

Research article

# Outcome of the upper limb in cervical spinal cord injury: Profiles of recovery and insights for clinical studies

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**Background:** Improved appreciation of recovery profiles of sensory and motor function as well as complex motor functions (prehension) after cervical spinal cord injury (SCI) will be essential to inform clinical studies to consider primary and secondary outcome measures for interventions and the optimization of dosing and timing of therapies in acute and chronic SCI.

**Objectives:** (1) To define the sensory, motor, and prehension recovery profiles of the upper limb and hand in acute cervical SCI and (2) to confirm the impact of AIS severity and conversion on upper limb sensorimotor recovery.

**Methods:** An observational longitudinal cohort study consisting of serial testing of 53 patients with acute cervical SCI was conducted. International Standards of Neurological Classification of Spinal Cord Injury, Graded Redefined Assessment of Strength Sensibility and Prehension (GRASSP), Capabilities of Upper Extremity (CUE-Q) Questionnaire, and Spinal Cord Independence Measure III (SCIM-III) were administered at 0–10 days, 1, 3, 6, and 12 months.

**Analysis:** Change over time was plotted using mean and standard deviation of the total and subgroups of the sample.

**Results:** Individuals with traumatic tetraplegia show distinct patterns of recovery. Factors that distinguish homogeneous subgroups of the sample are: severity of injury (level of injury, completeness) at baseline and conversion from a complete to an incomplete injury.

**Conclusions:** In cervical SCI, clinical recovery can be assessed using standardized measures that distinguish levels of activity and impairment. Specific recovery profiles of the upper limb over the 1-year timecourse provide new insights and opportunity for combined analysis of recovery profiles for different clinical assessment tools of upper limb function which are meaningful to inform the design of study protocols.

**Keywords:** Upper limb, Tetraplegia, Recovery, Outcome measure, Sensorimotor function

## Introduction

Understanding the course of neurological recovery in traumatic cervical spinal cord injury (SCI) is essential for the provision of optimal rehabilitative approaches and the study of new interventions. The diverse neurological presentation of cervical SCI<sup>1–4</sup> produces

challenges in predicting endpoints, dosing of interventions, and designing and executing clinical studies/trials. To understand and define more homogeneous subgroups of SCI existing databases such as the European Multicenter Study of SCI and the Model Systems in the USA have been studied to determine spontaneous recovery profiles.<sup>5,6</sup> Much of this research has been conducted using the International Standards of Neurological Classification of SCI (ISNCSCI) as

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the main outcome measure of study. The American Spinal Injury Association Impairment Scale (AIS) and motor score change have been predominant variables of interest in this work.

It is well documented that despite an injury to the spinal cord the potential for sensory and motor recovery is predictable based on sensorimotor completeness or incompleteness. The prevalence of incomplete injuries is greater and the conversion rates from AIS A to B, C, or D are higher than previously reported.<sup>7</sup> The impact of motor recovery in SCI has been used to predict independence as it relates to scores on the Spinal Cord Independence Measure (SCIM);<sup>8,9</sup> however, the impact of early neurological recovery (0–3 months) and conversion as they relate to upper limb and hand function have yet to be explored. Some work has been done to explore the relationship between ISNCSCI upper extremity motor scores (UEMS) to the self-care subscale of the SCIM, which identifies clinically meaningful change.<sup>10–12</sup> However, the presentation of upper limb recovery with more sensitive assessments, such as: the Graded Redefined Assessment of Strength Sensibility and Prehension (GRASSP) has not been presented to date.

In this observational study, we evaluated the spontaneous change specific to the upper limb in a cohort of individuals with traumatic cervical SCI. We evaluated the sensorimotor impairment and function of the arm and hand by way of the GRASSP Version 1.0,<sup>13</sup> SCIM III, and the Capabilities of Upper Extremity Questionnaire (CUE-Q).<sup>14</sup> The purpose of this work was to document neurological and functional recovery. In the case of this study, recovery refers to the reduction of impairment and improvement in function and independence over time. The work presented in this manuscript is an interim study analysis as these data are a subset of a larger project.

The objectives of this study were (1) to define the sensory, motor, and prehension recovery profiles of the upper limb and hand based on GRASSP parameters and (2) to confirm the impact of AIS conversion on upper limb sensorimotor recovery.

## Methods

A multi-center observational longitudinal study was conducted in Ontario, Canada, which included eight centers. Ethical board approval was attained at all sites; enrollment and follow-up data collection occurred between 2009 and 2013.

Patients were included if they sustained a traumatic cervical SCI and presented with a minimum motor grade of 1 in the C5 myotome on either side, complete

or incomplete. All patients enrolled were AIS A, B, C, or D, between the ages of 16 and 75 and were able to provide informed consent. Patients were excluded if they had any additional cause of upper limb neurological impairment and if there was a moderate-to-severe brain injury present.

Serial testing of study participants was conducted. ISNCSCI and GRASSP-partial were administered at 0–10 days (baseline). ISNCSCI, GRASSP-complete, CUE-Q, and SCIM were administered at 1, 3, 6, and 12 months post-injury. All assessments were performed by physical therapists or occupational therapists who had experience working with individuals with SCI and who were formally trained as GRASSP examiners. All trained examiners attended and participated in standardized study-related training by the lead investigators.

## Measures of change and assessments

All assessments were conducted by occupational and physical therapists; who were trained as examiners, by the primary investigator. All examiners were provided a theoretical and practical 6-hour teaching module regarding study implementation and assessment administration. The outcome measures used in the study were selected based on their use in the field of SCI assessment and/or their established qualities.

The ISNCSCI provides a sensory and motor level based on the most normal caudal spinal cord level represented by the dermatomes and myotomes tested. The ISNCSCI was administered according to the 2003 version.<sup>15,16</sup> Inter-rater reliability of ISNCSCI motor and sensory testing has been confirmed to be above 0.80 where a standardized training has been provided. The ISNCSCI was selected for use in the study to define the sample according to an international classification method and to define the severity of injury for individuals involved in the study.

The SCIM III is a global measure of function specific for individuals with SCI,<sup>17</sup> and was used to define the function and independence of the sample in this study. Inter-rater reliability is above 0.8 when assessed by agreement statistics for most SCIM items, and ICC for the total score is 0.94. Concurrent validity of the SCIM with the Functional Independence Measure used for other populations as well as SCI is 0.79.<sup>18</sup> The SCIM total and self-care subscale (SCIM-SS) were used as comparator scores. The SCIM-SS includes items solely related to the use of the upper limb; therefore, comparisons between the GRASSP subtests are made with the SCIM-SS. Subscales of the SCIM are reliable and useful quantitative representations of the specific constructs of independence in SCI.<sup>17</sup>

The CUE-Q is a 32-item questionnaire developed to assess difficulty in performing certain activities with the upper extremities. Psychometric properties of the CUE-Q have been reported as 0.92 for test-retest reliability, tested by Cronbach's alpha and 0.74 for concurrent validity with the Functional Independence Measure, tested by Pearson correlation coefficient.<sup>14</sup> The CUE-Q was selected as a measure to establish relationships between impairment and self-perceived function.

The GRASSP is an impairment measure specific to the upper limb for individuals with tetraplegia. The psychometric properties of reliability and validity are well established; GRASSP was administered according to the GRASSP Version 1.0, 2008 manual.<sup>13,19</sup> The purpose of using the GRASSP was to define upper limb impairment with a sensitive tool.

### Analysis

Change over a 1-year timecourse was plotted by way of mean and standard deviation at each timepoint for the total sample and subgroups of the sample stratified by AIS classification and conversion. Sensation of the ISNCSCI was calculated with the light touch total of dermatomes C6–C8, with a score range of 0–6. Recovery profiles for the ISNCSCI-UEMS (0–25), ISNCSCI-LT and GRASSP (0–50, 0–24, 0–30) were all plotted. The presence of AIS conversion was used to further group the sample to observe the differences between strength, sensation, and prehension.

## Results

### Sample

A total of 59 study participants were enrolled. Fifty-three individuals had more than one assessment available for inclusion in the analysis. Data available for analysis included 46 sets for baseline assessment, 51 for 1 month, 38 for 3 months, 43 for 6 months, and 38 for 12 months. The mean age of the sample was  $49.6 \pm 15.6$ ; 87% of the sample was male. Of the 53 participants included in the analysis, at baseline 11 were AIS-A, 5 were AIS-B, 16 were AIS-C, and 21 were AIS-D. The analysis consisted mainly of descriptive results. All data for each measure were plotted by mean and standard deviation across the 1-year timecourse. This presentation of the data defines recovery over time, which is the subject of interest in this study. The sample was stratified on the basis of their initial baseline presentation as either motor complete SCI (AB) or motor incomplete (CD) SCI. The figures present the total sample and/or two subgroups (AIS-AB and AIS-CD). The AIS-AB group consists of the

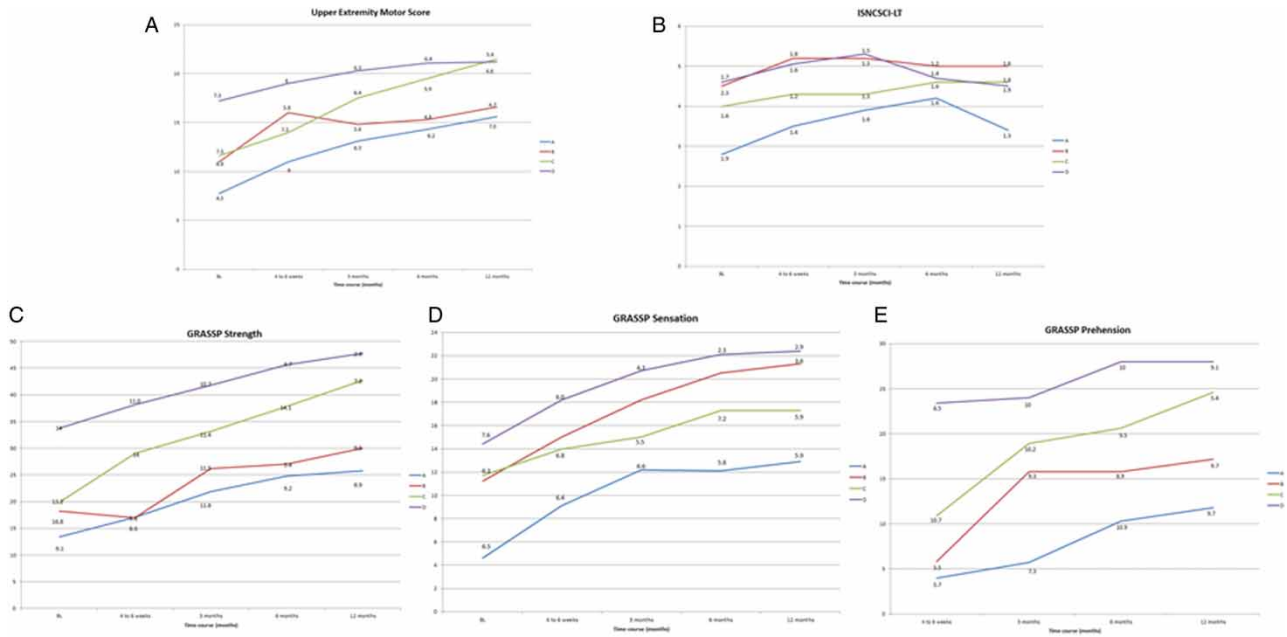
individuals that present as A or B at baseline. The AIS-CD group consists of the individuals that present as C or D at baseline. These two groups are further stratified by conversion. Thus, the AIS-AB-S group consists of the individuals that do not convert over the 1-year timecourse, the AIS-AB-V group consists of the individuals that do convert, the AIS-CD-S group consists of the individuals that do not convert, and the AIS-CD-V group consists of the individuals that do convert. The timing of conversion is not considered in this stratification.

### AIS conversion

The overall conversion rate (AIS) of the sample was 45%. Of the 11 baseline AIS A patients, 3 converted to B, 2 converted to C, and 1 converted to D, 5 remained as A. Of the five baseline B patients, one converted to C and two converted to D, two remained as AIS B. Of the 16 AIS C patients at baseline, 13 converted to D, 3 remained as AIS C. Of the 21 AIS D patients at baseline, all remained stable at D. A total of 22 participants converted AIS grade, 36% of these conversions were assessed at 1 month post-injury, 45% at 3 months post-injury, and 18% at 12 months post-injury. No conversions were assessed at 6 months post-injury. Furthermore, conversion to AIS-C occurred in four participants (two AIS-A, two AIS-B), one of which eventually became an AIS-D. One AIS-A participant, who converted to AIS-C, did not recover any lower extremity muscle strength. The remaining AIS-A and two AIS-B participants all recovered some lower extremity muscle strength that was significant enough to enhance movement and transfers, however, not substantial enough for functional walking.

### Timecourse profiles

All measures administered showed recovery of the upper extremity over the 1-year timecourse post-traumatic tetraplegia, except for the ISNCSCI-LT. Fig. 1 defines the recovery profiles of the sample grouped by baseline AIS grade for UEMS, ISNCSCI-LT, GRASSP strength sensation and prehension. The purpose of this figure is to simply provide a visual representation of the differences in recovery profiles of the four different grades. The subgroups are small and strong conclusions cannot be made from this figure; however, it does provide an opportunity to see the heterogeneity of the sample. The CUE-Q and SCIM were also administered from the 1-month timepoint. Table 1 defines the mean and SD values for SCIM and CUE-Q at each time point measured again with the sample grouped by baseline AIS grade.



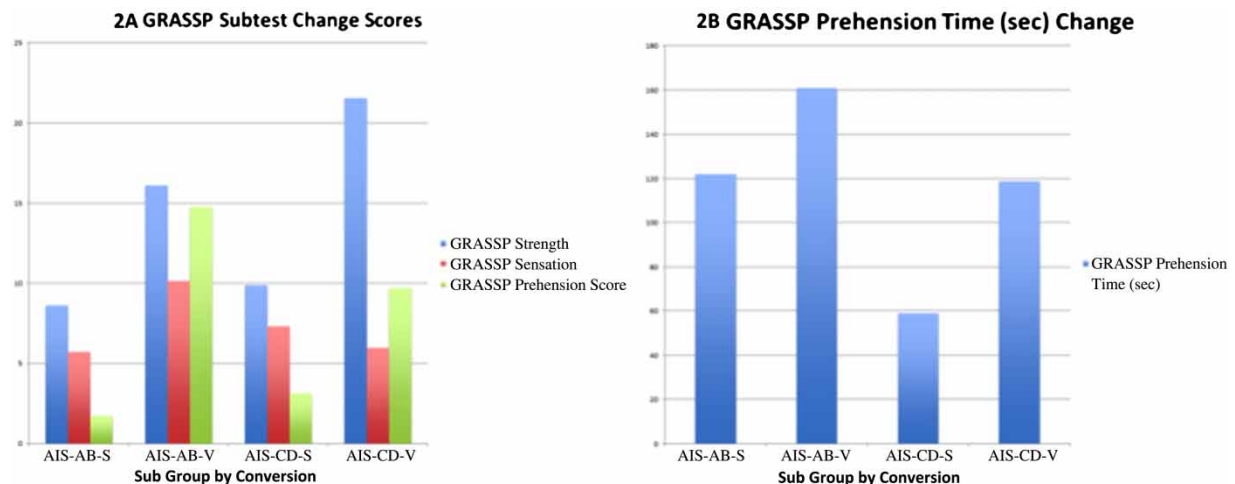
**Figure 1** Recovery profiles stratified by AIS grade. Figures A through D define the mean and SD at each time point across one year for UEMS, ISNCSCI-LT, GRASSP subtests, sub-grouped by AIS grade.

Fig. 2A and B define the cumulative change for the GRASSP subtest scores. The plots are defined according to four groupings (AIS-AB-S, AIS-AB-V, AIS-CD-S, and AIS-CD-V). Of note, the AIS-CD subgroup of the sample that converts consists of Cs that convert only to D. The AIS-CD subgroup of the sample that does not convert consists of Ds that remain as Ds. Fig. 2A and B express the values as total cumulative change in score over the year. The figure outlines the change in mean of each group, which describes the recovery. Changes occurring in the AIS AB-V subgroup show significant improvements in sensation, strength, and prehension; the mean score changes for sensation

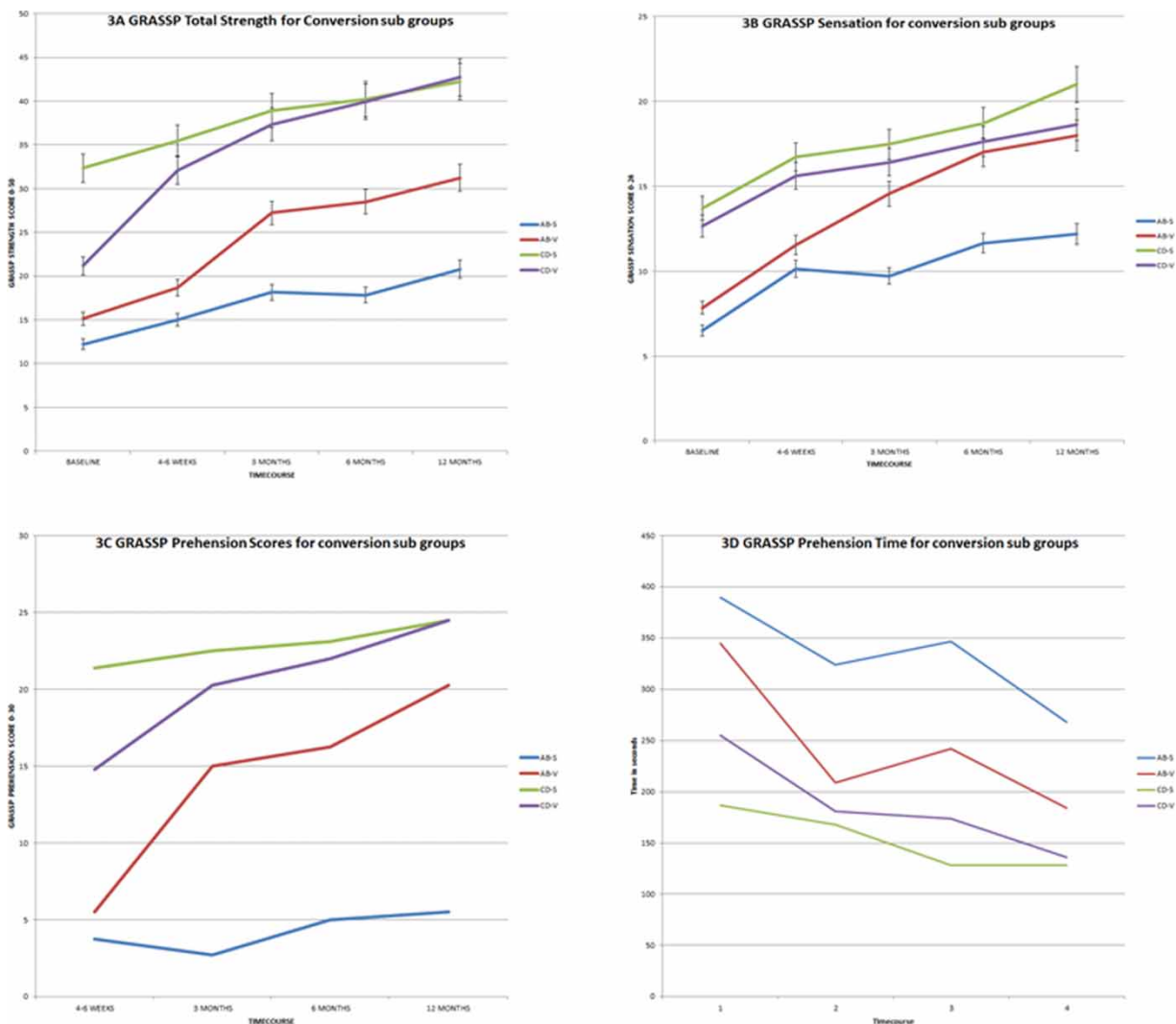
and prehension are greater than any of the other subgroups. Fig. 3 defines the sample by test administered, grouping the sample by the four subgroups (AIS-AB-S, AIS-AB-V, AIS-CD-S, and AIS-CD-V). Distinct recovery profiles for each group can be noted, recovery is influenced by the baseline degree of impairment and the severity of SCI.

### Discussion

The impact of recovering neurological impairment on functional outcomes after cervical SCI is of great interest to the field of SCI researchers, clinicians, and consumers. It is well documented that there is mild-to-



**Figure 2** Change scores of GRASSP subscores over 1 year.



**Figure 3** Recover profiles of GRASSP for conversion stratification.

moderate recovery for most individuals with traumatic tetraplegia.<sup>2</sup> To date there is an understanding of the extent of recovery in the tetraplegia subgroup based mainly on ISNCSCI UEM scores, LEM scores, and AIS grade.<sup>3,4,20</sup> The work presented in this study provides the field with some new preliminary findings that represent recovery according to a more sensitive upper extremity measure. The recovery profiles, although, from a small sample do inform the clinician and researcher of some of the more subtle sensory and motor changes occurring during the 1-year timecourse, which have the potential to inform study/trial design as well as clinical decision-making.

#### *AIS as it relates to upper limb recovery*

Incompleteness of SCI or severity of injury plays a significant role in the endpoint of neurological and functional recovery. The presence of incompleteness and conversion to incomplete injury are one factor that

contributes to the recovery profile and endpoint.<sup>7</sup> In this sample the conversion rate is 45%, 22 individuals in total convert and 18 have converted by the 3-month assessment. Thus, the known impact conversion has on recovery and what constitutes it should be considered when studying the SCI population. By considering conversion as one method to group participants, associations of subtle changes in strength, sensation, and prehension can be seen in these recovery profiles.

With respect to the upper limb AIS A and B subjects that did not convert, they show the least amount of recovery (Fig. 3). Thus, making them the ideal study group for application of interventions directed towards enhancing recovery; making potential large or important score changes observable. Change scores of >5 for GRASSP strength, 2 for GRASSP sensation, and 3 for GRASSP prehension are indicative of true clinical change as these values are the smallest real difference values. Minimally, clinical important change is yet to

be defined by the developers and awaits a large sample size for robust analysis. The AIS A and B groups that convert show the greatest changes across all measures (Fig. 2A). Of interest, sensation has the largest recovery in this group with respect to the hand even greater than strength when the values are normalized. This presentation of recovery would support the concept that sensory improvement is associated with prehension and strength recovery.

The AIS C and D groups that did not convert were entirely comprised of AIS D patients that remained AIS D. This group showed recovery across the 1-year timecourse, however, the magnitude of change was only in the range of 5–10% greater than the magnitude of change occurring in the AIS AB non-converting group (Fig. 2A and B). In essence, the AIS-D endpoint was much higher than the AIS AB non-converting group; however, the magnitude of recovery was not. AIS D patients could potentially be studied with interventions as well if the outcome measures used do not have ceiling effects for the AIS D subgroup. For studies including cervical AIS D patients, measures such as electrical perceptual thresholds,<sup>21</sup> and measures of manual dexterity<sup>22</sup> could be employed to avoid the challenges of a ceiling effect that are inherent in the more conventional measurement techniques used.

The AIS CD group that converted was entirely made up of AIS C patients that converted to D. This group generally started at a lower point than the AIS D patients; showed significant recovery in the first 3 months and then followed a similar recovery profile as the AIS D group. The change scores were greatest for strength, and least for sensation, and the magnitude of recovery when normalized in this group was slightly less than that of the AIS AB converting group (Fig. 2A and B).

### *Recovery of function and independence*

Just as recovery is present in the sample with respect to impairment throughout the 1-year timecourse, self-perceived upper limb function (CUE-Q) and independence (SCIM-SS) also improve (Table 1). Similar to the impairment profiles, the AIS grade does differentiate according to function. Although, the subgroups are small, the functional differences between AIS grade are notable.

### *Strength, sensation, and prehension*

Specific elements of strength are useful in differentiating the four groups (AIS AB non-converting, AIS AB converting, AIS CD non-converting, and AIS CD

converting). These four groups also present with unique recovery profiles when strength, sensation, and prehension are studied (Fig. 3A–C). Sensation and prehension according to the GRASSP assessment also differentiated the four groups. These recovery profiles established from the use of the GRASSP over a 1-year timecourse are useful as they define strength with a greater number of muscles, palmar sensation tested with monofilaments, and task-related prehension performance. Of importance, this is the first time that these elements of hand assessment have been characterized longitudinally in the cervical SCI population. Furthermore, the change scores (Fig. 2) over the 1-year timecourse warrant further investigation for their value in determining clinical endpoints for interventional studies, particularly those engaging individuals with acute traumatic cervical SCI.

### *Limitations of the study*

This work is a presentation of the observational findings of a small SCI sample. It provides some insights into how the upper limb shows recovery over the 1-year timecourse. The data provide information regarding the unique differences in upper limb recovery among subgroups of SCI individuals. Inherent challenges do exist with this interim analysis, mainly due to sample size limitations. Heterogeneity in the cervical SCI population limits successful analysis of the whole sample. Thus, subgrouping is required which creates even smaller groupings for analysis. The total sample size is small for this analysis, therefore, the findings cannot be considered evidence, but rather an initial step in establishing recovery profiles and developing concepts for analysis of the upper limb, once more data are available.

### **Conclusions**

It has been shown over the past 15 years that the SCI population is changing with a greater potential for recovery post-injury. Clinicians and researchers can have the opportunity to exploit this phenomenon by having a strong understanding of the spatiotemporal recovery profile and an outcome tool that has the specificity to assess this recovering subgroup (tetraplegia) of SCI. The observational work done in this study provides some specific insights regarding recovery that have not been reported in the past.

As clinical studies and trials move forward by studying cervical SCI, the informatics and sensitivity of the measures used should be tailored to capturing the distinct recovery occurring as a result of the natural history and new and novel treatment interventions.

**Table 1 Mean and SD for CUE-Q and SCIM-SS scores for AIS grade across the 1-year timecourse**

CUE	4–6 weeks	3 months	6 months	12 months
A	38.6 (16.7)	55.1 (15.7)	64.5 (18.2)	74.5 (15.3)
B	59.4 (27.1)	70 (30.3)	78.7 (32.4)	85.8 (31.0)
C	62.8 (23.3)	81.4 (26.2)	87.5 (24.3)	95.38 (25.6)
D	97.48 (32.3)	100.6 (33.1)	106.5 (31.9)	105.8 (25.9)
SCIM-SS				
A	1.8 (3.7)	3.7 (3.4)	6.2 (4.8)	6.6 (4.9)
B	4.4 (3.2)	9.4 (3.4)	10.5 (6.7)	12.2 (5.8)
C	5.1 (6.2)	9.1 (7.3)	12.3 (7.1)	14.3 (6.4)
D	13.8 (6.4)	16.2 (4.4)	17.7 (2.2)	17.5 (2.9)

CUE-Q, Capabilities of Upper Extremity Questionnaire; SCIM-SS, Spinal Cord Independence Measure Self-Care Subscore.

This prospective approach to documenting detailed changes in important outcomes serves as an initial step in elucidating upper limb recovery in traumatic tetraplegia and establishing endpoints that may be useful for future clinical studies and trials.

### Acknowledgments

The investigative team would like to acknowledge Dr Henry Ahn, Dr Christopher Bailey, Dr Brian Drew, Dr Dalton Wolfe, Heather Askes, Jean Brown, Kathy Butler, Naaz Desai, Deborah Tsui, Kayee Tung, Jennifer Urquhart, and Vera Zivanovic for their commitment to this study.

### Disclaimer statements

**Contributors** SK-R – design, implementation, analysis, and synthesis of manuscript. DB – study design, analysis. AC and MGF – study design and study support. MCV – study design, implementation, analysis, and synthesis of manuscript.

**Funding** This research was supported by the Rick Hansen Institute, the Ontario Neurotrauma Foundation, and the Physiotherapy Foundation of Canada. The postdoctoral funding for SK-R was provided by the Canadian Institutes of Health Research and the Craig H. Neilsen Foundation.

**Conflicts of interest** None.

**Ethics approval** REB boards from University of Toronto, University Health Network, Toronto Rehab Institute, Hamilton Health Sciences Centre, St Michaels Hospital, and London Health Sciences Centre.

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