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(Review Article)

Peripheral Nerve Rehabilitation Techniques: A Systematic Review

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Abstract

Background: The peripheral nervous system connects the brain to the body and enables us to feel and move. When its nerves are injured by trauma or disease, pain, weakness, or loss of sensation may occur. Previously, treatment focused on physical therapy and surgery. Today, these methods are combined with new therapies such as grafts, stem cells, and electrical stimulation. The current goal is not only to repair the nerve, but to truly and completely restore its function.

Methods: A systematic review was carried out following the PRISMA framework, a search strategy was used to analyze 1210 studies (cohorts, clinical trials, and cross-sectional trials) on rehabilitation for peripheral nerve injuries in adults, and 30 studies were reviewed according to the inclusion and exclusion criteria. Conventional and novel techniques were compared, evaluating muscle strength (MRC), electromyography, functionality (DASH), pain (VAS), and safety. The search was carried out between August and September 2025 in PubMed, Scopus, Web of Science, and Google Scholar. Data were organized by type of intervention and clinical outcomes, and bias was assessed using Cochrane and the level of evidence using the SIGN scale.

Results: A total of 1210 studies were identified, of which only 30 met the inclusion criteria. The analyzed studies, from Europe, the Americas, and Asia, evaluated traditional techniques and innovative therapies for peripheral nerve rehabilitation. Conventional techniques were generally safe, but innovative techniques showed better results in motor and sensory recovery, especially in complex cases. Randomized clinical trials had a low risk of bias and a high level of evidence (SIGN 1+ to 1++), with a grade of recommendation of A, while retrospective or cohort studies had a higher risk of bias and a lower level of evidence (2+ or 2++), with grade B or C.

Conclusion: Peripheral nervous system injuries remain a significant challenge due to their impact on functionality and quality of life. Traditional techniques such as neurorrhaphy, autologous grafts, and physical therapy remain effective and safe, although their recovery is often slow and sometimes partial. Innovative therapies such as stem cells, photobiomodulation, bioactive polymers, and non-conventional transfers are showing promising results by accelerating reinnervation and improving strength and sensitivity, with a low risk of complications. Evidence indicates that the most effective approach is not to replace traditional methods, but rather to combine both, integrating traditional surgery with modern regenerative strategies to achieve a faster, more functional, and longer-lasting recovery.

Keywords: Peripheral Nerve Injury; Rehabilitation; Prognosis; Treatment

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1. Introduction

The Peripheral Nervous System (PNS) is a network of nerves and ganglia that extends beyond the brain and spinal cord, connecting the Central Nervous System (CNS) to the rest of the body, including the limbs, organs, and skin. It plays crucial roles in perception by conveying information from the internal and external environment to the central nervous system, as in movement, by sending commands from the brain and spinal cord to the muscles and glands. It is divided into two main components: the somatic system, which is responsible for regulating voluntary movements and conscious sensations, and the autonomic nervous system, which controls involuntary functions such as heart rate, digestion, and breathing. (1)

The nerves of the peripheral nervous system are responsible for transmitting information between the brain, spinal cord, and the rest of the body. They enable us to move, feel, and react to stimuli. These nerves are divided into motor, sensory, and mixed types, and their proper functioning is essential for coordination and sensitivity. Peripheral nervous system injuries can occur from trauma, compression, metabolic diseases, or infections. Depending on the severity, symptoms range from pain, weakness, loss of sensation, or even paralysis. (2)

Treatment is aimed at restoring nerve function as quickly as possible. Traditionally, physical therapy, mobility exercises, electrical stimulation, and surgery have been used to directly repair the nerve. However, in recent years, new techniques have emerged, such as the use of nerve grafts, nerve transfers, stem cell therapies, and targeted electrical stimulation, which seek to accelerate regeneration and improve functional recovery.

The approach to peripheral nervous system injuries has advanced considerably. Today, it's not just about repairing a nerve, but about restoring its function as completely as possible. Combining traditional therapies with new technologies offers real hope for patients to regain sensation and movement in the affected areas. (3)

2. Methodology

A search was conducted for cohort studies, randomized controlled trials, clinical trials, and cross-sectional studies reporting on different treatments for peripheral nerve injury.

2.1. Study design

The systematic review is conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

2.2. Eligibility criteria

We are seeking studies reporting on the efficacy of different peripheral nerve rehabilitation techniques. Studies should report data on standardized neurological assessment test outcomes and safety, neuroimaging, and quality of life. Table 1 demonstrates the development of the PICO strategy for the study question, and Table 2 shows the inclusion and exclusion criteria.

Table 1 PICO strategy (P-population, I-intervention, C-comparison, O-results, S-studies)

Population	**Adult population (>18 years) with peripheral nerve injury**
Intervention	Conventional rehabilitation techniques (grafts, electrical stimulation, physiotherapy)
Comparison	Novel rehabilitation techniques (non-conventional transfers, new materials)
Results	Electromyographic evaluation tests, safety (adverse events, mortality), angle of movement, Medical Research Council (MRC) muscle strength scale, visual analogue pain scale (VAS). Safety (adverse events, mortality)
Studies	Cohort studies (both prospective and retrospective), randomized controlled trials, clinical trials (stages I, II and III, controlled clinical trials) and cross-sectional observational studies

Table 2 Inclusion and exclusion criteria

Inclusion Criteria	Prospective study, retrospective cohort study, randomized controlled trials
	Studies published in the last 10 years
	Adult patients (≥18 years)
	Nerve rehabilitation technique described
	Data on adverse events or effects of the procedure were reported.
Exclusion Criteria	Systematic reviews and meta-analyses
	Letters to the editor, Report articles or case series
	Conferences
	Studies in languages other than English.
	Studies published more than 10 years ago
	Animal studies
	Protocol studies without results

2.3. Search strategy and information sources

As a first step, a search was conducted in the PROSPERO database to ensure there was no previously published research addressing the topic of this review. The search was then conducted using Mesh terms (medical subject headings produced by NLM), taking care to use the different meanings, spellings, and synonyms. Searches were conducted in PubMed, MEDLINE, Scopus, and Web of Science, and Google Scholar records were also reviewed between August and September 2025. The search strategy is described in Table 3.

Table 3 Search strategies

Database	Search	Comments
PubMed	("Peripheral nerve injuries"[MeSH] AND "peripheral nerve injury"[tiab] AND "peripheral nerve injuries"[tiab] AND "nerve trauma"[tiab] AND "nerve injury*"[tiab]) AND ("Rehabilitation"[MeSH] OR "rehabilitation"[tiab] OR "physiotherapy"[tiab] OR "functional recovery"[tiab] OR "motor recovery"[tiab] OR "sensory recovery"[tiab]) OR ("Nerve transfer"[MeSH] OR "nerve transfer"[tiab] OR "nerve grafting"[tiab] OR "nerve repair"[tiab] OR "nerve regeneration"[MeSH] OR "nerve regeneration"[tiab])	Filters applied: *Clinical trial (stages I, II and III, controlled clinical trials) *Randomized controlled trial *Cohort study *Cross-sectional study *Last 10 years *Adults: 18+ years *Language: English
Web of science	TS=(peripheral nerve injury OR nerve injury OR nerve trauma) AND TS=(rehabilitation OR motor recovery OR sensory recovery OR recovery)	Filters applied: *Advanced search *Last 10 years
Scopus	TITLE-ABS-KEY (peripheral nerve injury OR nerve injury OR nerve trauma) AND TITLE-ABS-KEY (rehabilitation OR motor recovery OR sensory recovery OR recovery)	Filters applied: *Advanced search *Last 10 years *Published article *English language

2.4. Selection of studies

After conducting the search, the articles were selected. First, the titles and abstracts of the studies were read to ensure they met the selection criteria. Articles that passed this initial screening were read in full to determine whether they met all the selection criteria; those that did were selected for this review.

2.5. Data collection

A complete and exhaustive reading of the articles was performed. The results obtained were: 1) to evaluate the results of the procedure in improving different measures of functional recovery such as the Medical Research Council (MRC) muscle strength scale and the Disabilities of the Arm, Shoulder and Hand (DASH) scale, 2) to identify unwanted events resulting from the intervention; and 3) to compare the different rehabilitation techniques according to whether they were conventional or novel. The data were organized according to author, type of study, year of publication, patient population, objective, baseline characteristics of the participants before the intervention such as age, sex, Medical Research Council (MRC) muscle strength scale, time since LNP, and results of functional tests. The outcomes of interest in the follow-up included the Disabilities of the Arm, Shoulder and Hand (DASH) scale, electromyography results, quality of life parameters, and disability rating scale.

2.6. Summary of results

To organize the syntheses of the different studies, Table 4 was prepared, which describes the identifying name of the article, with its author and year, characterization of the patient group, intervention, measures, evaluation and conclusion.

Table 4 Summary of the main characteristics of the included studies**.**

Study	Country	Design	Patients	Intervention	Results
Fasce et al., 2021	Italy	Single-center prospective	Patients with mixed C5-C6 avulsions with an average age of 4.7 months	Different nerve transfers were performed as needed: spinal accessory nerve (SAN) via trapezius with prior end-to-end neurotization, radial nerve via axillary nerve using end-to-end microsuture, and ulnar nerve via cutaneous muscle using epinerurotomy.	Significant recovery of movement strength in external rotation, internal rotation, abduction, and elbow flexion at 24 months. No deficits in sensation or strength were observed in the hands.
Verdins et al., 2018	Latvia	Single-center retrospective	Patients with brachial plexus injury with grade between 0 and M1 on the Medical Research Council (MRC) muscle strength scale for biceps, with an average age of 11.7 months	For the rehabilitation of the musculocutaneous nerve, a traditional Oberlin transfer was performed via the ulnar nerve and for the biceps nerve, a motor branch of the flexor carpi ulnaris was performed.	In an average of 43.6 months, there was recovery to M5 and M5/M4 in the biceps, a DASH disability questionnaire score of 27.5 and a visual analogue pain scale (VAS) for activities of daily living of 3.2/8.
Widodo et al., 2024	Brazil	Randomized clinical trial	Patients with neglected brachial plexus injury (between 6 to 18 months)	For median nerve rehabilitation, intercostal nerves 3-5 were transferred, and umbilical cord mesenchymal stem cells (UC-MSC) or secretome were injected, and a neuromuscular junction (NMJ) biopsy was performed at the time of transfer, which was repeated at 8 months.	There was a significant improvement in overall physical functioning across the entire cohort. DASH scores improved significantly in the secretome group but not in the UC-MSC group, a trend that continued for the SF-86 questionnaire results.
Head et al., 2020	Canada	Retrospective	Patients with proximal neurothetic or axonotmetic lesions with denervation of intrinsic ulnar muscles.	Anterior interosseous motor nerve transfer via end-to-side ulnar with superload, a procedure previously described by Barbour et al.	Significant improvement in the strength of the first dorsal interosseous and abductor of the fifth finger, with an increase in the average MRC scale from M1 to M4 and from M1 to M3, respectively. A greater motor amplitude was also evident in these muscles.

Nemani et al., 2024	USA	Randomized clinical trial	Patients with complete nerve transection in the upper extremity (digital, ulnar, median) with concomitant damage at the level of multiple injuries and vascular damage, within 72 hours of the injury.	The usefulness of neurorrhaphy alone in the control group in early sensory recovery was compared with an intervention group with end-to-end neurorrhaphy with polyethylene glycol (PEG) application.	Sensitivity mediated by the Medical Research Council Classification (MRCC) scale demonstrated significantly greater recovery in the intervention group at one month postoperatively; at 3 months, both groups had similar outcomes; this trend was maintained on the Michigan Hand Outcomes Questionnaire (MHQ) scale.
Chen et al., 2024	China	Single-center retrospective	Patients with complete axonal injury of the common peroneal nerve	Either a direct nerve suture or graft was performed along the entire length of the nerve with subsequent fixation of the nerve with a flap obtained from the gastrocnemius muscle, and the ankles and toes were immobilized for 6 weeks.	There were improvements in the Lower Extremity Functional Scale (LEFS) for both groups. On the British Medical Research Council (BMRC) scale, those treated with sutures had better results than those with grafts.
Hsu et al., 2019	Taiwan	Prospective	Patients with complete peroneal nerve palsy with tibial nerve transfer less than 10 months ago who show evidence of reinnervation of the tibialis anterior muscle.	An intervention group was compared with a progressive biofeedback gait training program that maximized electromyographic activity isolated from the tibialis anterior muscle. The control group wore their ankle-foot orthosis full-time.	Patients with gait training showed better results on the Stanmore scale and the MRC scale than the control group.
Baltzer et al., 2017	USA	Single-center retrospective	Patients with brachial plexus injury who lacked external rotation and abduction of the shoulder with paralysis of the supraspinatus and infraspinatus muscles.	SAN transfer via the suprascapular nerve (SSN) using the technique described by Bertelli et al. End-to-end tension-free. The coaptation site was protected with a collagen conduit and fibrin glue. Immobilization was applied for 3 weeks.	There was postoperative reinnervation measured by electromyography especially in the infraspinatus with 85%, the numbers for the supraspinatus was 65% and for both muscles it was 60%, however these electromyographic results do not relate to the clinical evidence of recovery, which was also modest.
Satbhai et al., 2016	Japan	Single-center prospective	Patients with traumatic brachial plexus injury	Three shoulder reconstruction strategies were compared, chosen	Shoulder abduction and flexion were similar between groups, external

				according to the time of injury and patient wishes: ulnar nerve graft transfer for shoulder reconstruction, and intercostal nerve (ICN) graft transfer for musculocutaneous nerve reconstruction at the elbow. In single free muscle transfer (SMT) patients more than 8 months post-injury underwent transfer for shoulder reconstruction and functional free muscle transfer (FFMT) for finger flexion or extension. Double free muscle transfer (DFMT) was performed: nerve transfer to the shoulder and muscle transfer of the gracilis muscle with its nerve and SAN for elbow flexion, gracilis muscle and its nerve with ICN for finger flexion.	rotation was better in the DFMT group, as was elbow flexion, manual muscle testing (MMT). In all groups there was clinical improvement according to the DASH scale.
De George et al., 2019	France	Single-center retrospective	Patients with brachial plexus injury with upper trunk paralysis or panplexus paralysis, with prior restoration of elbow flexion by ulnar nerve transfer.	To rehabilitate the SSN, a SAN transfer was performed with lateral elbow immobilization for 1 month. The comparison group underwent shoulder arthrodesis as a primary strategy or, if the previous transfer failed, the arthrodesis was performed using a posterior approach with compression screw fixation. A splint was worn for 2 months with prior evidence of bone fusion.	In the upper trunk paralysis group, arthrodesis had better results than nerve transfer in antepulsion and external rotation, with no differences on the DASH scale. In the panplexus paralysis group, arthrodesis showed better results in retropulsion, external rotation, and retropulsion, with no differences on the DASH scale. There were no significant differences between primary and secondary osteoarthritis, except in the primary group, which had greater degrees of antepulsion and abduction. Complications occurred in 18% of

					patients who underwent arthrodesis.
Curran et al., 2021	Canada	Randomized clinical trial	Patients with median or ulnar nerve repair between the mid-palm and elbow	Both groups received training for 12 weeks. The intervention group received mirror therapy based on tactile observation and tasks, while the control group received regular manual therapy and physical therapy.	Significant improvement was observed in the pinch-holding-up activity test (FR $_{Peak}$, FR $_{Mean}$ and percentage of maximum pinch strength) in the intervention group, in the Purdue Pegboard Test (PPT) there were significant improvements in the intervention group in Unilateral Pin Insertion and Bilateral Pin Insertion.
Gunasagaran et al., 2023	Malaysia	Prospective	Patients with complete brachial plexus injury without clinical recovery of elbow flexion (M0) within three months.	Traditional phrenic nerve transfer is compared with sural nerve grafting via SSN as a control group; and complete musculocutaneous phrenic nerve transfer using video-assisted thoracoscopic surgery (VATS) for restoration of elbow flexion.	In the VATS complete phrenic nerve transfer group, recovery of elbow flexion strength was faster and better than in the control group. Hospitalization was longer in the complete transfer procedure, and no patient experienced a major complication in either procedure.
Horteur et al., 2019	France	Single-center retrospective	Patients with common peroneal nerve injuries with various injury mechanisms. Most were M0 on the MRC scale (only one M2). They underwent emergency surgery for open wounds and an average of 152 days for closed wounds.	The procedures for neurolysis, direct suture, and sural nerve grafting were decided based on the surgeon's observation. Immobilization for 1 month was required for direct suture or nerve grafting; no immobilization was performed after neurolysis.	Average follow-up was 48 months. Motor recovery (M4-M5) was recorded in most patients with neurolysis (7/9) and direct suture (⅘), but none with nerve grafting; the numbers were similar for sensory recovery (S3) except for the nerve graft group, where some (3/6) recorded recovery. The average Kintaoka score was higher in the direct suture group. Complications included one hematoma requiring drainage and one infection requiring surgical revision.
Neubrech et al., 2018	Germany	Multicenter randomized clinical trial	Patients with finger nerve injury.	Sensory recovery was compared between a control group with end-to-end epineural microsuture, and	The mean two-point discrimination score was better in the intervention group. Results on the Semmes-

				an intervention group in which, in addition to the end-to-end microsuture, a chitosan tube was attached to the center of the surgical suture.	Weinstein test were also better for the intervention group. Pain was infrequent in both groups, and there were no complications in the intervention group.
Lin et al., 2025	Taiwan, Argentina	Multicenter retrospective	Patients with severe brachial plexus injury with avulsion or rupture of C5-T1 or C5-C8.	The efficacy of phrenic nerve transfer for restoring shoulder abduction (Ph-shoulder) and elbow flexion (Ph-Ef) was compared.	In the Ph-shoulder group, the average range of motion (ROM) was 75.6°, with a high standard deviation of 49.6°, at an average of 16.8 months. In the Ph-Ef group, the average MRC score was M3.3, at an average of 18.6 months.
Saeki et al., 2018	Japan	Prospective non-randomized trial	49 patients with peripheral sensory nerve repair with collagen conduits and 38 with autologous graft (7 from the study + 31 historical data)	Repair of peripheral nerves (≤30 mm) with an artificial collagen nerve conductor with longitudinal filaments, compared with autologous graft	At 12 months, sensory recovery occurred in 75% of patients with conduit and 73.7% with autologous graft. There were no serious adverse events. Conduit demonstrated non-inferior efficacy and safety, making it a valid alternative to autologous nerve graft.
Li et al., 2019	China	Multicenter retrospective	510 patients with traumatic brachial plexus injuries treated surgically in 74 hospitals between 2004 and 2016. Average age: 29 years; 88.24% of injuries were closed; 64.71% were caused by traffic accidents.	Neurolysis, nerve grafting, direct reconstruction, nerve transfers, spinal accessory nerve, phrenic nerve, intercostal nerve, contralateral C7 nerve, and tendon transfers were performed.	Useful functional recovery (grade ≥3) was 76.8% for C5–C6 injuries, 58.7% for C5–C7 injuries, and 48.2% for C5–T1 injuries. Neurolysis had the best success rate (79.45%). Neuropathic pain persisted in 64.6% of patients, and anxiety/depression in 81.2% of patients.
Foo et al., 2020	Malaysia	Prospective, randomized, controlled clinical trial	14 patients (all men, 18–34 years old) with upper brachial plexus injuries underwent Oberlin-type neurotization. They were divided into two groups (n=7): a control	PBM with an 808 nm, 50 mW, 4 J/cm^2 Ga-As laser for 10 consecutive days (excluding weekends), applied directly to the neurotization site. Compared with standard rehabilitation without PBM.	At 3 months, the PBM group showed greater biceps muscle power (MRC 1.43 +/- 0.53 vs. 0.43 +/- 0.78; p = 0.026) and 100% reinnervation vs. 28.6% in the control group (p = 0.005). At 6 months, all patients showed reinnervation, with no

			group and a postoperative photobiomodulation (PBM) group.		adverse effects. It is concluded that PBM accelerates nerve regeneration after neurotization.
Simske et al., 2024	USA	Retrospective cohort study .	265 adult patients with ankle fractures treated surgically between 2019 and 2020.	Review of medical records and surgical records of patients undergoing posterior or lateral surgery. The incidence of iatrogenic sural nerve injury and associated factors were evaluated.	Iatrogenic sural nerve injury occurred in 9.8% of patients, all of which occurred with the posterior approach in the prone position. Sixty-two percent of those affected fully recovered nerve function within six months. It was concluded that the posterior approach significantly increases the risk of sural nerve injury.
Lam et al., 2024	Vietnam	Retrospective, observational and analytical study	59 patients with post-traumatic peripheral facial paralysis treated between 2017 and 2021 at the Ho Chi Minh City National Dental Hospital.	Facial nerve rehabilitation surgery: 25 cases with end-to-end anastomosis, 22 with nerve graft (sural) and 12 with combined technique.	All assessment scales improved significantly after surgery ($p < 0.001$). 78.4% achieved moderate recovery and 11.8% achieved good recovery. End-to-end anastomosis showed better functional results than other techniques.
Zhang et al., 2023	China	Prospective, non-randomized, comparative, controlled clinical trial.	114 patients with peripheral nerve injury of the upper limb treated between August 2017 and November 2019.	Control group: conventional rehabilitation. Experimental group: rehabilitation + Jiaji electroacupuncture.	After treatment, both groups improved, but the experimental group showed significantly greater increases in the Barthel index, Fugl-Meyer scale, SF-36 and nerve conduction velocity, with the combination therapy showing greater functional efficacy and quality of life.
Safa et al., 2019	USA	Retrospective, multicenter observational study	20 patients with 22 mixed or motor nerve repairs in upper extremities, head and neck, treated between 2008 and 2015.	Nerve repair using processed nerve allografts. Follow-up ≥ 12 months.	82% of the repairs achieved significant functional recovery. The results were comparable to those obtained with autologous grafts, with no serious adverse events related to the ANP.

Carlson et al., 2018	USA	descriptive observational study	16 patients with peripheral and cranial nerve injuries of different locations (mainly in the upper extremities), most of them secondary to trauma.	Nerve reconstruction with cadaveric nerve allografts in lesions with gaps ≥10 mm; without the use of immunosuppression.	Good or excellent sensory recovery was achieved in 91.7% of cases and significant motor recovery in 33%. The prognosis was better for sensory nerves and gaps smaller than 50 mm. There were no serious complications or rejection.
Gezercan et al., 2016	Turkey	Single-center retrospective	25 patients (30 nerves) with peripheral nerve injuries due to penetrating and cutting wounds, with a mean time between injury and surgery of 11.5 months.	Late surgical treatment with different techniques depending on the type of injury: external neurolysis, epineurotomy, epineural or fascicular repair, and sural nerve graft.	Significant improvement in muscle strength and electromyographic results. The best results are observed in median nerve injuries and in cases treated with neurolysis or epineural repair. They conclude that even delayed repairs can achieve good functional recovery.
Chu et al., 2023	China	Prospective	23 patients (15 men, 8 women, 10–70 years) with complete median nerve transection treated with neurorrhaphy. They were assigned to 2 groups: percutaneous electrical nerve stimulation (PENS) (n=12) and transcutaneous electrical nerve stimulation (TENS) (n=11).	Ultrasound-guided PENS with parallel needles spaced 3 cm apart, applied at 20 Hz, 0.2 ms, 1 h/session, 4 times per week for 5 weeks, after neurorrhaphy. Compared with TENS with the same parameters. Both received conventional rehabilitation.	The PENS group showed significant improvement in: Grip strength (0.08±0.10 vs. 0.02±0.03; $p = 0.048$) Global function of the median nerve ($p = 0.046$) Decrease in DASH score ($p = 0.022$) Higher number of patients with sensory recovery ≥ S2 and motor recovery ≥ M3 ($p < 0.05$). The PENS protocol based on finite element modeling accelerates regeneration and improves motor and sensory function without adverse effects.
Suszyński et al., 2025	Poland	Single-center prospective	31 patients with traumatic peripheral nerve injuries in the upper extremities: 19 treated with	Predegenerated sural nerve graft (sectioned and left in situ for 7 days before microsurgical reconstruction), compared with traditional fresh autologous graft.	The pre-degenerated graft group showed better results in: Hand volume index ($p = 0.0254$) Sensory recovery ($p = 0.0368$)

			predegenerated autologous sural grafts and 12 with fresh grafts. Mean age: 36 years.		More adequate motor and sensory nerve conduction.
Li et al., 2016	China	Retrospective multicenter observational study	64 patients of the hand and upper extremity, followed for 3 years after reconstruction with human acellular nerve allografts.	Reconstruction of peripheral nerves using acellular human nerve allografts, variables analyzed were: age, nerve type, site, delay time, graft length and follow-up time.	75% of the nerves achieved significant functional recovery Graft length ≤30 mm was associated with better outcomes; there were no infections or rejections. Graft length was an independent predictor of functional recovery.
Wong et al., 2015	Canada	Randomized, double-blind, placebo-controlled clinical trial	36 patients with complete transection of the digital nerve treated with primary epineural repair.	Experimental group: postoperative electrical stimulation after nerve coaptation. Control group: sham stimulation.	At 6 months, the stimulation group showed better sensory recovery and a higher percentage of complete recovery, with no serious complications. They conclude that brief postoperative electrical stimulation accelerates sensory reinnervation.
Bai et al., 2015	China	Prospective	13 patients with peripheral nerve injuries in upper extremities (mean age: 32.6 years).	Repair with intraoperative nerve elongator that allows tension-free suturing, compared to conventional technique (elbow flexion or nerve stretching).	The group with the stretcher showed: Significantly better early neurological recovery ($p = 0.027$) Better elbow function and less immobilization (4 vs. 6 weeks) Without complications or additional deficits.

2.7. Risk of bias and levels of evidence of individual studies

Table 5 shows the analysis of the Cochrane bias scale, assessed on 6 criteria: random sequence generation, concealed allocation, blinding of investigators and participants, blinding of assessors, incomplete outcome data, and selective reporting of results. Table 6 was developed with the description of the level of evidence and grade of recommendation of included studies, according to the SIGN tool. In this scale, the evidence is evaluated in eight levels (4, 3, 2- , 2+, 2++, 1-, 1+, 1++), in which level 4 has a lower level of evidence and 1++ has a higher level of evidence that is characteristic of high-quality meta-analyses, systematic reviews of clinical trials or high-quality clinical trials with low risk of bias. The degree of recommendation is based on the five-level scale (A, B, C, D, √), in which √ is characterized by being a practice recommended in the clinical experience and consensus of the writing group and A corresponds to those articles valued with the level of evidence 1++, applicable in the target population or studies classified as 1+ with great consistency between them.

Table 5 Bias risk scale assessment

Study	Criterion 1	Criterion 2	Criterion 3	Criterion 4	Criterion 5	Criterion 6
Fasce et al., 2021	-	-	-	?	+	+
Verdins et al., 2018	-	-	+	?	+	+
Widodo et al., 2024	+	+	+	?	+	+
Head et al., 2020	-	-	-	?	+	+
Nemani et al., 2024	+	+	-	?	+	+
Chen et al., 2024	-	-	-	?	+	+
Hsu et al., 2019	-	-	-	?	+	+
Baltzer et al., 2017	-	-	+	?	+	+
Satbhai et al., 2016	-	-	-	?	+	+
De George et al., 2019	-	-	+	?	+	+
Curran et al., 2021	+	+	-	?	+	+
Gunasagaran et al., 2023	-	-	-	?	+	+
Horteur et al., 2019	-	-	+	+	+	+
Neubrech et al., 2018	+	+	+	+	+	+
Lin et al., 2025	-	-	+	?	+	+
Saeki et al., 2018	+	+	+	?	+	+
Li et al., 2019	-	-	-	?	+	+
Foo et al., 2020	+	+	+	?	+	+
Simske et al., 2024	-	+	+	?	+	+
Lam et al., 2024	+	+	+	?	+	+
Zhang et al., 2023	-	-	-	?	+	+
Safa et al., 2019	-	-	+	+	+	+
Carlson et al., 2018	-	-	+	?	+	+
Gezercan et al., 2016	-	-	+	+	+	+
Chu et al., 2023	+	?	+	?	+	+
Suszyński et al., 2025	-	-	-	?	+	+
Zhu et al., 2016	-	-	+	+	+	+

Wong et al., 2015	+	+	+	+	+	+
Bai et al., 2015	+	?	-	?	+	+

3. Results

The search identified a total of 1209 records (PubMed 117, Web of Science 878, Scopus 117, and Google Scholar 21). After screening, 770 studies were excluded for not meeting the inclusion criteria, leaving 29 studies for analysis. The search system is shown in Figure 1.

Table 6 Level of evidence and grade of recommendation according to the SIGN tool.

Study	**Level of evidence**	**Recommendation level**
Fasce et al., 2021	2+	D
Verdins et al., 2018	2++	B
Widodo et al., 2024	1++	A
Head et al., 2020	2+	A
Nemani et al., 2024	1+	B
Chen et al., 2024	2+	D
Hsu et al., 2019	2+	D
Baltzer et al., 2017	2++	B
Satbhai et al., 2016	2+	D
De George et al., 2019	2++	B
Curran et al., 2021	1+	B
Gunasagaran et al., 2023	2+	D
Horteur et al., 2019	2++	B
Neubrech et al., 2018	1++	A
Lin et al., 2025	2++	B
Saeki et al., 2018	1+	A
Li et al., 2019	2+	B
Foo et al., 2020	1++	A
Simske et al., 2024	2+	D
Lam et al., 2024	2+	D
Zhang et al., 2023	2+	D
Safa et al., 2019	2++	B
Carlson et al., 2018	2+	D
Gezercan et al., 2016	2+	D
Chu et al., 2023	1+	A
Suszyński et al., 2025	2+	B
Zhu et al., 2016	2+	D
Wong et al., 2015	1++	A
Bai et al., 2015	2++	D

3.1. Characteristics of the studies

The characteristics of the included studies are summarized in Table 1, following the PICO strategy (type of study, participants, intervention, results, and conclusions). A total of 30 studies were included, of which 13 were retrospective. Geographically, 31% of the studies were conducted in Europe, 31% in the Americas, and 38% in Asia. The reported results addressed various rehabilitation techniques and their associated adverse events.

The studies identified as innovative included those by Fasce et al. (4), Widodo et al. (5), Nemani et al. (6), Chen et al.(7), Hsu et al. (8), Baltzer et al. (9), Satbhai et al. (10), DeGeorge et al. (11), Curran et al. (12), Gunasagaran et al. (13), Horteur et al. (14), Neuberch et al. (15), Saeki et al. (16), Foo et al. (17), Suszyński et al. (18), Zhu et al. (19), Safa et al.(20), Carlson et al. (21), Gezercan et al. (22), Chu et al. (23), Li et al. (24), Wong et al. (25), and Bai et al. (26). These studies incorporated novel or rarely used interventions such as bioengineered conduits, cell-based therapies, or neurostimulation. Except for Baltzer et al. (9), most reported favorable outcomes regarding sensory and motor recovery, although sample sizes and follow-up periods varied considerably.

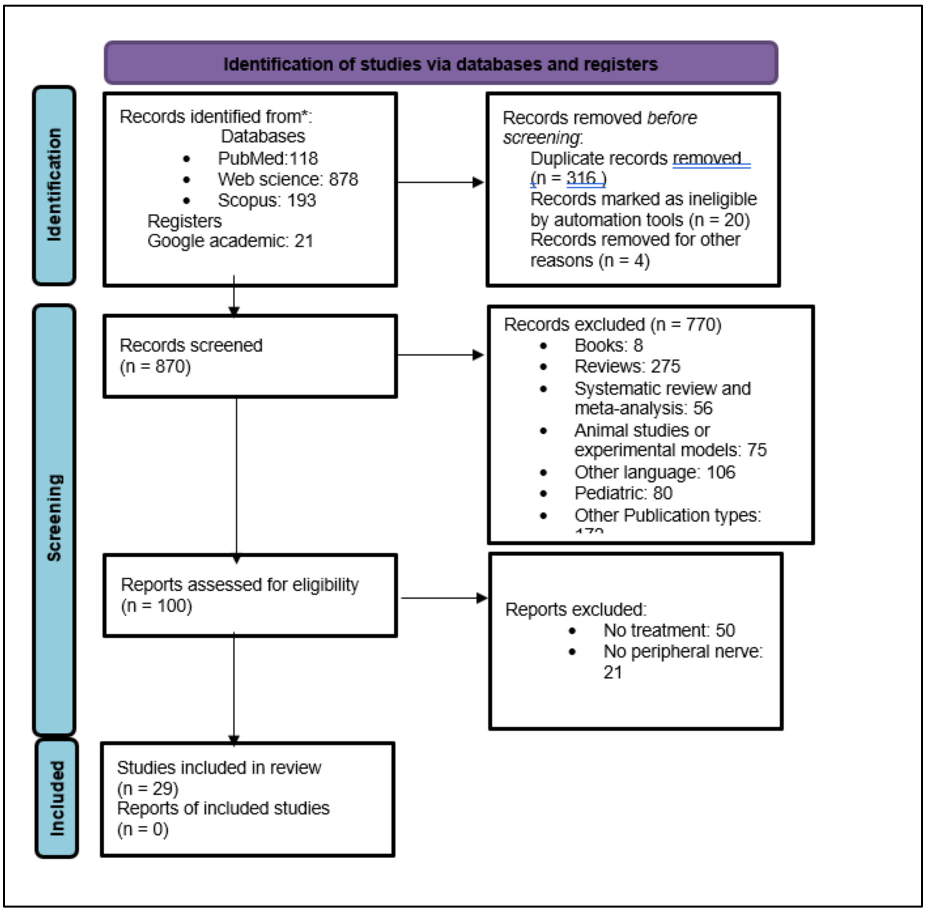

Figure 1 PRISMA diagram**.**

Conversely, studies by Verdins et al. (27), Head et al. (28), Lin et al. (29), Li et al. (30), Simske et al. (31), and Lam et al. (32) focused on conventional techniques, including neurorrhaphy, autologous grafts, and structured physical therapy. These were used as comparative models to establish current standards in peripheral nerve rehabilitation. Overall, conventional methods demonstrated acceptable safety profiles and consistent, though often incomplete, functional recovery. Innovative interventions, while still experimental in many settings, showed potentially superior motor and sensory outcomes, albeit with a greater need for validation through larger, controlled trials.

Across the reviewed literature, the primary objectives of the studies were to accelerate peripheral nerve healing, reduce donor site morbidity, and explore alternative strategies for injuries with traditionally poor prognoses.

3.2. Summary of results and interpretation

*Nerve transfer and conventional microsurgical techniques: Fasce et al. compared different nerve transfers in C5–C6 avulsions, reporting significant strength recovery at 24 months without sensory or distal weakness. Verdins et al. evaluated the Oberlin transfer for musculocutaneous and biceps nerve rehabilitation, achieving M4–M5 recovery at a mean of 43.6 months, with moderate DASH and VAS scores. Head et al. observed improved motor amplitude following anterior interosseous branch transfer to the ulnar nerve. Lin et al. compared phrenic nerve transfers for shoulder and elbow recovery, reporting moderate improvements in range of motion and muscle strength. Li et al. found superior outcomes in patients with C5–C6 injuries treated by neurotization alone, though neuropathic pain and psychological symptoms were common. Lam et al. showed that end-to-end anastomosis yielded better facial nerve recovery than grafting or combined techniques. Simske et al. reported a 9.8% incidence of iatrogenic sural nerve injury following ankle ORIF, with most patients achieving full recovery at 6 months.

**Innovative and regenerative interventions: Widodo et al. demonstrated that umbilical cord mesenchymal stem cell (UC-MSC) injections improved DASH and SF-36 scores compared with intercostal nerve transfer. Nemani et al. found that polyethylene glycol (PEG) adjunct therapy accelerated early sensory recovery after neurorrhaphy, though results equalized at three months. Hsu et al. showed that progressive biofeedback gait training enhanced tibial nerve function compared to orthotic use alone. Baltzer et al. found partial electromyographic recovery after CN XI–SSN transfer with collagen conduit protection, though motor improvement was limited. DeGeorge et al. reported that shoulder arthrodesis achieved greater abduction and antepulsion than CN XI–SSN transfer, despite an 18% complication rate. Curran et al. found that tactile observation and task-based therapy improved dexterity and grip tests versus conventional rehabilitation.

Neubrech et al. reported superior sensory recovery with the use of chitosan tubes in digital nerve repair, with no complications. Foo et al. observed early reinnervation and increased MRC scores at 3 months following photobiostimulation, though differences were not sustained at 6 months. Horteur et al. noted better outcomes with neurolysis and direct suture compared with nerve grafting in common peroneal nerve injuries. Safa et al. found comparable outcomes between processed allografts and autologous grafts with no adverse events. Gezercan et al. observed improved strength and EMG findings following late neurolysis or epineural repair in chronic peripheral nerve injury. Zhu et al. demonstrated a 75% overall recovery rate using acellular nerve allografts, with grafts <30 mm associated with better outcomes and fewer complications. Wong et al. reported enhanced sensory recovery after electrical stimulation post-coaptation in digital nerve repair compared to sham stimulation.

***Neurorehabilitation and adjunct therapies: Zhang et al. found that Jiaji electroacupuncture significantly improved Barthel Index, Fugl-Meyer, SF-26, and nerve conduction scores compared to standard rehabilitation. Across studies, innovative techniques—particularly cell-based therapies, bioactive scaffolds, and neuromodulation—showed potential to accelerate sensory and motor recovery; however, these benefits were often based on small samples, heterogeneous methodologies, and limited follow-up.

3.3. Risks of bias in individual studies

Table 5 explains Cochrane's risk of bias assessment. Randomized clinical trials have very low risk of bias due to their rigorous methodologies; however, prospective and retrospective cohort studies were also included, which increased the risk of bias in some of these studies due to the lack of a control group or the generation of random sequences. Table 6 indicates the level of evidence and grade of recommendation according to the scale proposed by SIGN. All randomized clinical trials have a low level of risk, so the level of evidence will vary between 1++ and 1+, and their grade of recommendation will be A. However, for cohort or case-control studies, the level of evidence will vary between 2++ or 2+, and their grade of recommendation will be between B and C.

4. Discussion

Peripheral nervous system (PNS) rehabilitation is a constantly evolving field, where technological and biological advances have transformed traditional therapeutic approaches. The results of this systematic review demonstrate a trend toward integrating conventional strategies such as physical therapy, electrical stimulation, and reconstructive surgery with innovative techniques that seek to optimize axonal regeneration, muscle reinnervation, and functional recovery.

Overall, the included studies demonstrate that innovative techniques such as selective nerve transfers, acellular nerve grafts, photobiostimulation (PBM), the use of mesenchymal stem cells (UC-MSCs), and the topical application of biocompatible polymers such as polyethylene glycol (PEG) offer superior results in terms of motor and sensory recovery compared to conventional procedures. In this line, the works of Widodo et al. (5) and Nemani et al. (6) showed a significant improvement in quality of life and early sensitivity, respectively, suggesting that the combination of biological interventions with microsurgical techniques may accelerate nerve repair.

Likewise, nerve transfer-based interventions have shown promising results in brachial plexus and major peripheral nerve injuries. Studies by Fasce et al. (4), Verdins et al. (27), and Baltzer et al. (9) demonstrated significant functional recovery in the treated groups, especially in muscle strength and joint mobility. These findings are in agreement with previous research supporting that selective transfers allow for more targeted reinnervation and lower donor site morbidity. However, the variability in clinical outcomes, particularly in the recovery of shoulder external rotation or grip strength, highlights the need for rigorous selection of surgical candidates and individualized rehabilitation protocols.

On the other hand, studies evaluating autologous nerve grafts and acellular allografts (such as those reported by Zhu et al. (19) and Safa et al. (20)) agree that these strategies represent viable alternatives when tension between nerve ends prevents direct repair. In particular, acellular allografts have demonstrated regeneration rates comparable to autografts, with lower morbidity and no increase in complications, which positions them as a safe and effective option in nerve reconstruction.

Regarding neuromodulation and advanced physiotherapy techniques, the findings of Hsu et al. (8), Curran et al. (12), Foo et al. (17) and Head et al. (28) support the fundamental role of electrical stimulation, tactile observation-based therapy and laser photobiostimulation in enhancing cortical plasticity and motor recovery. These techniques, by promoting functional reorganization of the central and peripheral nervous system, complement surgical approaches and offer a therapeutic window even in long-standing injuries.

Despite the progress made, this review identified important methodological limitations. While the included randomized controlled trials present a low risk of bias and high methodological quality (evidence levels 1++ and 1+ according to the SIGN scale), a considerable proportion of the studies were retrospective or observational, which reduces the strength of the evidence. Furthermore, the heterogeneity in functional assessment methods (MRC, DASH, SF-36, Purdue Pegboard, among others) hampers direct comparisons across studies and limits the possibility of conducting quantitative meta-analyses.

Another relevant aspect is the lack of standardization in follow-up times and postoperative rehabilitation protocols, which directly influence functional outcomes. Most studies reported follow-up periods of less than two years, an insufficient period to fully assess nerve regeneration, which can extend up to 36 months or more. In terms of safety, the review shows that complications were rare and generally minor (hematomas, superficial infections, or mild neuropathic pain). The innovative techniques, although more complex, did not significantly increase adverse events, which reinforces their safety profile and clinical applicability.

Finally, the findings of this review highlight the need for comprehensive, multimodal rehabilitation, combining precise surgical procedures, biotechnological interventions, and personalized physical therapy programs. This synergistic approach can optimize neuroplasticity, shorten recovery times, and improve the quality of life of patients with PNS injuries. The studies analyzed present marked heterogeneity in terms of injury type, technique applied, follow-up time, and success criteria, which limits the extrapolation of results. Multicenter clinical trials with homogeneous designs that standardize the evaluation of emerging techniques, and their long-term effects are needed. Furthermore, future research should focus on combining regenerative therapies with artificial intelligence and predictive modeling to optimize the selection of strategies according to the type and extent of the injury.

Abbreviations

- CNS: Central Nervous System
- DASH: Disabilities of the Arm, Shoulder and Hand
- ER: external rotation
- VAS: Visual Analogue Scale
- MRC: Medical Research Council
- NLM: National Library of Medicine
- PBM: photobiostimulation therapy
- PEG: polyethylene glycol
- PICO: population, intervention, comparison, outcomes
- PNS: Peripheral Nervous System
- PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses

- PROSPERO: International Prospective Register of Systematic Reviews
- ROM: range of motion
- SD: standard deviation
- SIGN: Scottish Intercollegiate Guidelines Network
- SSN: suprascapular nerve

5. Conclusions

Peripheral nerve injuries remain a major therapeutic challenge due to limited regenerative capacity and incomplete functional recovery with conventional treatments. Emerging regenerative approaches such as stem cell therapy, bioactive scaffolds, and photobiomodulation show encouraging potential to enhance axonal regeneration and accelerate recovery. However, methodological heterogeneity, lack of standardized protocols, and insufficient long-term data prevent definitive conclusions about their superiority. Future clinical integration should emphasize combined, evidence-based strategies that merge traditional repair with biological and technological innovations for optimal outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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