

R E V I E W

Sural nerve graft in peripheral nerve injuries: Systematic review of the literature and analysis of the donor site complications

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Abstract. *Background and aim:* Traumatic injuries of the peripheral nerves commonly occur in the workplace or in traffic accidents and affect young people, mostly males. When possible, acute repair should always be performed. But this is not always possible, and it is necessary to use autologous graft with sural nerve. The purpose of this review is to illustrate the effectiveness of the sural graft for the management of these lesions. We also evaluated complications related to the donor site. *Methods:* This systematic review was conducted according to PRISMA guidelines. After the full-text analysis, 8 articles were included in the review. We extracted data on the number of patients, gender, mean age, damaged nerve, time between trauma and surgery, mean follow-up, nerve gap, percentage of patients who reported scores of S3 or higher and M3 or higher. The second part of the review analyzed complications related to the donor site. *Results:* The sural graft was effective in managing nerve damage in both upper and lower limbs, obtaining percentages close to 50% for the restoration of sensitivity and function higher than S3 and M3, respectively. 92.6% of patients complained of sensory deficit at the donor site, followed by allodynia reported by 36 patients (26.7%) and chronic pain only in 9.6% of cases. *Conclusions:* Our systematic review highlights how the sural nerve graft effectively manages peripheral nerve injuries, with acceptable outcomes at the donor site. (www.actabiomedica.it)

Key words: sural nerve graft, peripheral nerve injuries, donor site, nerve gap, systematic review

Introduction

Injuries to peripheral nerves are highly debilitating pathological conditions resulting from various traumatic mechanisms, such as workplace and vehicle accidents (46%) or ballistic injuries. In most cases, the upper limbs are involved (60.5%), particularly the ulnar nerve, followed by the radial nerve and the median nerve (1,2). In Europe, hand trauma has a variable incidence between 7 and 37 per 1000 inhabitants per year, and about 3% of these involve peripheral nerves. Less common are lesions of the nerves in the lower limbs. Specifically, the external popliteal sciatic nerve can be injured during surgical procedures on the

knee. The incidence of peripheral nerve injuries is 0.4 per 1000 inhabitants per year (3). Between 2005 and 2020, the male incidence of peripheral nerve lesions in England was 15.8 (95% CI 15.2, 16.3) per 100,000 males per year compared to a female incidence of 6.7 (95% CI 6.5, 6.8) per 100,000 females per year (4). Patients suffering from peripheral nerve lesions experience a significant reduction in the quality of life due to dysfunctions in sensitivity, mobility, and sometimes chronic pain syndromes. Additionally, these lesions typically affect young people. The decision to perform nerve repair or reconstruction depends on a correct diagnosis and the timing of the trauma. Direct repair is possible immediately after trauma but is not always

feasible, especially if there is a loss of substance (5). The clinical outcome of reconstruction is often suboptimal, influenced by factors such as correct diagnosis, extent and timing of trauma, surgeon's technical skills, and post-operative rehabilitation. Comorbidities like diabetes and kidney failure can profoundly compromise the recovery of nerve function. Treatment of these injuries requires an understanding of the biological processes that lead to success or failure. Peripheral nerves can suffer different types of damage depending on the trauma, ranging from simple compressions/strains to large lacerations with loss of nerve substance. Various classifications exist for nerve injuries. Seddon divides nerve injuries into neurapraxia, axonotmesis, and neurotmesis (6). Sunderland formulates a more articulated classification, better categorizing the damage (7). Treatment is surgical for grade 4 and higher lesions, with recovery outcomes variable and conditioned by numerous factors from grade 3 onwards. Neurological trauma triggers various cellular reactions attempting repair, with nerve regeneration favored by Schwann cell proliferation and local growth factors. Schwann cells also guide the direction of regeneration. The clinical outcome is connected to the central nervous system's ability to reorganize itself, explaining better outcomes in children due to developed "neuronal plasticity" (8,9). Any traumatological patient with symptoms compatible with neurological deficits must be considered a potential carrier of an injury, necessitating nerve exploration. A direct acute repair should be attempted whenever possible (10). The correct diagnosis relies on a thorough clinical examination, including strength evaluation using a specific scale, sensitivity assessment through the two-point discrimination test, and evaluation of the patient's ability to perceive the difference between heat and cold. Electromyography is a fundamental diagnostic test affected by the time of trauma and should not be performed before 2-4 weeks post-trauma in open trauma cases. Surgical exploration is mandatory, involving extensive debridement of injured tissues and repair of associated tendon and/or vascular injuries. If repair is necessary, it should be done immediately or postponed if substance loss requires a graft. The sural nerve is commonly used for grafts, and the procedure should be performed in

a bloodless field, avoiding torsion of the graft and ensuring suture without tension. In light of the debilitating effects and prevalence of peripheral nerve injuries, particularly among the younger population, exploring effective treatment strategies is crucial. Autologous sural nerve grafts have been frequently utilized due to their distinctive properties. However, a comprehensive understanding of their efficacy is required, considering factors such as injury severity, patient comorbidities, and post-operative care (11-13). This review aims to systematically assess the outcomes of peripheral nerve injuries in upper and lower limbs treated with autologous sural nerve grafts, drawing upon the most recent and relevant studies. The review also aims to highlight existing gaps in knowledge and propose directions for future research. Therefore, this review seeks to address the question: How effective is the use of autologous sural nerve grafts in the treatment of upper and lower limb nerve lesions?

Methods

We conducted a systematic review of the literature according to the PRISMA guidelines, involving the use of sural graft in peripheral nerve injuries. The search engines used were: PubMed / Medline, Scopus, Web of Science and Google Scholar (14).

Study eligibility criteria

All prospective randomized, observational and case-control retrospective studies published before March 2024 available as full text were included. We included English and non-English papers, evaluated after using translation tools. Case-reports and systematic reviews were excluded.

Search strategy

The search included the following items: (("peripheral nerve injuries"[MeSH Terms] OR ("peripheral"[All Fields] AND "nerve"[All Fields] AND "injuries"[All Fields])) OR "peripheral nerve injuries"[All Fields] OR ("peripheral"[All Fields]

AND “nerve”[All Fields] AND “injury”[All Fields]) OR “peripheral nerve injury”[All Fields]) AND (“nerve”[All Fields] OR “nerve s”[All Fields] OR “nerved”[All Fields] OR “nerves”[All Fields]) AND (“graft s”[All Fields] OR “grafted”[All Fields] OR “graftings”[All Fields] OR “transplantation”[MeSH Subheading] OR “transplantation”[All Fields] OR “grafting”[All Fields] OR “transplantation”[MeSH Terms] OR “grafts”[All Fields] OR “transplants”[MeSH Terms] OR “transplants”[All Fields] OR “graft”[All Fields])) AND (“sural”[All Fields] AND (“graft s”[All Fields] OR “grafted”[All Fields] OR “graftings”[All Fields] OR “transplantation”[MeSH Subheading] OR “transplantation”[All Fields] OR “grafting”[All Fields] OR “transplantation”[MeSH Terms] OR “grafts”[All Fields] OR “transplants”[MeSH Terms] OR “transplants”[All Fields] OR “graft”[All Fields])). After the main analysis, the authors also added to the search keywords “donor site”, “sensory deficit” and “chronic pain” to evaluate discomfort due to donor site.

Study selection and data collection

Two reviewers performed the data extraction independently. In case of disagreement, the first author was sought to resolve the divergences. The first selection of studies was performed on the basis of titles and abstracts: Only papers that clearly reported the words “sural nerve graft” and/or “peripheral nerve lesions” or synonyms in the title and abstract were considered. Duplicates were identified and excluded. Studies that passed this selection were evaluated as “full-text.” The following data were extracted: authors, year of publication, number of patients, gender, trauma-repair interval (weeks), injured nerve, mean age (years), mean follow-up (months), extent of the gap (cm), number of patients with recovery of sensitivity greater than or equal to S3, number of patients with recovery of muscle function greater than or equal to M3. When any of these parameters were not reported in the study under analysis, the paper was excluded. This systematic review aims to highlight the effectiveness of the sural nerve graft as a treatment for nerve injuries of the upper and lower limbs. Firstly, we analyzed any clinical differences obtained from the enrolled papers

based on the time elapsed between trauma and repair. We then moved on to evaluate any differences between the use of the graft between the upper and lower limbs in terms of clinical outcomes and complications. Finally, data relating to residual symptoms on the donor site were reported. Scoring for motor function is based on the M system: M0, no contraction; M1, palpable contraction, barely visible; M2, horizontally along the bed surface; M3, against gravity only; M4, against gravity and resistance; M5, full strength (15). Scoring for sensory function is based on the S system: S0, no sensation; S1, deep pain re-established; S2, some response to touch and pin, with over-response; S3, good response to touch and pain, without over-response; S3 +, location and some tactile discrimination; S4, complete recovery (16).

Quality assessment and statistical analysis

Two reviewers performed the quality evaluation of the studies independently. In case of disagreement, the first author sought to resolve the disagreements. The quality assessment of the included studies was performed using the Cochrane risk of bias tool (17). Data were recorded using Microsoft Excel. The statistical analysis was performed by STATA version 17 (StataCorp, College Station, TX) and Review Manager 5.4 (New York, NY). Parametric tests were used to compare the data relating to the upper and lower limbs. In that case, a p-value 0.5 (or 50%) indicates high heterogeneity. The potential sources of heterogeneity were investigated as follows: measuring the influence and entity of the threshold effect, realizing a bivariable box plot to identify the sources of heterogeneity among studies and exclude them from the further analysis; performing a meta-regression and subgroup analysis to identify the independent factors. If the heterogeneity is statistically significant, with $p < 0.05$, the estimated effect resulting from the analysis may not represent the real treatment effect. In this case, it is necessary to re-evaluate the studies included in the analysis, to identify substantial differences between the characteristics of the various studies and/or patients enrolled: a sensitivity or subgroup analysis.

Surgical procedure

The injured nerve preparation procedure is similar to the acute procedure before direct repair. After cutting away the suffering edges of the injured nerve, the exact length of the gap can be established. The careful preparation of the receiving bed is essential to allow the correct re-vascularization of the graft by the neighboring tissues; otherwise, the procedure will fail. At this point, the graft is taken from the distal-lateral third of the leg. A distal incision of approximately 2 cm is made between the posterior edge of the lateral malleolus and the Achilles tendon. Once the nerve has been identified, it is dissociated with a probe similar to the one used for the release of the carpal tunnel up to the desired length. At this point, a second proximal incision is made, the nerve is found, and after having dissected it at the level of the first distal incision, it is made to come out of the proximal incision and sectioned. This allows picking up grafts up to 38 cm (13). Often it is necessary to fold the graft on itself several times to obtain a diameter corresponding to the receiving nerve. Furthermore, it is always good to take a quantity of sural nerve slightly greater than the length of the gap to prevent the suture from being in tension. Hypoesthesia of the dorsal-lateral region of the foot will remain (Figure 1).

Results

The search led to the identification of 209 studies. The in-depth analysis of the entire text of the manuscripts led to the selection of only 8 studies valid for the systematic review (18-25) (Figure 2).

The heterogeneity of the included studies was low (I² value <0.5); therefore, it was not necessary to perform a subgroup analysis. The included studies were published between 2002 and 2021, involving a total of 195 patients, 162 males and 33 females. The female sex is involved in a significantly reduced way ($p < 0.001$), probably due to the fact that the prevalence of this type of trauma is higher in the male sex for occupational reasons. The average age of the patients was 34.3 years (min: 2; max: 67; SD: 6.84). The average age is also affected by the fact that these traumas often occur in the workplace or as a result of road accidents, in which young people are more involved. The mean follow-up of the included studies was 37.4 months (min: 12; max: 76; SD: 22.20). The studies showed a good level of quality in the absence of significant bias. No study reported a high risk of bias according to the Cochrane risk of bias tool. "Unclear" results are reported in a low number of cases, as shown in Table 1.

The mean time elapsed between trauma and repair of the nerve injury with sural graft (data reported in 6 of 8 papers included) was 31 weeks (min: 5; max: 120; SD: 11.25). In the case of an upper limbs' injury, 5 papers reported the ulnar nerve as damaged, 4 the radial nerve, 3 the median nerve, and 1 digital nerves. While regarding the lower limbs, 2 papers reported cases relating to lesions of the femoral, tibial, and fibular nerve, while 3 papers reported data relating to lesions of the sciatic nerve.

Among papers about upper limbs, 5 of these reported data relating to the width of the nerve gap, while among those about lower limbs, the extent of nervous gap was reported only in 2 cases. In 3 papers, it is generally reported that the amount of the gap treated was on average less than 5 centimeters, while

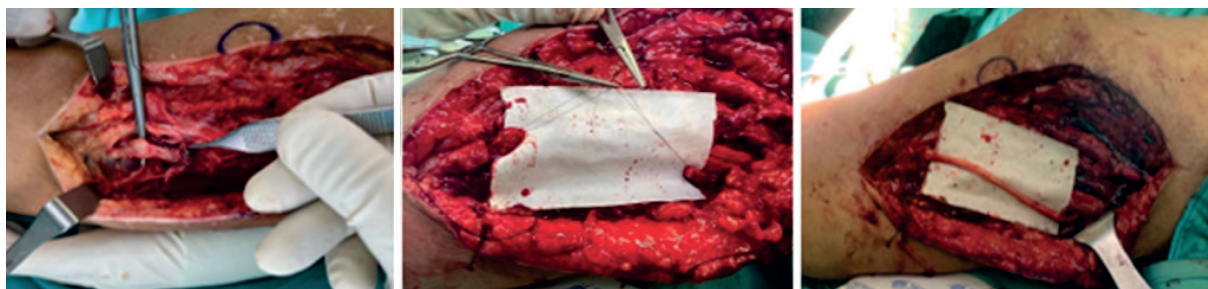


Figure 1. Intraoperative view of a damaged nerve repaired with a sural nerve graft.

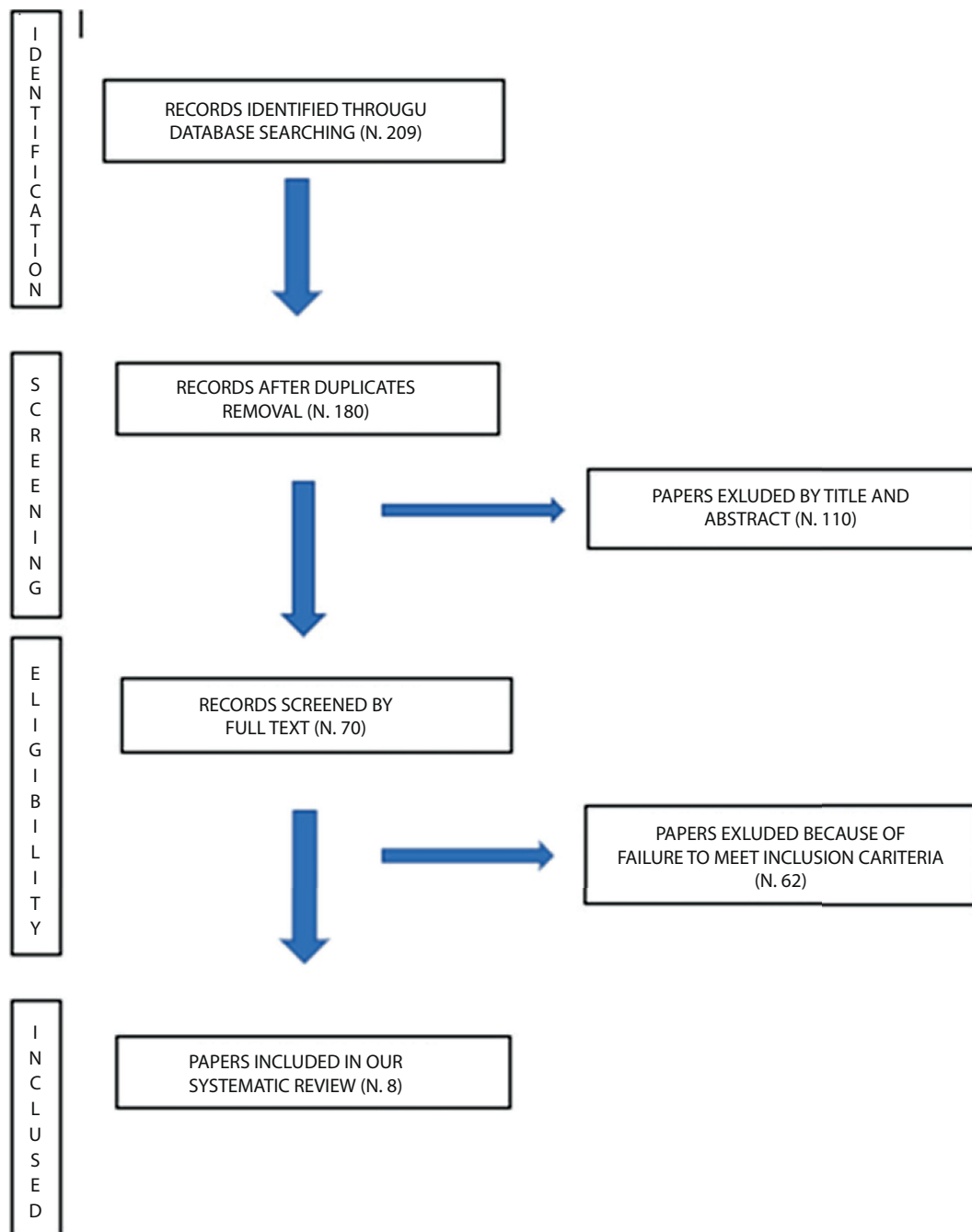


Figure 2. Flow diagram of the first step.

in the remaining cases the average value was reported. The pooled mean gap was 6.3 cm (min: 1; max: 19; SD: 1.92). Data relating to the recovery of sensitivity was reported in 5 papers. Out of a total of 155 patients, 86 (55.5%) reported a recovery of sensitivity with a score

greater than or equal to S3. The functional recovery was greater than or equal to M3 in 107 patients (67.7%). Therefore, it was possible to analyze the correlation between the recovery of muscle function and the extent of nervous gap. We obtained that even in the presence

Table 1. First step studies quality assessment using Cochrane risk of bias tool.

N	Author	Selection bias Random sequence generation	Selection bias Allocation concealment	Reporting bias Selective reporting	Other bias Other sources of bias	Performance bias Blinding (participants and personnel)	Detection bias Blinding (outcome assessment)	Attrition bias Incomplete outcome data
1	Lin et al. ⁽¹⁸⁾	LOW	UNCLEAR	LOW	LOW	LOW	LOW	UNCLEAR
2	Debski et al. ⁽¹⁹⁾	LOW	LOW	LOW	LOW	LOW	LOW	LOW
3	Kapoor et al. ⁽²⁰⁾	LOW	LOW	LOW	LOW	UNCLEAR	LOW	LOW
4	Sallam et al. ⁽²¹⁾	LOW	LOW	UNCLEAR	LOW	LOW	LOW	LOW
5	Schwaiger et al. ⁽²²⁾	LOW	UNCLEAR	LOW	UNCLEAR	LOW	UNCLEAR	LOW
6	Gezercan et al. ⁽²³⁾	LOW	LOW	LOW	LOW	UNCLEAR	LOW	LOW
7	Matejcik et al. ⁽²⁴⁾	LOW	LOW	UNCLEAR	LOW	LOW	LOW	LOW
8	Vayvada et al. ⁽²⁵⁾	LOW	LOW	LOW	LOW	LOW	LOW	LOW

of average gaps greater than 6 centimeters, the functional outcomes were comparable to those with nerve gaps less than 5 cm. On the other hand, there is no evidence of a correlation between younger age and better functional outcome. Moreover, we found that the time interval between trauma and grafted reconstruction significantly influenced the outcome. In fact, it can be noted that in the studies that report average waiting times of more than 30 weeks, the percentage of patients who obtained scores higher than or equal to S3 and / or M3 decreases (Table 2A, 2B).

The autologous graft implies harvesting and therefore discomfort in the donor area. The second phase of the review on the outcome of the donor site made it possible to identify 25 titles. After the analysis of the abstract and the full text, only 4 studies were included in the review with a total of 135 patients, mostly males (103, 76.3%) (Figure 3).

The mean age was 29.5 years (min: 10; max: 72, SD: 6.86) (26-29). (Figure 3) The mean follow-up was 126 months (min: 3; max: 468; SD: 136.6). Quality assessment using Cochrane risk of bias tool of the studies included in the second step of our systematic review are reported in Table 3.

The extrapolated data were related to the deficit of sensitivity in the dorsal-lateral region of the foot, the presence of allodynia / intolerance to cold, the presence of chronic pain, expressed in percentages. Consistent with prior research, the most frequently reported symptom by patients was sensory deficit (125 out of 135 patients, 92.6%). Followed by allodynia: reported by 36 patients (26.7%) and chronic pain only in 9.6% of cases (13 patients) (Table 4).

Discussion

The gold standard for bridging a nerve gap remains a nerve autograft. Since the first implementation of a nerve graft in 1870 by Philipeaux and Vulpian, significant contributions to micro-suturing technique, neural topography, and the biology of nerve regeneration have transformed the way we approach nerve gap (30). Among the usable nerve grafts, the sural nerve certainly represents the autologous donor of choice, as it is easy to withdraw, emits few branches along its course, and is of adequate length and caliber. Furthermore, the use of sural nerve involves discomfort from

Table 2A. Data relating to the studies included on the upper limbs' injuries.

N	Author	Year	N. of patients	Time between injury and surgery (weeks)	Injured nerve	Gender (M/F)	Mean age (years)	Mean Follow-up (months)	Nerve gap (cm)	% > S3	% > M3
1	Lin et al. ⁽¹⁸⁾	2007	15	-	Median, ulnar, radial	13M, 2F	27.5 (2-48)	49.7	5.7 (2-11)	11/15 (73,3%)	7/15 (46,7%)
2	Debski et al. ⁽¹⁹⁾	2021	61	33.1 (5-430)	Sensitive digital nerves	55M, 6 F	33.8 (17-63)	76	3.6 (1-9)	28/61 (45,9%)	-
3	Kapoor et al. ⁽²⁰⁾	2020	16	14 (8-20)	Ulnar	13M/ 3 F	31.3 (16-53)	12	9.4 (2-19)	-	10/16 (62,5%)
4	Sallam et al. ⁽²¹⁾	2017	28	32 (28-64)	Ulnar	17M/11 F	31.8 (21-50)	26.8	< 5	15/28 (53,6%)	26/28 (92,9%)
5	Schwaiger et al. ⁽²²⁾	2020	6	16 (6-40)	Radial	7 M/ 5 F	51.2 (7-67)	51	-	-	3/6 (50%)
6	Gezercan et al. ⁽²³⁾	2016	18	44 (12-120)	Median, ulnar, radial	14 M/ 5 F	30.1 (16-66)	18	-	-	12/24 (50%)
7	Matejcik et al. ⁽²⁴⁾	2002	42	36 (9 pz >48 weeks)	Median, ulnar, radial	37 M/5 F	36 (no range reported)	-	31 pz < 5 cm	27/42 (64,3%)	37/42 (88,1%)

Table 2B. Data relating to the studies included on the lower limbs' injuries.

N	Author	Year	N. of patients	Time between injury and surgery (weeks)	Injured nerve	Gender (M/F)	Mean Age (years)	Mean Follow-up (months)	Nerve gap (cm)	% > S3	% > M3
1	Gezercan et al. ⁽²³⁾	2016	6	44 (12-120)	Fibular, sciatic, tibial	5 M/ 1 F	30.1 (16-66)	18	-	-	3/6 (50%)
2	Matejcik et al. ⁽²⁴⁾	2002	14	29 (5 pz > 24)	Fibular, sciatic, femoral, tibial	9 M/ 5 F	39.7 (no range reported)	-	2 pz > 5 cm	-	4/14 (28,6%)
3	Vayvada et al. ⁽²⁵⁾	2013	9	-	Sciatic	6 M/ 3 F	31.7 (20-42)	48	6.5 (3.4-13.6)	5/9 (55,6%)	5/9 (55,6%)

the donor site, but well tolerated over time. As demonstrated by the second part of our review, in fact, the residual sensitivity deficit is a constant, while more rarely there are major complications such as intolerance to cold / heat or chronic neuropathic pain. However, these symptoms tend to decrease over time, thanks to neuronal plasticity, more developed in children, so that the patient adapts to the hypoesthesia of the dorsal-lateral region of the foot. The original graft harvesting technique involved a long incision along its course halfway between the Achilles tendon and the

posterior edge of the fibula. Nowadays, minimally invasive techniques, such as the one used by the authors of this manuscript, have been described. This offers the advantage of avoiding both long incisions and the use of other minimally invasive techniques such as stripping. Stripping can cause significant damage to the nerve intended for transplantation, especially to the epineurium, as documented by Jaroszynski et al (31). Therefore, the withdrawal technique is of fundamental importance to ensure the success of the procedure, but not only that. The type of trauma that caused the nerve

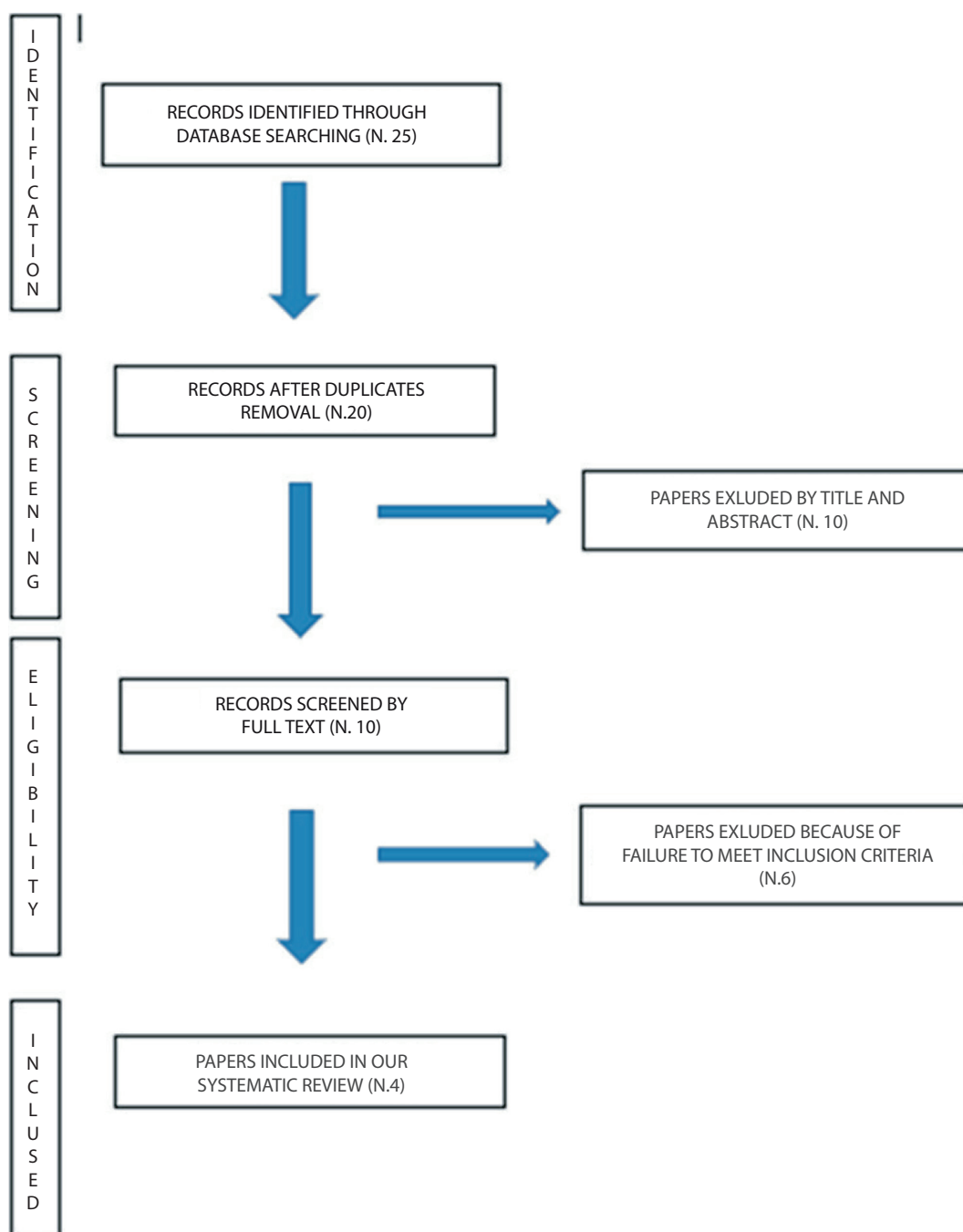


Figure 3. Flow diagram of the second step.

injury can also affect the outcome of the procedure. As mentioned in the introduction, the integrity of the receiving bed is essential for the nourishment and correct re-vascularization of the graft. Consequently, the presence of vascular deficits and associated bone or

tendon injuries invariably affects functional recovery, as occurs, for example, in the case of gunshot injuries (32). It is essential to guarantee an optimal receiving bed, but the time elapsed between the trauma and the surgical repair procedure could also play a role in the

Table 3. Second step studies quality assessment using Cochrane risk of bias tool.

N	Author	Selection bias Random sequence generation	Selection bias Allocation concealment	Reporting bias Selective reporting	Other bias Other sources of bias	Performance bias Blinding (participants and personnel)	Detection bias Blinding (outcome assessment)	Attrition bias Incomplete outcome data
1	Hallogren et al. ⁽²⁶⁾	LOW	UNCLEAR	LOW	LOW	LOW	LOW	UNCLEAR
2	Martins et al. ⁽²⁷⁾	LOW	LOW	LOW	UNCLEAR	LOW	LOW	LOW
3	Ijpma et al. ⁽²⁸⁾	LOW	LOW	UNCLEAR	LOW	LOW	LOW	LOW
4	Miloro et al. ⁽²⁹⁾	LOW	LOW	LOW	LOW	UNCLEAR	LOW	LOW

Table 4. Data related to the donor site.

N.	Author	N. of patients	Mean Follow-up (months)	Gender (M/F)	Mean age (years)	% deficit sensoriale	% allodinia	% chronic pain
1	Hallogren et al. ⁽²⁶⁾	41	144 (14-468)	35 M / 6 F	23 (10-72)	38/41 (92,7%)	20/41 (48,8%)	8/41 (19,5%)
2	Martins et al. ⁽²⁷⁾	39	12 (3-16)	37 M / 2 F	25 (14-40)	39/39 (100%)	0/39 (0%)	0/39 (0%)
3	Ijpma et al. ⁽²⁸⁾	29	312 (192-408)	21 M / 8 F	38 (18-49)	22/29 (75,9%)	10/29 (34,5%)	5/29 (17,2%)
4	Miloro et al. ⁽²⁹⁾	26	36 (no range reported)	10 M / 16 F	32 (19-45)	26/26 (100%)	6/26 (23%)	0/26 (0%)

outcome, as demonstrated in our review. This is confirmed by some studies, such as that of Cornelius et al., on the lingual nerve and the inferior alveolar nerve. The minimum duration of follow-up was 14 months. After direct nerve coaptation, 69% of the patients exhibited protective sensation, and 41% regained discriminative function. In contrast, grafting resulted in the restoration of protective function in 39% and discriminative function in 17% of the patients (33). Whenever possible, reconstruction should be performed within 3 weeks after the trauma. Simultaneously, the quality and the degree of tension of the microsurgical suture can significantly influence the outcome (34). It is known that microsurgical sutures on peripheral nerves performed using many stitches lead to failure. Furthermore, it is important not to

over-tension the wire during knotting because this leads to overlapping of the two nerve segments, which cannot promote nerve regeneration (35). It is also necessary to mention the “polarity” of the graft. Traditionally, it is believed that by reversing the graft with respect to its position in the donor site, axonal escape is avoided. In all the cases we dealt with (20 cases), the polarity was never reversed, and it seems that this did not affect the outcome. We find confirmation of this in the literature thanks to experimental studies on the rat. Nakatsuka et al. have shown that there are neither histological nor electrophysiological differences, disproving this dogma (36). Finally, our review showed that average waiting times of more than 30 weeks between trauma and graft reconstruction are associated with a worse functional outcome. We also find confirmation

of this fact in the literature. Roganovic et al. demonstrated how a wait longer than 5.5 months is associated with a worse outcome. The authors reported data about 128 patients with missile-caused complete ulnar nerve injury managed surgically in the Neurosurgical Department of the Belgrade Military Medical Academy. They demonstrated that preoperative interval ($P = 0.001$) and length of the nerve defect ($P < 0.001$) were independent predictors of a successful outcome (37). In the same way, a more recent paper of Mathieu et al. confirmed the importance of direct, when possible, and early repair of peripheral nerve injuries, especially in extreme conditions, such as ballistic lesions (2). While the study by Moor et al. on the reconstruction of the axillary nerve showed that even in the face of a considerable delay (on average 12 months), the result was optimal. Authors evaluated 12 patients, mean age 37 years old, who underwent axillary nerve repair with sural nerve graft with an average 11-month delay between trauma and surgery. They observed an improved deltoid function of at least M3 in all the patients, demonstrating that also delayed sural grafting achieved optimal results (38). We believe that, when performing nerve grafting, the elapsed time alone does not represent a variable capable of changing the outcome, as it is the set of local conditions and the accuracy of the suture that are most relevant to the final result. Finally, a relevant role in the outcome is given by the patient's age. Several studies report that patients under the age of 25 have better results (39,40). Obviously, the presence of comorbidities can also affect the outcome, such as diabetes. As is known, hyperglycemia decreases the ability of nerve cells to react to oxidative stress and also affects microcirculation. So, in the case of diabetes, the possibility of re-vascularization of the graft decreases (41). Our systematic review presents some limitations. First, some studies were excluded because the full text was not found or because the English text was not available. Secondly, even in the absence of relevant bias, some of the included studies were missing some data that would have further enriched the results of our study (e.g. range, no mean values reported). In addition, all the included studies were retrospective. The number of patients treated for upper limb nervous injury was higher than the number of patients affected from lower limbs injuries. On the other hand, the

strengths of our study are multiple: we recorded low high heterogeneity among studies; studies involved a good number of patients so that the results can represent the reality; most of the studies included are recent ones (published after 2010). The results obtained in this systematic review confirm that the sural graft is a valid therapeutic choice in all those lesions that cannot be subjected to direct acute repair. Furthermore, sural grafting can correctly conduct nerve regeneration even if surgically performed many months after the trauma that caused the peripheral nerve injury. Peripheral nerve injuries also have a significant impact on patients' psychosocial aspects of life. Hundepool et al. conducted a prospective multicenter study on 61 patients to identify prognostic factors for functional recovery in the first postoperative year following injuries of the median nerve, ulnar nerve, or combined lesions at forearm level. One year after injury, 84.6% of patients had returned to work. The authors found gender, level of education as well as posttraumatic levels of stress at one- and three months post-injury as highly predictive in regard to functional recovery (42). Heary et al. investigated the relationship between psychosocial factors and pain relief following peripheral nerve surgery. 331 patients who underwent surgery for peripheral nerve injuries and returned for at least two postoperative follow-ups were included. They reported that increased impact of neurological pain on daily activities or persistent nervous deficits were predictive for psychological discomfort and depression (43). In conclusion, surgeons should be aware that functional recovery following the repair of peripheral nerve lesions can be significantly influenced by the prevalence of postoperative stress and psychosocial sadness and depression.

Conclusions

Microsurgical reconstruction of nerve injuries is an essential aspect of treating penetrating wounds. Whenever possible, direct acute repair should be performed, along with tendon sutures or osteosynthesis for associated bone fractures. In situations where direct repair is not feasible, such as major nervous losses or wounds with a high infectious risk, autologous graft

reconstruction becomes the mandatory treatment, as demonstrated in our review. The use of the sural nerve is considered the gold standard due to its simplicity in harvesting, minimally invasive nature, and ability to yield good functional outcomes with few complications. Our review emphasizes that, when direct repair is impossible, sural grafting proves to be the optimal treatment for these patients, resulting in significant gains in function and sensitivity with low complication rates.

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Authors Contribution: MS and EP formulated the search strategy and collected data for the review, MS performed the statistical analysis, GM revised critically the manuscript.

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