MEDICINE

Research Highlights

Expected functional loss and factors affecting recovery in patients with traumatic peripheral nerve injury in the upper limb

Harris Mangal
Year 2, Medicine, University of Exeter
Email: hm549@exeter.ac.uk

Abstract

Traumatic peripheral nerve injuries are nerve injuries that occur in the upper and lower extremities of the body initiating a variety of neurological symptoms. These range from motor to sensory deficits in the affected limb based on the severity and type of nerve injured. While there is increasing knowledge of the mechanisms of injury and regeneration, treatment is suboptimal resulting in major incapacities in the most active populations of society. Studies have purported many factors that can affect the recovery of a nerve and ameliorate functional outcomes. However, given the complexity of nerve anatomy and topography prognosis is highly unpredictable. This paper aims to review the effects of the type of nerve injured, age and gender, and how time between nerve injury and repair affects functional recovery. The case study format provides essential insight into factors that need to be considered in a clinical setting by physicians in order to produce better outcomes for patients. Furthermore, the case study concludes that the aforementioned factors have a significant impact on nerve recovery and functional outcomes in patients. In general, younger female patients with shorter axonal lengths, less atrophy following trauma and with the endoneurium intact had a better prognosis. Furthermore, surgical delays reduced good neurological recovery. Expected functional loss and factors affecting peripheral nerve recovery are multifaceted and the need for a meta-analysis of many other factors in conjunction to those mentioned is crucial.

Abbreviations

BDNF - Brain-derived neurotrophic factor
TPNI - Traumatic peripheral nerve injury
VEGF - Vascular endothelial growth factor

Introduction

Traumatic peripheral nerve injuries (TPNI) are common, especially in injuries affecting the upper limb. The nature of the injury is usually attributed to motor vehicle accidents, violence, sporting and recreational injuries, as well as iatrogenic injury during surgery. In addition to the posttraumatic stress a patient endures, if a length of nerve is damaged, functional recovery is substantially affected. Patients can be left severely debilitated with chronic neuropathic pain and neurological deficits, jeopardising their ability to work and return to a normal life.[1]

This study will aim to discuss how the significance of the type of nerve trauma, age and gender, and the time between injury and nerve repair impact functional recovery providing essential consideration for physicians. The article will revolve around a case-based analysis of a patient with peripheral upper limb nerve trauma at the Princess Elizabeth Orthopaedic Centre in Exeter. The patient provided consent for use of their data (for patient details, see **Text box: Patient case summary**).

Patient case summary

Initials: CA

Age: 21

Gender: Male

Operation: Exploration right elbow wounds and repair ulnar nerve

History: Fall onto broken tiles 4 days ago

Findings:

- Multiple ragged wounds over extensor and medial aspect of elbow
- 50% division of ulnar nerve at medial epicondyle with motor to intrinsic bundle and sensory to hand bundle affected
- Multiple ceramic fragments in wound including within ulnar nerve

Discussion

Clinically, outcomes of peripheral nerve injuries have been poor even with the intervention of the most experienced surgeon. While there have been little changes in surgical repair techniques over the past decade, other factors may impact functional loss to a greater extent. Some of these factors include: age, gender, type of trauma, repair time, adjuvant therapy, duration of follow ups and lengths of nerve grafts. However, independent predictors of successful outcomes can be hard to identify conclusively.

Nature and extent of nerve trauma Patient CA explained, *"I fell into some broken tiles four days ago and my elbow was hurt really bad. I couldn't move my arm or my fingers because of the unbearable pain and it was bleeding a lot. Even now, after surgery, I still have pain that keeps me up at night but I am taking Amitriptyline for it. As most university lectures are online, I feel I can manage the pain and I am now able to make a fist. I do occasionally get pins and needles and shooting pain in my ring and long fingers and it affects my ability to type and write."*

The nature and extent of nerve trauma plays an important role in neurological recovery. Typically, a nerve trauma may be categorised into tidy and untidy wounds, whereby tidy wounds (glass, knife and other sharp instruments) contain no devitalised tissue and have a better prognosis than untidy wounds (shrapnel, bullets, contamination).[2] Tidy wounds involve less damage to longer lengths of nerve, requiring less excision and hence recovery is quicker and functional loss is minimal.[2] Untidy wounds can present with loss of nerve vascularisation, especially when axons are inhibited from renewing in areas where trauma has left the distal nerve non-vascularised.[2] Patient CA experienced an untidy wound with penetration of ceramics fragments into his ulnar nerve causing motor deficits to the intrinsic muscles of his hand and sensory loss to his hand bundle. The injury caused a 50% division of the ulnar nerve at the medial epicondyle resulting in these functional losses.

In the case of patient CA, he had weakness in his intrinsic muscles and paraesthesia that improved very slightly postoperatively, along with his ongoing neuropathic pain. This indicates that he had a neurotmesis (**Table 1**). It is crucial that the type of nerve injury is identified as it acts as a strong indicator of prognosis and rehabilitation time.

Table 1. The types of nerve trauma as classified by Seddon (1954)[3] during his World War 2 experiences of nerve injuries.[3-5]

Type of nerve injury	Layers of nerve involved	Is the axon involved?	Symptoms expected
Neuropraxia	Damage to myelin sheath	No	Transient functional loss
Axonotmesis (2nd degree)	Axon severed, myelin degeneration, endoneurium intact	Yes	Complete denervation. Excellent prospect for recovery
Axonotmesis (3rd degree)	Axon division, endoneurial tube discontinuity, perineurium and fascicular bundles preserved	Yes	Complete denervation
Axonotmesis (4th degree)	No axonal continuity, no endoneurial tube continuity, no perineurium and fascicular continuity, epineurium intact	Yes	Complete denervation
Neurotmesis	Entire nerve trunk affected	Yes	Complete functional loss and denervation without surgical intervention

When a TPNI presents proximal to the site of injury, recovery of the nerve and functionality is usually poor. In a study of 2210 gunshot wound patients with peripheral nerve injuries, like CA, poor muscle strength levels (≤M2) preoperatively were found in 86.73% of the 407 ulnar nerve injuries (**Table 2**). Median, tibial and peroneal nerves followed in strength levels respectively.[6] Useful good muscle power recovery (≥M3), postoperatively, was second to last for ulnar nerves (56.76%) following the brachial plexus (49.01%; **Table 2**). Poor sensory levels (≤S2), preoperatively, were second highest for ulnar nerves (94.1%) after radial nerves (94.51%; **Table 3**). Postoperatively, useful good sensory recovery (≥S3) was second to last for ulnar nerves at 64.86% (**Table 3**).[6]

> *Therefore, ulnar nerve injury was associated with poor muscle strength and poor sensation levels pre-operatively, with poor post-operative outcomes for muscle strength and sensation, in comparison to most other nerve injury types.*

Despite the study involving high-velocity and high-level injuries to the ulnar nerve, the findings corroborate the functional outcomes the patient spoke about. Functional recovery depends on regeneration of nerve fibres from the site of the injury to the distal site of innervation. Therefore, a proximal nerve injury at the medial epicondyle for CA will take longer to recuperate with a risk of neuronal necrosis at the site of the injury affecting functional recovery.[7] Although, this is highly dependent on the type of nerve trauma, as a neuropraxia would have resulted in less motor and sensory dysfunction.

Table 2. Muscle strength grading. Adapted grading of muscle strength for peripheral nerve injuries caused by gunshot wounds in adults.[6]

Grade of muscle strength	Description of response elicited
M0	No contraction
M1	Minimal muscle contraction
M2	Perceptible contraction without gravity
M3	Active movement against gravity
M4	Active movement against resistance performing all independent and synergistic movements
M5	Normal strength and complete recovery

Table 3. Sensory grading. Adapted grading of sensory function for peripheral nerve injuries caused by gunshot wounds in adults.[6]

Grade of sensory strength	Description of response elicited
S0	No response to any pressure stimulus
S1	Testing gives hyperesthesia, paraesthesia or pain
S2	Overresponse to sensory stimuli; sensory response slow but can grip adequately
S3	Some overresponse to sensory stimuli; response to touch and pin pressure
S4	Abnormal localised response to sensory stimuli with no overresponse
S5	Normal response to any sensory stimulus in all body fields

Consequently, the type of nerve trauma is an important factor in the recovery of nerves following injury and functional loss can vary according to the extent of the nerve injury, especially if it is an untidy wound involving Wallerian degeneration. From a patient perspective, the extent of the nerve injury can be both alarming and life changing, such as hindering CA in his university studies and daily activities (for patient remarks, see **Text box: Patient comments**). So this is an important consideration for both patients and physicians.

Patient comments

"I was told by the therapists not to play rugby until I recovered and that I would not be able to sense anything on inside of my palm. They said I could get serious injuries if I was not careful and that I have to wait longer until I can feel again. But I am finding that moving my fingers is becoming better day by day."

Age and gender Studies clearly support that younger patients are more likely to have better outcomes and regain functionality following peripheral nerve injury compared to elderly patients.[8,9] In a univariate analysis by He *et al*.,[10] for every increase in age by a year the odds ratio for a good to excellent recovery in sensory functionality following repair was 0.98 (95% CI: 0.96-0.99, P<0.05). The odds ratios for motor recovery was 0.97 (95% CI, 0.96-0.99, P<0.05). Age is therefore an important consideration, especially when evaluating whether a patient may be eligible for surgery and how many potential quality-adjusted life years this would give them.

> *Younger patients may show better outcomes due to shorter axonal lengths, more efficient regenerative abilities and less atrophy following trauma.*

However, other studies allude to the fact that age may be related to declining expression of vascular endothelial growth factors (VEGFs), which are required for axon regeneration.[11] This is central to the fact that endoneurial vasculature is needed for angiogenesis and the outgrowth of axons from the proximal nerve stump.[12] In a patient, such as CA, age may have ameliorated poorer outcomes due to better vascularisation but vascular features may differ from person to person despite age differences. Moreover, encouraging vascularisation in patients older than CA may yield better neurological recovery, particularly if there is ischaemia in the damaged area.

Gender may be a factor that is overlooked following nerve injuries and the lack of studies regarding gender and recovery substantiates this. Univariate analyses following nerve repair of mixed nerve injuries in females versus males showed that the odds ratio was 2.19 (95% CI: 1.06-4.52, P<0.05) for motor recovery and 1.53 (95% CI: 0.82-2.85, P<0.05) for sensory recovery.[10] As suggested from this study,

> *females have better outcomes in terms of functionality (motor and sensory) when compared to their male counterparts*

but this does not warrant a causal link between gender and recovery. Various animal studies have presented different results with regards to how gender may affect recovery making it difficult to come to conclusions. Androgens have been found to play a vital role in axon regeneration, causing the expression of brain-derived neurotrophic factor (BDNF) via different mechanisms in males and females.[13,14] However, the use of hormones to increase recovery of damaged peripheral nerves requires more studies. In addition, expected functional loss may be due to factors that were not considered in the previous studies such as fewer women partaking in labour intensive activities and female engagement with post-operative therapy differing from male engagement.

Therefore, age and gender are pivotal factors in nerve recovery and it is important for a physician to consider these variables in assessing functional loss. In the case of CA, a young 21-year-old male, sensory function remained impaired 3 weeks after surgical intervention and follow ups, but motor function of intrinsic muscles improved considerably (for patient remarks, see **Text box: Patient comments**).

In a clinical setting, knowing the age of the patient may provide a physician with a more informed choice as to what surgical interventions can be used, whereas gender may provide an indication into better postoperative rehabilitation.

All in all, this will reduce expected functional losses and aid recovery.

Time between injury and nerve repair There is a strong link between the time taken to repair a nerve and functional recovery, with various studies supporting this. A study of 242 repairs of radial nerves found that 49% of the repairs that took place within 14 days of the injury achieved a good result, and only 28% of the later repairs had similar results. Good results consisted of proximal muscles having a grade of M5 or M4 (powerful elbow extension) and distal muscles having a grade of M3 (wrist extension against gravity).[2] Furthermore, the same study also showed that when surgery was delayed, good neurological recovery falls to 30% and fails for 42% of patients. Therefore, direct anastomoses of distal nerve stumps or even a stage of repair is required early on to improve prognosis. Leaving the injury for more than 6 months can reduce recovery leading to outstanding neurological deficits.[15] Repairs left for more than 10 months showed no functional recovery postoperatively due to the predominant atrophy of terminal receptors and scarring of distal nerve endings.[16] Given that nerve regeneration takes place at a rate of 1mm/day it is crucial that there is no delay in surgical intervention to ensure good outcomes.[17]

Hence, repair time is a vital factor in the recovery of nerves and so delaying it, particularly after 6 months, will result in significant sensory and motor dysfunction. Even though ulnar nerve repairs tend to have poor outcomes, CA managed to achieve a substantial recovery due to the immediate surgical response. CA's success may lie in the careful management and triaging of his case, which can be used for other patients with more traumatic injuries.

Conclusion This case-based analysis of expected functional loss and factors affecting recovery of peripheral upper limb nerves has shown the gravity that age, gender, type of nerve trauma and repair time can have on prognosis. Patient voice has been incorporated throughout this article, giving first-hand outcomes of patient experiences and providing essential considerations for physicians. It is difficult to maintain homogeneity of results due to the disparity in types of trauma. Furthermore, small samples sizes and a lack of statistical tests and randomised controlled trials may have caused limitations to this article. Overall, expected functional loss and factors affecting peripheral nerve recovery are multifaceted and the need for a meta-analysis of other factors, including those mentioned, is key.

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