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Original Article

Characterization of Spinal Cord Injury Patients for Arm Functional Restoration through Nerve Transfer

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ABSTRACT: ***Introduction:*** Traumatic spinal cord injuries (tSCI) are common, often leaving patients irreparably debilitated. Therefore, novel strategies such as nerve transfers (NT) are needed for mitigating secondary SCI damage and improving function. Although different tSCI NT options exist, little is known about the epidemiological and injury-related aspects of this patient population. Here, we report such characteristics to better identify and understand the number and types of tSCI individuals who may benefit from NTs. ***Materials and Methods:*** Two peripheral nerve experts independently evaluated all adult tSCI individuals < 80 years old admitted with cervical tSCI (C1–T1) between 2005 and 2019 with documented tSCI severity using the ASIA Impairment Scale for suitability for NT (nerve donor with MRC strength ≥ 4/5 and recipient ≤ 2/5). Demographic, traumatic injury, and neurological injury variables were collected and analyzed. ***Results:*** A total of 709 tSCI individuals were identified with 224 (32%) who met the selection criteria for participation based on their tSCI level (C1–T1). Of these, 108 (15% of all tSCIs and 48% of all cervical tSCIs) were deemed to be appropriate NT candidates. Due to recovery, 6 NT candidates initially deem appropriate no longer qualified by their last follow-up. Conversely, 19 individuals not initially considered appropriate then become eligible by their last follow-up. ***Conclusion:*** We found that a large proportion of individuals with cervical tSCI could potentially benefit from NTs. To our knowledge, this is the first study to detail the number of tSCI individuals that may qualify for NT from a large prospective database.

RÉSUMÉ : Caractérisation de patients ayant subi une blessure médullaire en vue du rétablissement fonctionnel des bras par transfert de nerfs. ***Introduction :*** Les blessures médullaires (BM) sont un type fréquent de trauma qui se solde, dans bien des cas, par un état irrémédiable de débilité. Aussi est-il nécessaire de concevoir de toutes nouvelles formes de traitement, telles que le transfert de nerfs (TN), afin d'atténuer les lésions secondaires et d'améliorer le fonctionnement d'organes. Il existe différentes possibilités de TN dans les cas de BM, mais on en connaît peu sur l'épidémiologie de ces blessures et les aspects qui y sont liés dans la population concernée. Il sera donc question, dans l'article, de la caractérisation de ces éléments afin de mieux comprendre le type de personnes susceptible de bénéficier d'un TN après une BM, et de mieux en cerner le nombre. ***Matériel et méthode :*** Deux experts en matière de transfert de nerfs périphériques ont évalué, chacun de leur côté, tous les adultes < 80 ans, ayant subi une BM et hospitalisés entre 2005 et 2019 pour des lésions cervicales (C1–T1), dont le degré de gravité avait été documenté à l'aide de l'échelle ASIA Impairment Scale (AIS) aux fins de détermination de la compatibilité du TN (force selon l'échelle du MRC : donneur : ≥ 4/5; receveur : ≤ 2/5). Des données sur des variables démographiques, les lésions traumatiques et les lésions neurologiques ont été recueillies, puis analysées. ***Résultats :*** Au total, 709 patients ayant subi une BM ont été repérés, dont 224 (32 %) satisfaisaient aux critères de sélection pour participer à l'étude, selon le niveau des lésions (C1–T1). De ce nombre, 108 (15 % des BM toutes confondues; 48 % des BM cervicales) étaient considérés comme de bons sujets au TN. Par contre, 6 candidats initialement jugés admissibles au TM ne répondaient plus aux critères en cours de suivi en raison de leur rétablissement. En revanche, 19 patients non considérés comme de bons candidats au départ sont devenus admissibles en cours de suivi. ***Conclusion :*** D'après les résultats, une bonne proportion de patients ayant subi une BM cervicale pourrait bénéficier d'un TN. À notre connaissance, il s'agit de la première étude sur le nombre de personnes atteintes de BM susceptibles de profiter d'un TN, qui repose sur une imposante base de données prospective.

Keywords: Spinal cord injury; nerve regeneration; neurosurgery; clinical epidemiology

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Introduction

Traumatic cervical spinal cord injuries (tSCIs) are devastating life-altering events that often leave individuals irreparably debilitated. Unfortunately, tSCIs are not uncommon.[1] Moreover, although the proportion of tSCI due to central cord syndrome is increasing given an aging population,[2,3] the majority of tSCIs still occur in younger individuals resulting in high healthcare costs and many living with lifetime disabilities. [4] Despite this, little advancement has been made in the treatment of tSCI. Few therapeutic options exist that help repair the primary spinal cord damage. However, much progress has been made with respect to mitigation of secondary damage in SCIs, as well as restoration of function through secondary procedures such as tendon transfers and nerve transfers (NTs). Although NTs have been in use for the treatment of peripheral nerve injuries, brachial plexus injuries (BPIs) for some time,[5–7] the use of NTs in the setting of SCI,[8,9] has only recently started to become more commonplace.

With approximately half of all tSCIs being cervical in nature and given an aging population,[10] the use of NTs for functional restoration and improvement is only likely to continue to increase. Although previous reports and observational cohort studies[10,11] detail the feasibility and efficacy of NTs in this patient population, few previous studies have examined the number of tetraplegics undergoing upper extremity surgery.[12,13] Of these, none has examined the number of individuals with tSCIs that may be appropriate candidates for NT surgery. Here, we sought to better characterize this patient population by examining the total number of tSCI individuals that would qualify for functional restoration surgery through NTs in Central and Northern Alberta. In addition, we aim to quantify traumatic and neurological injury-related characteristics in order to better delineate the potential volume of individuals with tSCI that may be served, and specific patterns of injury that may benefit from NT surgery.

Methods

All individuals presenting to hospital with an acute tSCI were identified through the use of a prospective SCI patient registry and database (PRAXIS, formerly the Rick Hansen Spinal Cord Injury Registry) since its inception in 2004 to answer research questions and to facilitate best practices.[14] All PRAXIS sites have obtained local research ethics board approval prior to enrolling individuals with tSCI with each site having data-sharing agreements in place. Individuals with tSCI were included if: i) ≥18 years old and ≤80 years old; ii) admitted with tSCI (C1–L1) between 2005 and 2019 with an SCI ranging in severity from an American Spinal Injury Association (ASIA) Impairment Scale (AIS) A-D identified at the time of initial presentation, upon admission to a rehabilitation center, or upon discharge. Individuals with tSCI were excluded if they had a concomitant peripheral nerve injury or traumatic head injury.

These individuals were then further selected based on the level of injury (C1–C8), and on their neurological deficits as documented on their International Standards for the Neurological Classification of Spinal Cord Injury (ISNCSCI) examination.[15] The last available patient ISNCSCI examination upon discharge was used to determine NT candidacy. Two peripheral nerve surgery (PNS) experts independently evaluated each patient for their potential to benefit from NT. Disagreement between the PNS experts was resolved through review of the involved cases. The following patient variables were included: i) demographic variables (age at the time of injury, sex), ii) injury-related variables (mechanism of injury, co-incident peripheral nerve injury or head injury), iii) AOSpine Trauma Classification System for sub-axial cervical spine, primary injury diagnosis and injury location, secondary injury diagnosis and injury location, injury severity score (ISS, ≥25 indicating major trauma in addition to the spine), and iv) neurological injury-related variables (AIS grade, motor neurological level of injury [NLI], sensory NLI). In keeping with previous observational cohort studies,[10] individuals with tSCI were deemed suitable candidates for NT surgery if they fulfilled the following criteria:

- had a cervical tSCI ASIA A-D,
- had ≤2/5 Medical Research Council (MRC) grade motor strength in one of the key muscle groups tested from C5 to C8 as a potential NT recipient
- ≥4/5 MRC grade motor strength in one of the key muscle groups tested from C5 to C8 that could serve as a potential NT donor.

Individuals with tSCI were then subcategorized based on the types of NTs that they were deemed candidates for based on their neurological deficits. NTs that tSCI individuals were considered for included:

- axillary nerve to radial tricipital nerve
- musculocutaneous nerve to anterior interosseous nerve
- supinator branch of radial nerve to posterior interosseous nerve

Statistical Analysis

Patient demographics, trauma-related, and neurological injury-related were summarized using descriptive statistics (mean ± s.e.). Medians and ranges were used to measure ISS and percentages were calculated to measure agreement between evaluators.

Results

A total of 709 tSCI individuals were identified with 224 being selected based on their tSCI level (C1–C8) (see Fig. 1). Motor vehicle collision was the most frequent mechanism (45/108; 42%) followed by fall-related injuries (29/108; 27%). The average ISS was 19.8 (median: 17, range: 4–54). Forty-seven individuals with SCI had an ISS ≥ 25 indicating severe multisystem trauma. The range of tSCI severity included: 54 (50%) individuals with tSCI being AIS A, 17 (16%) AIS B, 34 (31%) AIS C, and 3 (3%) AIS D. The AIS motor level ranged from C4 to C8 with 7 (6%) C4, 40 (37%) C5, 22 (20%) C6 individuals with tSCI, 38 (35%) C7 individuals with tSCI, and 1 (1%) C8 patient. Mechanisms and demographics are summarized in Table 1. After initial review, there was 94% agreement among the PNS reviewers regarding which patients were considered eligible for which specific NT based on nerves donor and recipient availability. The cause of disagreement between the two PNS reviewers in the majority of these cases was due to most individuals with SCI being eligible for multiple NTs in which there was an initial discrepancy in the number of NTs recorded between the two reviewers that these SCI individuals would qualify for. For example, individuals with a C6 level of motor injury were often eligible for axillary nerve to tricipital radial nerve branch transfer, musculocutaneous nerve to anterior interosseus nerve transfer, and supinator radial nerve branch to posterior interosseus nerve transfer. Details of these discordant cases were discussed individually before reaching a final consensus.

From the total sample of 709 individuals with tSCI, 108 (15% of all tSCIs and 48% of all cervical tSCIs) were deemed to be appropriate NT surgery candidates. At last follow-up, six NT

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Table 1: Baseline patient characteristics

Patient characteristic	Value (%)
Age (mean, years)	43
Sex (male)	82 (76)
Mechanism	
Motor vehicle collision	45
Fall	29
Sport-related	23
Blunt assault	4
Other trauma	4
Penetrating assault	2
Unspecified	1
Injury Severity Score (mean)	19.8
ASIA Impairment Score	
A	54 (50)
B	17 (16)
C	34 (31)
AIS Motor Level	
C4	7 (6)
C5	40 (37)
C6	22 (20)
C7	38 (35)
C8	1 (1)

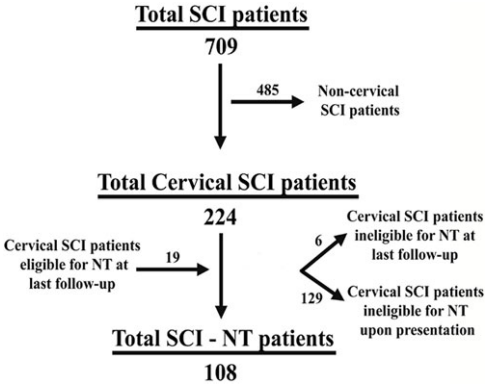

Figure 1: Depiction of the inclusion and exclusion of individuals with traumatic spinal cord injury described in the study.

candidates with tSCI no longer qualified, and 19 individuals with tSCI not initially considered NT candidates became candidates by their last follow-up (Fig. 1). The changes in eligibility were due to SCI recovery with a recipient myotome recovering to at least a MRC 3/5 (and thus being excluded due to longer qualifying for NT) or a donor myotome recovering to at least a MRC 4/5 (and thus being included and qualifying for NT). As shown in Table 1, average patient age was 43 ± 2 years and the majority of individuals with tSCI were male (82/108, 76%).

Of the 108 total individuals with tSCI deemed eligible for NT, 37 (34%) were found to be candidates for unilateral NTs, whereas 71 (66%) were found to be candidates for bilateral NTs. Moreover, eight (7%) were found to potentially benefit from a single NT,

Table 2: Spinal cord injury patient reanimation nerve transfer options

Nerve transfer				
Donor	Recipient	No of patients (%)	Unilatera	Bilateral
AN	RT	78 (72)	30	48
MSC	AIN	84 (78)	27	57
RS	PIN	85 (79)	27	58

AIN=anterior interosseous nerve; AN=axillary nerve; MCN=musculocutaneous; PIN=posterior interosseous nerve; RT=radial tricipitalk; RS=radial supinator.

whereas 100 (93%) were deemed to potentially benefit from multiple NTs. In our dataset, 78 individuals with tSCI were found to be candidates for axillary nerve to radial tricipital nerve transfers (30 unilateral and 48 bilateral), 84 were found to be candidates for musculocutaneous nerve to anterior interosseous nerve transfers (27 unilateral and 57 bilateral), and 85 were found to be candidates for radial supinator branch nerve to posterior interosseous nerve transfers (27 unilateral and 58 bilateral) (see Table 2).

Given that the majority of individuals with tSCI were found to be candidates for multiple NTs, characteristic patterns of NTs were evident for a given motor NLI. More specifically, individuals with tSCI with a motor level C5 were frequently candidates for axillary nerve to radial nerve transfer. Those with a motor level of C6 were frequently candidates for musculocutaneous nerve to anterior interosseous nerve transfer, supinator nerve to posterior interosseous nerve transfer, in addition to the NTs described for the C5 motor level above. For individuals with tSCI with a C7 motor level, the latter C6 motor level NTs described were frequently possible. Patterns are shown in Table 2.

Discussion

Spinal cord injury is of global concern with significant physical, social, and financial implications for individuals with tSCI and their caregivers.[16] Cervical tSCIs disrupt sensory and motor signal conduction to particular muscle groups that significantly affect hand functions.[17] Restoration of hand and arm function can enhance an individual's quality of life and relieve them of their dependance on others for mobility and other activities of daily living.[18] Moreover, a recent study by Javeed, et al. showed that restoration and recovery in select upper extremity muscle groups after SCI is strongly correlated with individuals with tSCI regaining independence.[19] This restoration of upper extremity function in individuals with tSCI can be accomplished through both tendon and/or nerve transfers. Although tendon transfers have been widely used to restore function in tSCI cases,[7,20] there are a number of drawbacks. These include the risk of inadequate tendon tensioning, adhesions, and mechanical failure post-transfer, to name a few.[5]

Compared to tendon transfers, NTs are capable of providing fractionated movements to individual muscles, which is crucial in fine motor control with minimal postoperative immobilization.[10] The goals of NTs in the setting of SCI are two-fold: (1) to restore volitional control to an intact recipient lower motoneuron (LMN) and its target below the NLI by transferring a donor from above the NLI, and/or (2) to rescue an injured LMN recipient undergoing Wallerian degeneration (due to injury to the spinal cord anterior horn cells of the LMN) by transferring an intact donor from above the NLI. Over time, the intact donor nerve will re-innervate its recipient to its neuromuscular target, reestablishing voluntary

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control of the recipient's muscle. In doing so, NTs make use of the peripheral nervous system's ability to regenerate after injury to overcome the disrupted central nervous system. NTs for SCI aim to restore distal upper extremity functions such as elbow extension, grasp, key pinch, and release, which have been associated with post-SCI independence. [10,19] Previous studies have demonstrated successful restoration of elbow extension using teres minor branch of the axillary nerve transfer to the tricipital branch of the radial nerve,[21] improved finger flexion with a brachialis branch of the musculocutaneous nerve transfer to the anterior interosseous nerve, and improved hand grasp/grip strength (MRC ≥3/5) through a supinator branch of the radial nerve transfer to posterior interosseous.[10,22]

Recovery of hand function has been attempted using diverse tendon transfers, with many individuals with tSCI showing considerable improvement.[23] However, due to the heterogeneous nature of SCIs, tendon transfers may not represent the ideal surgical option in all individuals with tSCI[10] as outcomes from some tendon transfers can be unpredictable.[24] On balance, long-term solutions for restoration of upper extremity function will ultimately involve using both tendon and NTs. Indeed, tailored procedures based on patient-specific neurological deficits after SCI, including both nerve and tendon transfers, have recently demonstrated significant improvements in patient function highlighting the role that NTs (with or without tendon transfers) can play in this patient population.[11]

Early NT can promote improved outcomes and earlier recovery in individuals with tetraplegia.[11] However, unlike NTs for BPI in which the goal is to help restore what has been lost based on prioritizing what is likely to be successfully re-innervated, the decision to perform NTs in tSCI is based on the restoration of functions that will help the patient regain independence.[10,19,25,26] Our data shows that a greater number of individuals would have qualified for and potentially benefitted from multiple NTs, potentially resulting in greater recovery of function and thus independence. Of all the individuals with tSCI that were deemed to be eligible for NTs in this study, assuming no down-grading, which has been shown to be a very minor risk in this patient population,[10,27] as many as 72% would be eligible for procedures to improve elbow extension, 40% to improve elbow flexion, 78% to improve finger flexion, 79% to improve hand grasp, and 6% to improve pinch strength.

Although previous studies have detailed the different NT options that exist for individuals with tSCI, this study helped characterize this population from a large prospective database with respect to demographics, injury-related characteristics, and volume of individuals with tSCI that may benefit from NT. This has allowed us to gain insight into the volume of individuals with tSCI that should be screened to prevent under-treatment. Herein, we found that as many as 15% of all tSCIs and 48% of cervical tSCI individuals may be candidates, similar to previous reports.[10,12] Curtin *et.al.* found that while 50% of tetraplegia individuals would benefit from an upper extremity procedure, only 14% of individuals with tSCI actually received a procedure.[12] Although our results may be an overestimation due to individuals with tSCI refusing the procedure, electrodiagnostic findings, or patient attrition, this still represents a significant volume of individuals with tSCI currently being undertreated. Furthermore, it is also likely that so many individuals with cervical tSCI are found to be candidates for NT in this study because of the fact that the NLI typically targeted and shown to benefit from NT (C5, C6, C7) coincides with the most common levels injured (C4, C5, C6).[28] Our data also shows that the majority of candidates are relatively young, healthy males having been in a motor vehicle collision. Previous NT studies have shown improved outcomes in such individuals suggesting this subset of the tSCI population is also likely to benefit most as they possess favorable factors (such as young age and few co-morbidities) that would promote nerve regeneration, and brain plasticity for rehabilitation, among others. Interestingly, epidemiological tSCI studies have shown a bimodal age distribution (early peak due to higher mechanism trauma and later peak due to lower mechanism causing central cord syndrome), which was not shown here. This is potentially due to the fact that older individuals with SCI presenting with traditional central cord syndrome have more mild deficits and potentially a better natural history than other tSCI individuals resulting in them not qualifying for NT at follow-up.

Upon stratifying individuals with tSCI into specific NT options that they would be eligible for, the majority of this tSCI patients subset were found to be eligible for both bilateral and multiple NTs. This is in keeping with what previous cohort studies have demonstrated where bilateral procedures were performed in 33%–87% of the population.[10,11] In this series, greater than 50% of the individuals would be eligible for bilateral procedures independent of level and transfer type. Due to the somatotopic organization of the spinal cord, the function of numerous myotomes originates from within a confined area. As a result, tSCI results in numerous myotomes and thus upper extremity functions being affected. It is therefore not surprising that in this study, the majority of tSCI individuals were found to be candidates for multiple NTs. As experience grows with these techniques, refinements around the NT procedures will lead to guidelines on timing, staging, and optimal set of nerve transfers to be performed.

Although a substantial number of individuals with tSCI are potentially eligible for NTs, the actual number of procedures performed in Canada is relatively low.[13] Furthermore, there are significant regional variations with the surgery being less common in the Prairie and Maritime provinces. Identifying the influencing factors and potential barriers would be of great practical importance.

Limitations

To our knowledge, this is the first study to detail the number of tSCI individuals from a large prospective database who may qualify for NTs in an attempt to restore hand function. That being said, this was a retrospective study of prospectively collected data and as such is prone to specific biases. Although several quality assurance projects have been completed since inception of the database to ensure institutional data fidelity, it is possible that some tSCI individuals were missed, which could bias our results. However, our institution is the only one in the region to which all tSCI individuals are referred. This results in a low risk of ascertainment bias or loss of follow-up.

The NT candidates identified in this study were reviewed independently by two PNS evaluators with a resultant high level of agreement with respect to NT eligibility between them indicating the relatively straightforward nature of patient selection based on clinical criteria. Finally, the lack of electrodiagnostic information for tSCI patient selection for NT also represents a potential drawback to our study as the availability of a sufficient number of intact motor axons in the donor's nerve is of crucial importance in determining the success of the NT.[29,30] Electrodiagnostic studies also provide valuable information to guide surgical planning.

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If lower motor neuronal loss is found to be present in the recipient's nerve, nerve transfer needs to be done within 6 months of injury when the distal stump and the target muscles are still receptive to regeneration. Due to the nature of the study, it was not possible to overcome this limitation, which could potentially result in an overestimation of the number of eligible individuals with tSCI.

Conclusion

Although several NT options for upper extremity functional restoration have been previously described, to our knowledge this is the first study to examine the number and characteristics of tSCI individuals who may benefit from NT surgery. Here, we found that a large proportion of individuals with cervical tSCI could potentially benefit from this treatment option and as such that this patient cohort is likely undertreated. Depending on the specific NLI, characteristic patterns of NTs are possible, often bilateral and multiple in nature. Better characterization of the epidemiological and injury patterns of this patient population forms an important first step to increase awareness and inform tSCI NT candidate identification.

Competing interests. None.

Statement of authorship.
AJ – Manuscript preparation, data analysis.
MR- Manuscript preparation.
CW- Manuscript preparation.
MC- Manuscript preparation.
JO- Manuscript preparation.
MM- Manuscript preparation.
LJ - Manuscript preparation.
KMC- Manuscript preparation, data analysis.

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