Functional Outcome Following Traumatic Peripheral Nerve Injury Repair in a Tertiary Care Hospital in South India - An Observational Study

Joyal Jose[1], Sabu Chaniveliyil Parameswaran[2], Aniraj Rajappan[3]

[1, 2, 3] Department of Plastic and Reconstructive Surgery, Government Medical College, Thiruvananthapuram, Kerala, India.

ABSTRACT

BACKGROUND

Peripheral nerve injuries (PNIs) often accompany trauma to limbs and is a major cause of morbidity. Various surgical techniques are described for nerve repair and various factors influence the functional outcome after repair. This study intends to assess the functional outcome following PNI repair and various factors affecting the final outcome post repair. In this study we wanted to assess the functional outcome of PNI repair done at our institute.

METHODS

This is a prospective observational study conducted at the Department of Plastic and Reconstructive Surgery, Government Medical College, Thiruvananthapuram, India, from September 2017 to September 2019 (24 months) in patients with a diagnosis of traumatic peripheral nerve injury. Data collected were analysed by statistical programme for social sciences (SPSS) version 20. Quantitative variables were expressed in mean & standard deviation (SD) and qualitative variables were expressed in proportions. Associations were tested by chi-square test.

RESULTS

A total of 100 patients were studied. Overall satisfactory sensory outcome was found to be 45.2% in median nerve and 45.5 % in ulnar nerve injuries (P value - 0.492). Overall satisfactory motor outcome was found to be 45.2 % in median nerve and 36.3 % in ulnar nerve injuries (P value - 0.391). Age < 40 years was found to be significantly associated with a good sensory and motor recovery. Diabetes mellitus was associated with a poor sensory and motor outcome compared to patients without any comorbidities. Use of nerve grafts was associated with less sensory recovery compared to primary nerve coaptation (P value - 0.496). Nerve repairs done between 4 - 7 days of injury had better sensory and motor outcome.

CONCLUSIONS

Traumatic peripheral nerve repair has a variable functional outcome and is dependent on various factors like age and other patient related factors, mechanism of injury and the type of nerve repair. Accurate diagnosis, attention to detail and timely intervention can improve the overall functional outcome.

KEYWORDS

Peripheral Nerve Injury, Nerve Repair, Functional Outcome

Corresponding Author:
Dr. Joyal Jose,
Eluvathingal House,
Anakkal, Kanjirapally,
Kottayam -686508, Kerala, India.
E-mail: jozeerhymes@gmail.com

DOI: 10.18410/jebmh/2021/411

How to Cite This Article:
Jose J, Parameswaran SC, Rajappan A. Functional outcome following traumatic peripheral nerve injury repair in a tertiary care hospital in South India - an observational study. J Evid Based Med Healthc 2021;8(25):2197-2202. DOI: 10.18410/jebmh/2021/411

Submission 03-02-2021,
Peer Review 12-03-2021,
Acceptance 06-05-2021,
Published 21-06-2021.

Copyright © 2021 Joyal Jose et al. This is an open access article distributed under Creative Commons Attribution License [Attribution 4.0 International (CC BY 4.0)]

BACKGROUND

A neuron is made up of cell body, dendrites and an axon. Each axon is covered by Schwann cells and endoneurium. Nerve fibres can be myelinated or unmyelinated. The Schwann cells are a variety of glial cells that form the myelin sheath, in myelinated nerve fibres. The axons are bundled together into groups, called fascicles. Axonal bundle or fascicles are covered by perineurium and the whole nerve is covered by epineurium. Epineurium is divided into an internal and external epineurium. The terminal branch of each motor neuron forms a synapse called motor end plate or neuromuscular junction, which are filled with the neurotransmitter acetyl choline.

Nerve injuries result in a series of events in both the proximal and distal segment. In the proximal segment, there is collateral sprouting and axonal regrowth. In the distal end, Wallerian degeneration occurs, which is a scavenging process headed by Schwann cells making way for the regenerating axons. Nerve regeneration is a slow and unpredictable process with a regeneration rate of 1mm/day or 1 inch/month and hence distal injuries recover much faster than proximal injuries.

Peripheral nerve injuries often accompany trauma to limbs and is a major cause of morbidity. Upper limb is the most commonly affected, and most of the patients are young.[1,2]

Typical symptoms are motor and sensory defects like paralysis of affected muscles, numbness and neuropathic pain. Due to the morbidity associated with it, PNIs have a lot of social and economic implications.

Even though various surgical techniques are described for nerve repair, epineural repair remains the gold standard surgical reconstruction, with direct end to end nerve repair or using interposition nerve grafts, when there is excessive tension with primary repair. The nerves may also be repaired with fibrin nerve glues.

Recovery following repair is not predictable, and even with a technically perfect microsurgical repair, sensory and motor functions may recover variably, though improvement generally occurs. A meta-analysis in 2005[3] of median and ulnar nerve repairs demonstrated that only 51.6 % achieve satisfactory motor recovery (M4, M5) and only 42.6 % achieving satisfactory sensory recovery (S3 +, S4).

Various factors are found to influence the functional recovery after repair like age, mechanism of injury, level of injury and delay in presentation affect functional outcome. These prognostic factors were elucidated by various retrospective studies in the past.[4,5] Younger age and distal injuries had better outcome.

Objectives

1. Assess the functional outcome of PNI repair done at our institute (primary objective).
2. Study the influence of factors like age, mechanism of injury, nerves injured, delay in presentation and type of nerve repair in the functional outcome following repair (secondary objective).

METHODS

This is a prospective observational study conducted at Department of Plastic and Reconstructive Surgery, Government Medical College, Thiruvananthapuram, Kerala, India from September 2017 to September 2019 (24 months) in patients attending emergency department and outpatient department with a diagnosis of traumatic peripheral nerve injury of upper and lower limbs and who subsequently underwent nerve repair from our centre. Partial nerve injuries, brachial plexus and lumbar plexus injuries were excluded from the study.

A total of 100 patients were studied. History and physical examination were done, structured proforma was used for entering the data entry (details like age, sex, IP number, mechanism of injury, time since trauma, limbs involved, nerves involved, type of surgery, delay in surgery and motor and sensory recovery at follow-up were noted).

Sensory examination, being the most subjective part of the neurological examination, needs full patient cooperation. Patient was explained what is expected of him/her and were re-assured. Pain sensation assessment was done by pinprick test, fine touch assessment by Semmes-Weinstein monofilament and two-point discrimination by a Castroviejo caliper.[6,7] For motor assessment, manual testing of involved muscle groups are done.[8,9] Post-operatively patients were followed for a minimum of 6 months and assessment of outcome was assessed by Medical Research Council's scale (MRC) grading[10,11] into satisfactory (M4 or more, S3 or more) or unsatisfactory (M3 or less, S2 or less). Institutional ethical committee clearance was obtained, informed consent was obtained from the participants and confidentiality was ensured and maintained throughout the study. The study did not pose any additional risk to the subject nor interfere with existing treatment.

Statistical Analysis

Details collected from proforma were entered into a MS excel sheet and analysed using the statistical programme SPSS version 20. Quantitative variables were expressed in mean and standard deviation and qualitative variables expressed in proportions. Associations were tested by chi-square test.

RESULTS

Total study population consisted of 100 patients with 87 males and 13 females (M : F ratio 6.6 : 1). Study population was categorized into different groups based on their age groups and analysed (age < 20, 20 - 39, 40 - 59, 60 - 79). Minimum age was 11 and maximum age was 68 years. Most common age group was 20 - 39 age group consisting of 68 percentage of the entire study population. Mean age of the study population was 32.7 with a standard deviation of 10.8. The only comorbidity in the study group was diabetes mellitus which was present only in 5 patients. 16 percent of the population were smokers.

Type of initial injury helped in understanding the mechanism of injury and hence the impact on its final outcome. 75 % of the injuries were of accidental type, at work-place (cutter machine, glass, metal sheet injury etc.), 15 % of cases were due to deliberate self-harm and 10 % from road traffic accidents (RTAs).

Out of 100 cases, 96 cases were in the upper limb (50 cases-right, 44 cases-left). The most commonly injured nerve was the median nerve (42 %) followed by ulnar nerve (33 %). Combined median-ulnar nerve injuries constituted another 8 %, followed by digital nerve injury (7 %). Others were superficial branch of radial nerve – 4 %, tibial nerve - 3 %, posterior interosseous nerve - 2 %, and common peroneal nerve - 1%.

Primary nerve repair (within 72 hours) was possible in 40 cases. Delayed primary repair (72 hours -7 days) was done in 23 cases and secondary repair was done in the remaining 37 cases. The mean delay between injury and nerve repair was 9.96 days, with a standard deviation of 17.9.

Overall satisfactory motor and sensory recovery of the repaired nerves are shown in Table 1. Satisfactory motor and sensory recovery of median nerve was found to be 45.2 % each and that of ulnar nerve was 36.3 % and 45.5 % respectively.

Satisfactory motor and sensory recovery of combined median & ulnar injuries were 25 % each. Motor recovery was better with ulnar nerve injuries (45.5 %) and sensory recovery better with digital nerves (85 %), followed by superficial branch of radial nerve (75 %).

The various variables and their effect on sensory recovery was analysed (Table 2) and it was found that age of the patient was significantly associated with outcome, with age < 40 having 55.4 % sensory recovery compared to age > 40 having 34.4 % sensory recovery (P value 0.047). Patients with diabetes mellitus did worse than others (40 % Vs 49.5 %).

Patients in whom nerve repair was done without a nerve graft showed better outcome, compared with nerve repair with graft (50 % vs 37.5 %). Regarding injury-surgery delay, delay between 4 - 7 days after injury showed a good outcome (70.6 %) vs a delay of > 8 days (38.5 %), which was the worst. Since all nerves were repaired with epineural repair, comparison between various techniques could not be made.

Similarly, motor recovery was also studied with respect to different variables (Table 3). It was found that age < 40 had a 44.8 % motor recovery compared to age > 40 having a 33.3 % recovery (P value - 0.29). Patients with diabetes mellitus did worse than others (25 % vs 41.9 %) with a P value of 0.5.

Patients with accidental injuries showed a better outcome (42.3 %) compared to other mechanisms of injury. Regarding injury-surgery delay, delay between 4 - 7 days after injury showed good outcome (50 %) vs a delay of < 3 days (36.2 %), which was the worst. Since all the nerves were repaired with epineural repair, comparison between various techniques could not be made.

Nerve	Motor Recovery	Sensory Recovery
Median nerve	19 / 42 (45.2 %)	19 / 42 (45.2 %)
Ulnar nerve	12 / 33 (36.3 %)	15 / 33 (45.5 %)
Combined median+ ulnar nerve	2 / 8 (25 %)	2 / 8 (25 %)
Digital nerve	NA	6 / 7 (85 %)
Superficial branch of ulnar nerve	NA	3 / 4 (75 %)

Table 1. Overall Satisfactory Motor and Sensory Recovery

Variables		Unsatisfactory		Satisfactory		Chi-Square	P Value
		Count	%	Count	%		
Age	< 40	33	44.6 %	41	55.4 %	3.95	0.047
	> 40	21	65.6 %	11	34.4 %		
Comorbidity	NIL	51	50.5 %	50	49.5 %	0.17	0.678
	DM	3	60 %	2	40 %		
Mechanism of injury	Accidental	39	48.1 %	42	51.9 %	3.74	0.154
	DSH	11	73.3 %	4	26.7 %		
	RTA	4	40 %	6	60 %		
Nerve graft	No	49	50 %	49	50 %	0.46	0.496
	Yes	5	62.5 %	3	37.5 %		
Injury-surgery delay	0 - 3 days	25	50 %	25	50 %	4.92	0.085
	4 - 7 days	5	29.4 %	12	70.6 %		
	8 or more	24	61.5 %	15	38.5 %		

Table 2. Association of Sensory Recovery with Different Variables (DM - Diabetes Mellitus, DSH - Deliberate Self Harm, RTA - Road Traffic Accident)

Variables		Unsatisfactory		Satisfactory		Chi-Square	P Value
		Count	%	Count	%		
Age	< 40	37	55.2 %	30	44.8 %	1.12	0.290
	> 40	20	66.7 %	10	33.3 %		
Comorbidity	NIL	54	58.1 %	39	41.9 %	0.45	0.500
	DM	3	75 %	1	25 %		
Mechanism of injury	Accidental	41	57.7 %	30	42.3 %	0.15	0.929
	DSH	9	60 %	6	40 %		
	RTA	7	63.6 %	4	36.4 %		
Nerve graft	No	54	60.7 %	35	39.3 %	1.63	0.202
	Yes	3	37.5 %	5	62.5 %		
Injury-surgery delay	0 - 3 days	30	63.8 %	17	36.2 %	1.12	0.571
	4 - 7 days	8	50 %	8	50 %		
	8 or more	19	55.9 %	15	44.1 %		

Table 3. Association of Motor Recovery with Different Variables (DM - Diabetes Mellitus, DSH - Deliberate Self Harm, RTA - Road Traffic Accident)

Study	Motor Recovery			Sensory Recovery		
	Median Nerve	Ulnar Nerve	Median + Ulnar Nerve	Median Nerve	Ulnar Nerve	Median + Ulnar Nerve
Ruijs et al.		51.6 %			42.6 %	
Jaquet et al.	61.5 %	39.4 %	38.1 %	36.6 %	37.7 %	42.9 %
Be et al.	75 %	47.5 %	-	57.3 %	52.7 %	-
Our study	42.5 %	36.3 %	25 %	42.5 %	45.5 %	25 %

Table 4. Comparison of Motor and Sensory Recovery in Other Similar Studies.

Study	Factors Favouring Good Sensory Outcome	Factors Favouring Good Motor Outcome
He et al.	• Age < 25 (P value - 0.02) • Primary nerve coaptation without graft (P value - 0.01) • Median nerve > Ulnar nerve (P value - < 0.05) • Follow up period of 2 - 3 years (P value - 0.001)	• Age < 16 (P value - 0.02) • Female gender (P value - 0.03) • Injury-surgery delay of less than one day (P value - 0.00) • Primary nerve coaptation • (P value - 0.00) • Median nerve > Ulnar nerve (P value < 0.05) • Follow up period of 2 - 3 years (P value - 0.001)
Our study	• Age < 40 (P value 0.047) • Patients without DM • Primary nerve coaptation without nerve graft (P value - 0.496) • Injury- surgery delay less than 7 days (P value - 0.085)	• Age < 40 (P value - 0.29) • Injury-surgery delay of less than 7 days (P value - 0.571) • Median nerve > Ulnar nerve (P value-0.391)

Table 5. Variables Affecting Motor and Sensory Recovery – Comparison with Similar Study by He et al. (DM - Diabetes Mellitus)

DISCUSSION

Peripheral nerve repair dates back as far as Hippocrates era. In the 7th century, Paulus Aeginatus (626 - 696 AD) postulated a restoration of severed nerves, and the concept of repair of transacted nerves was described by Gabriele Ferrara (1543 - 1627) in Italy. In last few decades, specialized instrumentation, delicate suture materials and introduction of operative magnification, contributed to an improved surgical technique for nerve repair. Epineural repair is the most commonly done technique, in which the epineurium of the proximal and distal ends are approximated without tension. Another technique followed is the grouped fascicular repair in which the corresponding fascicles of the proximal and distal ends are approximated, i.e., motor to motor, and sensory to sensory. Grouped fascicular repair is of use in oligo-fascicular nerves, like ulnar nerve at wrist, where the nerve topography is predictable in most individuals. Studies have shown that immediate/primary repair gives the best results, compared with delayed primary and secondary repairs. Another factor affecting repair are the repair tension. A repair under tension gives sub-optimal results and, in such cases, utilizing a nerve graft is prudent. Potential donor sites for autogenous nerve grafts include sural nerve, Medial antebrachial cutaneous nerve (MABC), lateral antebrachial cutaneous nerve (LABC) etc. Other options to bridge the nerve gap is by utilising allogenous nerve grafts, nerve conduits (both biologic and engineered). Nerve transfer is also another method by which nerve gaps can be managed, especially if the proximal nerve end is missing & also in more proximal injuries.

Seddon, in 1947 classified nerve injuries into neuropraxia, axonotmesis & neurotmesis[12] and Sunderland in 1951 classified them into first - fifth degree injuries[13] with addition of sixth degree injuries by Mackinnon,[14] and these classifications continue to guide the management of nerve injury patients. Neuropraxia (first degree injury) is an ischemic injury that may have segmental demyelination but no interruption of axonal or connective tissue continuity. Remyelination and evidence of recovery is anticipated in up to 12 weeks.

Axonotmesis (Seddon) includes second, third and fourth-degree injuries (Sunderland). Second degree injury is characterised by axonal disruption but intact connective tissue sheaths. Recovery will be complete. The progress of regeneration can be followed by an advancing Tinel's sign. First and second degree injuries are managed conservatively.[15,16] Third degree injuries are uniquely characterised by fibrosis in the endoneurium that prevents the unencumbered regeneration of some injured axons. This leads to mismatched end-organ innervation and can be helped with surgical decompression. Fourth degree injuries represent an in-continuity neuroma with no potential for spontaneous recovery as the entire population of regenerating axons are blocked by scar. Neurotmesis (Seddon)/Fifth degree injury (Sunderland) can occur when the entire nerve (all the axons and connective tissue elements) is divided, which mandates surgical repair. Sixth degree injury demonstrates a mixed picture.

Regarding timing of nerve repair, primary nerve repair is defined as nerves repaired within 72 hours of injury, delayed primary repair defined as repair done between 72 hours to one week after injury. Secondary repair refers to any repair done after one week.[17]

Better results are obtained following microsurgical repair of nerves. Commonly performed nerve repair techniques include epineural repair and grouped fascicular repair. Using the native artery or fascicular patterns to align the proximal and distal nerve ends, with no tension and minimal sutures, epineural suturing technique is preferred. However, grouped fascicular technique can be used in oligo-fascicular nerves (ulnar nerve at forearm and wrist) with known sensory and motor topography.

Age of the patient is a very important variable that can affect the final outcome following repair. There are three reasons that make children attain better results after peripheral nerve repair. One is that children have less distance from site of injury to motor end plate, compared to adults which means with the same regeneration rate, children attain results faster than an adult. Second is children have better brain plasticity, which is defined as the ability of the brain to understand and adapt to the altered signals received from peripheral nerves after injury. Third reason is that children also have better regenerative capacity of nerves compared to adults, i.e. the regeneration rate of proximal neurons are slightly faster in children and also the regenerating axons are more specific to the target. Results also depends on the motivation level of the patient, his/her adherence to post-operative rehabilitation programme, and also intellectual level of the patient. Previous research has also shown that certain cognitive capacities, such as verbal learning and visuo-spatial logic capacity, are correlated with restitution of functional sensibility after nerve repair. There are many studies that report on motor and sensory recovery following peripheral nerve repairs and that assess the various prognostic factors affecting the final outcome.[5,16,18-22] Most of the studies conclude that younger patients recover better,[19,20] smoking is associated with a slower functional recovery and medical comorbidities like diabetes, hypothyroidism and peripheral vascular disease can affect nerve regeneration.[16,21]

After studying the 100 cases of traumatic PNI repair functional outcome, it was found that the overall satisfactory sensory recovery in median nerve was 45.2 % and in ulnar nerve 45.5 %, similarly the overall satisfactory motor recovery in median nerve was 45.2 % and in ulnar nerve was 36.3 % respectively. Also, it was found that age of the patient was the single most important factor having a statistically significant positive impact on sensory and motor recovery post repair, with age < 40 having a better sensory and motor recovery compared to the age > 40 group.

The results of our study were compared with studies by Jaquet et al.[5] Millesi et al.[23] Puckett et al. [24] and Daoutis et al.[25] The total sample size of 100 in our study was comparable to other studies and the male preponderance seen in our study was observed in similar studies too. The M : F ratio in current study was 6.6 : 1. Accidental injuries with sharp objects constituted the majority of cases (75 % in current study vs 62.2 % in the study by Jaquet et al.[5]

Comparing the nerves involved, median nerve was the most commonly injured nerve, probably related to its superficial position at the wrist level, followed by ulnar nerve and followed by combined median-ulnar nerve injuries. This pattern was also seen in the studies by Ruijs et al.[22] and Jaquet et al.[5]

Median and ulnar nerve injuries were the most common injuries in most of the similar studies and hence satisfactory motor and sensory recovery of median and ulnar nerves in our study were compared with outcomes studied by authors like Ruijs et al.[22] Jaquet et al.[5] and He et al.[26] (Table 4). Motor recovery of median nerve far out-weighed the ulnar nerve and this pattern was seen in our study also (42.5 % Vs 36.3 %). Combined median-ulnar injuries performed poorly in all study groups, probably due to the severity of injury, associated injuries like fractures and tendon injuries, and crush injuries associated with road traffic accidents (RTAs), and also the probable delay in peripheral nerve repair due to focus on other aspects of managing the patient, like other life-threatening injuries.

The secondary objective of our study was to assess the factors contributing to sensory and motor recovery. In motor recovery, it was found that along with the age of the patient, injury-surgery delay and the type of nerves injured also affected final outcome. This was in consensus with previous studies by He et al.[26] (Table 5). Age < 40 and injury-surgery delay less than 7 days were associated with better outcome. Median nerve had a better motor outcome than ulnar nerve in the previous studies compared. Coming to sensory recovery, primary nerve coaptation, absence of diabetes mellitus, age < 40 and injury-surgery delay less than 7 days were associated with better outcome. Median nerve had a better sensory outcome than the ulnar nerve in the previous studies compared.

CONCLUSIONS

In our study, it was found that motor recovery of median nerve was superior to ulnar nerve; the results of combined median-ulnar nerve injuries were poor, and results of purely sensory nerves like digital nerves were good. Also, in assessing variables affecting outcome, age of the patient was the single most important factor (lesser the age, better the outcome) followed by the type of nerves injured, injury-surgery delay (earlier, the better) and primary nerve coaptation (better outcome without a nerve graft) affected the final outcome.

Traumatic peripheral nerve injuries are debilitating injuries with an impact on overall function with its economic, social and psychological implications. Hence, accurate clinical assessment and surgical repair of peripheral nerves is of utmost importance. In our study, modifiable factors affecting functional outcome included the delay between injury and the definitive surgery, and primary nerve coaptation without a nerve graft. Hence, it is concluded that peripheral nerve injuries should be repaired early with meticulous technique to maximise the functional recovery following repair.

Limitations of the Study

There were some limitations in our study like relatively smaller sample size, variable follow-up period (ranging from 6 months to 24 months) which might have interfered with the final assessment. Also, the study did not incorporate assessment of muscle grip strength nor the use of electrophysiological studies. Various objective scoring systems or quality of life assessments were not done.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

[1] Taylor CA, Braza D, Rice JB, et al. The incidence of peripheral nerve injury in extremity trauma. The American Journal of Physical Medicine and Rehabilitation 2008;87(5):381-385.
[2] Kouyoumdjian JA. Peripheral nerve injuries: a retrospective survey of 456 cases. Muscle and Nerve 2006;34(6):785-788.
[3] Ruijs AC, Jaquet JB, Kalmijn S, et al. Median and ulnar nerve injuries: a meta-analysis of predictors of motor and sensory recovery after modern microsurgical nerve repair: discussion. Plastic and Reconstructive Surgery 2005;116(2):484-494, discussion 495-496.
[4] Desouches C, Alluin O, Mutaftschiev N, et al. Peripheral nerve repair: 30 centuries of scientific research. Rev Neurol (Paris) 2005;161(11):1045-1059.
[5] Jaquet JB, Luysterberg AJ, Kalmijn S, et al. Median, ulnar and combined median-ulnar nerve injuries: functional outcome and return to productivity. J Trauma 2001;51(4):687-692.
[6] Dellon AL, Kallman CH. Evaluation of functional sensation in the hand. J Hand Surg (Am) 1983;8(6):865-870.
[7] Novak CB, Mackinnon SE, Kelly L. Correlation of two point discrimination and hand function following median nerve injury. Ann Plast Surg 1993;31(6):495-498.
[8] Marx RG, Bombardier C, Wright JG. What do we know about the reliability and validity of physical examination tests used to examine the upper extremity? J Hand Surg Am 1999;24(1):185-193.
[9] Brandsma JW, Schreuders TA, Birke JA, et al. Manual muscle testing: intra- observer and inter-observer reliabilities for the intrinsic muscles of the hand. J Hand Ther 1995;8(3):185-190.
[10] Medical Research Council. Nerve Injuries Committee: Results of nerve suture. In: Seddon H, edr. Peripheral nerve injuries. London: Her Majesty's Stationery Office, 1954.
[11] Mackinnon SE, Dellon AL. Results of nerve repair and grafting: surgery of the peripheral Nerves. Thieme 1998: p. 115.
[12] Seddon HJ. Three types of nerve injury. Brain 1943;66(4):237-288.

[13] Sunderland S. A classification of peripheral nerve injuries producing loss of function. Brain 1951;74(4):491-516.
[14] Farber SF, Saheb-Al-Zamani M, Zieske L, et al. Peripheral nerve injury after local anaesthetic injection. Anesth Anlag 2013;117(3):731-739.
[15] Nguyen QT, Sanses JR, Lichtman JW. Pre-existing pathways promote precise projection patterns. Nat Neurosci 2002;5(9):861-867.
[16] Myckatyn TM, Mackinnon SE. A review of research endeavours to optimize peripheral nerve reconstruction. Neurol Res 2004;26(2):124-138.
[17] Weber RV, Boyd KU, Mackinnon SE. Repair and grafting of peripheral nerves. In: Neligan P, edr. Plastic Surgery. Vol. 1. 3rd edn. Maryland Heights, MO: Elsevier 2011.
[18] Altissimi M, Mancini G, Azzaras A. Results of primary repair of digital nerves. J Hand Surg (Br) 1991;16(5):546-547.
[19] Belin BM, Ball DJ, Langer JC, et al. The effect of age on peripheral motor nerve function after crush injury in the rat. J Trauma 1996;40(5):775-777.
[20] Hess JR, Brenner MJ, Myckatyn TM, et al. Influence of aging on regeneration in end to side neurorraphy. Ann Plast Surg 2006;57(2):217-222.
[21] Hentz VR, Narakas A. The results of microneurosurgical reconstruction in complete brachial plexus palsy: assessing outcome and predicting results. Orthop Clin North Am 1998;19(1):107-114.
[22] Ruijs ACJ, Jaquet JB, Kalmijn S, et al. Median and ulnar nerve injuries: a meta-analysis of predictors of motor and sensory recovery after modern microsurgical nerve repair. Plast Reconstr Surg 2005;116(2):484-496.
[23] Millesi H, Meissi G, Berger A. The interfascicular nerve grafting of the median and ulnar nerves. J Bone Joint Surg (Am) 1972;54(4):727-750.
[24] Puckett CL, Meyer VH. Results of treatment of extensive volar wrist lacerations: the spaghetti wrist. Plast Reconstr Surg 1985;75(5):714-721.
[25] Daoutis NK, Gerosthathopoulous NE, Efstathopoulous DG, et al. Microsurgical reconstruction of large nerve defects using autologous nerve grafts. Microsurgery 1994;15(7):502-505.
[26] He B, Zhu Z, Zhu Q, et al. Factors affecting sensory and motor recovery after the repair of upper limb peripheral nerve injuries. Neural Regen Res 2014;9(6):661-672.