Research Article

Factors associated with upper extremity contractures after cervical spinal cord injury: A pilot study

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Objective: To examine the prevalence of joint contractures in the upper limb and association with voluntary strength, innervation status, functional status, and demographics in a convenience sample of individuals with cervical spinal cord injury to inform future prospective studies.

Design: Cross-sectional convenience sampled pilot study.

Setting: Department of Veterans Affairs Research Laboratory.

Participants: Thirty-eight participants with cervical level spinal cord injury.

Interventions: Not applicable.

Main Outcome Measures: Contractures were measured with goniometric passive range of motion. Every joint in the upper extremity was evaluated bilaterally. Muscle strength was measured with manual muscle testing. Innervation status was determined clinically with surface electrical stimulation. Functional independence was measured with the Spinal Cord Independence Measure III (SCIM-III).

Results: Every participant tested had multiple joints with contractures and, on average, participants were unable to achieve the normative values of passive movement in 52% of the joints tested. Contractures were most common in the shoulder and hand. There was a weak negative relationship between percentage of contractures and time post-injury and a moderate positive relationship between percentage of contractures and age. There was a strong negative correlation between SCIM-III score and percentage of contractures.

Conclusions: Joint contractures were noted in over half of the joints tested. These joint contractures were associated with decreased functional ability as measured by the SCIM-III. This highlights the need for detailed evaluation of the arm and hand early after injury as well as continued monitoring of joint characteristics throughout the life course of the individual with tetraplegia.

Keywords: Spinal cord injuries, Contracture, Rehabilitation, Tetraplegia, Upper extremity

Introduction

Spinal cord injury (SCI) is the second leading cause of paralysis, with approximately 1.3 million people living with paralysis due to SCI. Joint contractures, reported to affect as much as 85% of persons with SCI, is a common complication in SCI.¹⁻³ Joint contractures

are an insidious co-morbidity of spinal cord injury that can lead to pain, deformity, loss of function, chronic pain, skin breakdown, sleep disturbance, increased caregiver needs, difficulty with bladder and bowel management, and ultimately contribute to decreased levels of independence and an overall lower quality of life.^{4,5} Furthermore, joint contractures may exclude individuals for eligibility or limit potential functional gains from upper extremity reconstruction surgery such as tendon transfers.⁶ Wrist and hand contractures may exclude individuals from tendon transfer surgeries aimed at restoring pinch and grasp. Elbow and shoulder joint contractures limit reach and

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workspace for the hand limiting function even if grasp is restored through tendon transfer and may exclude individuals from eligibility for tendon transfers to restore elbow extension.⁷⁻⁹

The literature describes multiple factors that may be associated with contractures. Eriks-Hoogland *et al.* prospectively studied patients as they were admitted to active rehabilitation, and subsequently at 3 months into rehabilitation, discharge, and 1 year post-discharge.² They examined passive range-of-motion of the shoulder and related it to demographic and personal characteristics, time-since-injury, spasticity, and pain. Tetraplegia was the cofactor most related to contractures of the shoulder. Other significant factors included shoulder pain, spasticity and time to admit to rehabilitation. Diong *et al.* followed 92 consecutively admitted patients with traumatic or nontraumatic SCI.¹ They assessed passive range of motion (PROM) of the shoulder, elbow, forearm, wrist, hand, hip, knee and ankle within 35 days of injury and used the following pre-selected factors to predict contracture development at 1 year follow up: neurologic status, motor scores (based on the International Standards for the Neurological Classification of Spinal Cord Injury¹⁰ sub-scores ranging from 0–25), spasticity, age, pain, and fractures. They found that contractures were significantly related to increased age, low motor scores, and spasticity. However, while prediction models were statistically significant they lacked sufficient predictive accuracy to be clinically useful. Other studies have noted a relationship between contractures and age, spasticity and lower motor scores.^{4,11-13}

Bryden *et al.* retrospectively reviewed 43 participants with C5 or C6 level chronic SCI.¹⁴ Voluntary muscle strength of the triceps, electrically stimulated muscle strength of the triceps, and PROM of the elbow were measured. A significant relationship was found between denervation of the triceps and elbow flexion contractures, presumably due to imbalances in muscle forces across the elbow when a voluntary biceps opposes a paralyzed, denervated triceps. Despite this relationship, questions still remain as this study retrospectively reviewed patient results. Other potential contributing factors such as spasticity, time since injury, age, and overall functional status were not included.

The aim of the present pilot study was to report the prevalence of varying degrees of joint contractures across all joints of the upper extremity in persons with Tetraplegia within a convenience sample and to examine the association with potentially predictive variables to inform future larger prospective studies.

Methods

Participants

Thirty-eight participants (76 arms) with chronic (>6 months) cervical level SCI (AIS A-D) were recruited from the Louis Stokes Cleveland Veterans Affairs Medical Center and the MetroHealth Medical Center, both in Cleveland Ohio, between November 2012 and January 2014. Participants were recruited from screening all of the annual check-ups for patients with SCI at the Cleveland VA Medical Center and from participants who were seen for evaluation for upper extremity surgeries such as tendon transfers at the MetroHealth Medical Center. All participants provided written informed consent prior to testing. The study was approved by the local institutional review boards of the Louis Stokes Cleveland VA Medical Center and the MetroHealth Medical Center.

Measurements

Subject and injury characteristics

Participant demographics and injury characteristics were recorded at the time of testing. These characteristics included: age, sex, level of injury (International Standards for Neurological Classification of SCI (ISNCSCI) exam), completeness of injury (using the American Spinal Injury Association Impairment Scale (AIS)), and time since injury.¹⁰

Range of Motion (ROM)

Passive ROM of the shoulder, elbow, wrist, and hand were measured in a seated position using standard goniometric techniques.¹⁵ A total of 46 measurements were made in each limb, as outlined in Table 1, and all subjects were evaluated bilaterally. All measurements were made by two experienced trained occupational therapists. The passive movement recorded at each joint was compared to standard normative data for these joints,¹⁵ as summarized in Table 1. Contractures were categorized using a quantitative method based on the qualitative approaches previously described in the literature.¹ The specific categories and definitions are:

1. *No Contracture*: No loss in range of motion.
2. *Mild Contracture*: Loss of up to one-third range.
3. *Moderate Contracture*: Loss of one-third to two-thirds range.
4. *Severe Contracture*: Loss greater than two-thirds range.

Muscle strength

Voluntary muscle strength of the deltoid, biceps, triceps, wrist flexors and extensors, and finger flexors and

Table 1 Normative passive range of motion values and definition of mild, moderate, severe contractures.

Joint		Movement	mild cut-off (norm) ¹	moderate cut-off	severe cut-off ²	Norm Range of Motion ¹⁵
Shoulder		Flexion	180	120	60	240
		Extension	60	40	20	
		Abduction	180	120	60	
		Horizontal Abduction	90	60	30	135
		Horizontal Adduction	45	30	15	
		Internal Rotation	70	47	23	150
		External Rotation	90	60	30	
Elbow		Extension	0	50	100	150
		Flexion	150	100	50	
Forearm		Supination	80	27	-26	160
		Pronation	80	27	-26	
Wrist		Flexion	80	30	-20	150
		Extension	70	20	-30	
		Ulnar Deviation	30	13	-3	
		Radial Deviation	20	3	-13	
Fingers (Index, Long, Ring, Small)	MP	Extension	-45	0	45	135
		Flexion	90	45	0	
	PIP	Extension	0	33	66	100
		Flexion	100	67	34	
	DIP	Extension	0	30	60	90
		Flexion	90	60	30	
Thumb	MP	Extension	0	17	33	50
		Flexion	50	34	17	
	IP	Extension	0	26	54	80
		Flexion	80	54	26	
	CMC	Extension	20	8	-3	35
		Flexion	15	3	-8	
		Abduction	70	47	23	

¹For example: shoulder flexion < 180° and ≥ 120° was defined as a mild contracture; shoulder flexion < 120° and ≥ 60° was defined as a moderate contracture; shoulder flexion < 60° was defined as a severe contracture.

²Negative numbers indicate the degrees lacking to neutral (0°). For example: -26° forearm supination is the same joint position as +26° forearm pronation.

extensors was measured using standard manual muscle testing (MMT) techniques.¹⁶

Innervation status

If a muscle was found to be paralyzed (volitional grade 0) during MMT, further testing was used to determine if the muscle was functionally denervated due to lower motor neuron damage. Electrical stimulation can be used to diagnose lower motor neuron damage in individuals with paralyzed limbs due to SCI.¹⁷⁻¹⁹ This is because muscle contractions elicited by electrical stimulation only occur if there is an intact nerve to the muscle; it takes much larger stimulus pulses than are produced by commercially available muscle stimulators to activate muscle fibers directly.²⁰ We determined functional innervation status with surface stimulation using a battery powered neuromuscular electric stimulation unit, with a maximum output of 100 mA, 300µs and 30 Hz (Empi Focus, Empi, Inc., DJO Global, Vista, CA, USA). Self-adhesive surface electrodes were placed over the muscle belly near the motor points using standard locations.^{16,21,22} A muscle was considered functionally denervated if

electrical stimulation failed to elicit a muscle contraction.

Spinal cord independence measure-III

The SCIM-III is similar in design to the more commonly utilized Functional Independence Measure (FIM), but the SCIM-III has been shown to be more sensitive to the functional changes typical in spinal cord injury (Ackerman *et al.* 2010; Anderson *et al.* 2011; Catz and Itzkovich 2007).²³⁻²⁵ The SCIM-III covers 19 activity of daily living (ADL) tasks, grouped into four areas of function (subscales): Self-Care (scored 0-20), Respiration and Sphincter Management (0-40), Mobility in Room and Toilet (0-10), Mobility Indoors and Outdoors (0-30). Subscales are added resulting in a composite score ranging from 0-100 with 100 referring to full independence. The measure is scored to reflect the participant's ability or level of independence to perform each task. We administered the SCIM-III as an interview where participants were asked to describe their typical performance of activities.²⁶

Table 2 Participant demographics.

Participants (n)	38
Men	35
Women	3
Age (y)	52 (43–62)
Time since injury (y)	10 (6.4–29.4)
Veterans (n)	30
Injury Level (n)	
High Tetraplegia (C1–C4) Motor Complete	12
High Tetraplegia (C1–C4) Motor Incomplete	4
Low Tetraplegia (C5–C8) Motor Complete	17
Low Tetraplegia (C5–C8) Motor Incomplete	5

Statistical analyses

One-way analysis of variance (ANOVA) was used to compare the percentage of contractures across the 92 joints in each participant across ISNCSCI levels: levels C1–4, C5, C6 (AIS A–D) and then differentiated by AIS (A/B and C/D), following up with *post hoc* analysis when appropriate. Pearson's product-moment correlation coefficients were calculated to determine the relationship between the percentage of joint movements with contracture and time post injury, age and SCIM-III score. Finally, one-way Kruskal-Wallis equality-of-populations rank test was used to explore the association between passive elbow extension range of motion and voluntary triceps strength, as well as response to electrical stimulation in participants with paralyzed triceps, using *post hoc* testing where appropriate. For this analysis, we included data from five additional participants who had valid measures of passive elbow extension, voluntary triceps strength and triceps excitation, however, they were excluded from the remaining analyses and overall numbers for the study due to incomplete data such as ISNCSCI or AIS. Significance was set at $P < 0.05$.

Results

Descriptive

Summary of participant characteristics are presented in Table 2. Seventy-six arms in 38 subjects were included in this study. The median age was 52 years (IQR 43–62), and included 35 men and 3 women. The median time since injury was 10 years (IQR 6–29). Neurological level ranged from C1 to C7, and 76% were classified as motor complete (AIS A or B). Because our main recruitment center was a VA Medical Center, our sample included 30 veterans.

Prevalence of contractures within the sample

An average of 91 (out of potential of 92) joint movements were measured in each participant. Participants were unable to achieve the normative values of passive movement in more than half of the joints tested (Median = 52%; IQR 45–58%). The most contracted

participant had contractures in 80% of joints tested. On average, participants were unable to achieve the normative values of passive movement in 52% of the joints tested. The most commonly contracted joint was the shoulder, particularly impacting the ability to be moved into abduction (100%; i.e. no participant could achieve the normative shoulder abduction value of 180°), forward flexion (99%) and horizontal adduction (91%). In the hand joint contractures were most commonly present in the the distal interphalangeal (DIP) joints into flexion (limiting extension) (80–90% of the fingers tested could not achieve normative movement) and the metacarpophalangeal (MP) joints into extension (limiting flexion) (>50%). Additionally, thumb CMC abduction was moderately or severely contracted in 61% of all thumbs tested.

To explore the prevalence of contractures according to injury level, we examined both ISNCSCI neurological and impairment levels. Figure 1 shows the percentage of abnormal joint passive range of motion across participants categorized by ISNCSCI levels C1–4, C5, C6 (AIS A–D) and then differentiated by AIS (A/B and C/D). There is no statistically significant difference in the percentage of joints with contracture across the cervical levels ($P = 0.3731$), (although the ranges are somewhat smaller and the middle 50% of the data are more condensed for individuals with C5 or C6 lesions, but some cervical levels had less representation). This absence of a statistically significant difference persists when including the AIS ($P = 0.1252$), although participants classified with C5–7 incomplete injury show the smallest percentage of joint contractures. Therefore, the prevalence of contractures in our sample is not associated with injury level.

Data were further analyzed to determine if there was an association between the percentage of joint contractures and time post injury. Figure 2 shows the percentage of contractures correlated with time post injury in years, for both any contractures and moderate plus severe contractures. A Pearson product-moment correlation was run to determine the relationship between length of time after injury and the percentage of contractures for each participant. There was a weak negative relationship between time post injury and the percentage of any contractures ($R = -0.3152$, $P = 0.0539$). There was a negligible relationship between time post injury and the percentage of moderate-severe contractures ($R = -0.1477$, $P = 0.3761$). We also investigated the relationship between the percentage of joint contractures and age (Fig. 3). There were moderate positive associations between age and the percentage of any contractures ($R = 0.3213$, $P = 0.0561$) and moderate/severe

Figure 1 Percentage of joint movements with contracture.

Note: The percentage of joint movements with contracture across participants as categorized by neurological level (A) and differentiated by AIS score (B). Median and mean measurements are represented by a line and a symbol, respectively. The box represents data within the 25th to 75th percentiles

contractures ($R=0.3306$, $P=0.0489$). Therefore, while there seems to be little to negligible association between years post injury and the percentage of contractures, there does seem to be a positive association between age and percentage of contractures.

To determine if there was an association between percentage of contractures and functional independence, a

Pearson product-moment correlation was run to determine the relationship between scores on the SCIM-III and the percentage of contractures for participants. The results are shown in Figure 4. There appears to be a statistically significant strong negative association between SCIM-III score and percentage of any contractures ($R=-0.4271$, $P=0.0094$) and moderate/severe

Figure 2 Percentage of contractures and time post injury.

Note: The percentage of joint movements with contracture according to both severity and years post injury. Any contracture ($R=-0.3152$). Moderate + Severe Contractures ($R=-0.1477$).

Figure 3 Percentage of contractures and age.

Note: The percentage of joint movements with contracture according to both severity and participant age. *Any contracture* ($R = 0.3213$). *Moderate + Severe Contractures* ($R = 0.3306$).

contractures ($R = -0.4472$, $P = 0.0062$), indicating that higher percentages of contractures are associated with lower scores on the SCIM-III indicating less independence.

Finally, the data were analyzed to determine the relationship between a specific joint's passive range of motion, the strength of its actuator (muscle) and the innervation status of that muscle if it is weak or paralyzed, following directly from the previous reports by Bryden.¹⁴ Specifically, we examined the relationship between passive elbow extension, voluntary triceps strength and innervation status of weak or paralyzed triceps. Figure 5a shows the passive elbow extension

for three groups of participants: those with grade 4–5 voluntary triceps strength, grade 1–3 voluntary triceps strength and no voluntary triceps strength. For this analysis, we included data from five additional participants who had valid measures of passive elbow extension, voluntary triceps strength and triceps excitation, however, they were excluded from the remaining analyses and overall numbers for the study due to incomplete data such as ISNCSCI or AIS. These five additional participants did not differ in recruitment. They had similar demographics with a median age of 47, and a median time since injury of 15 years. Using Kruskal-Wallis equality-of-populations rank test, there

Figure 4 Percentage of contractures and SCIM-III score.

Note: The percentage of joint movements with contracture according to both severity and SCIM-III score. *Any contracture* ($R = -0.4271$). *Moderate + Severe Contractures* ($R = -0.4472$).

Figure 5a Passive elbow extension and voluntary triceps strength.

Note: Passive elbow extension measurements for 3 groups: paralyzed voluntary triceps (MMT = 0), weak voluntary triceps (MMT = 1–3) and strong triceps (MMT = 4–5). Measurements of 0° indicate full passive elbow extension, whereas measurements of any degree of flexion indicate the minimum angle to which the elbow can be passively extended. Median and mean measurements are represented by a line and a symbol, respectively. The box represents data within the 25th to 75th percentiles. Participants with voluntary triceps had significantly fewer and less severe elbow flexion contractures than participants with paralyzed triceps.

was a significant difference in passive elbow extension across the three different groups by triceps strength ($\chi^2 = 12.89$, $P = 0.0016$). Post-hoc testing reveals significant differences in passive elbow extension between those without voluntary triceps and grade 1–3 strength ($P = 0.0267$), as well as between those without voluntary triceps and grade 4–5 strength ($P = 0.0005$). The

differences between those with grade 1–3 strength and 4–5 strength were not significant ($P = 0.2658$).

Figure 5b comprises only those participants with paralyzed triceps defined as those with a voluntary grade 0 on MMT. This cohort is then subdivided according to the triceps response to electrical stimulation, indicating the status of the lower motor neuron,

Figure 5b Passive elbow extension and triceps innervation status.

Note: Passive elbow extension measurements are shown for participants with paralyzed triceps (voluntary MMT grade 0) according to response to electrical stimulation. Participants were grouped according to the strength of their response to stimulation: no response (grade 0), weak response (1–3) and strong response (4–5). Median and mean measurements are represented by a line and a symbol, respectively. The box represents data within the 25th to 75th percentiles.

as follows: no response (grade 0), weak response (1–3) and strong response (4–5). Using Kruskal-Wallis equality-of-populations rank test, there was not a significant difference in passive elbow extension across the three different groups by triceps innervation status, or triceps stimulation strength ($\chi^2=3.372$, $P=0.1852$).

Discussion

Relationship to injury and participant characteristics

Our results show that none of the participants had normal passive range of motion in either arm and, in fact, most subjects had contractures in approximately half of the joints tested. Our prevalence within our convenience sample (100%) is significantly higher than any previous reports in the literature, which indicates a maximum contracture rate of 85%.¹ A possible reason for this discrepancy may be that every other study only evaluated a subset of the joints, whereas we evaluated every joint movement in each upper extremity, but definitive statements are limited due to convenience sampling. Thus, the prevalence of contractures in SCI has been significantly underreported and, likely, underappreciated.

In this study, we defined a contracture as any joint movement that did not achieve the normative value. Previous studies have utilized various definitions for contractures, generally in a qualitative manner. Given our quantitative definition, it is conceivable that participants only lacked one or two degrees of motion but still met the definition of a contracture. In order to assess this issue, we also defined “moderate” and “severe” contractures and assessed participants with respect to these more significant losses in joint range. Even within the more conservative analysis of only moderate and severe contractures, every participant in our study had at least one contracture that met this definition and, on average, 17% of all joints studied met this more stringent criteria. Ultimately, it would be desirable to classify contractures at each joint based on their functional impact, but such a definition would be difficult to achieve. For example, a loss of only 10 degrees of elbow extension was shown to impair a person with tetraplegia’s ability to lock the elbow for support.²⁷

It is likely that the accumulated loss of even relatively small ranges of motion at multiple joints in the upper extremity has a cumulative effect, which results in overall functional loss. This hypothesis is corroborated by the data shown in Figure 4, indicating a relationship between the percentage of joints with any type of contracture and the individual’s functional performance on the SCIM III. The relationship between contractures and loss of functional performance has been suggested

previously.^{1,2,13} The fact that the loss of passive joint movement is so ubiquitous for every participant argues for the important role of contractures if function is to be restored to this population. Contractures are a contraindication for upper limb reconstructive procedures such as tendon transfers, and must be remediated before function-restoring procedures can be considered. It is likely, therefore, that even if the spinal cord injury could be reversed in this population, they would still not achieve full functional recovery due to the loss of passive range of motion.

The data collected in this study was a cross-sectional snapshot of a cohort of individuals with cervical SCI. Time post-injury varied from six months to 40 years, and shows no obvious association in the prevalence of contractures with time post-injury. In fact, there was a weak negative correlation. This occurs despite the fact that contractures do appear to increase with age, as indicated by our data and that of others.^{1,2} Detailed longitudinal studies are warranted, but it seems likely that, for many individuals with SCI, contractures develop fairly quickly after injury (within six months) and then remain for the lifetime of the individual. In fact, for the five participants in this study who were less than 1.5 years post injury, the prevalence of contractures ranged from 45% to 74% of all joints tested, which may suggest a very rapid loss of range of motion throughout the entire upper extremity.

We identified specific joints with the highest and lowest rate of contractures. Most notably, none of the 76 shoulders we studied could achieve the normative value for shoulder abduction, and almost none could achieve the normative value for shoulder flexion. This may indicate difficulty in making these measurements, particularly while the subject is seated in a wheelchair. However, nearly 50% of the shoulders tested demonstrated moderate to severe contractures in shoulder abduction and shoulder flexion, so these movements are clearly impaired in this population.

Our study found that joint contractures were common in the hand, most commonly present in the DIP joints (90%), MP joints (50%) and thumb CMC (61%). Thumb CMC abduction was moderately or severely contracted in more than half of all thumbs tested. Lack of CMC abduction directly impacts the ability of the subject to position their hands around larger objects, and would be expected to directly impact functional independence. The DIP joints of each finger also had high rates of contractures (~90%), although it is not clear whether loss of range in the DIP joint has a significant functional impact.

Our analysis of passive elbow extension range of motion as a function of voluntary elbow extension

strength yielded significant differences, indicating that individuals with paralyzed or weak voluntary triceps are at greater risk for developing elbow flexion contracture. This matches results from a previous study examining this phenomenon.¹⁴ Bryden and colleagues also reported a statistically significant relationship between elbow flexion contracture and functional denervation (lack of response to electrical stimulation), in paralyzed triceps muscles. Importantly, individuals within this category are unable to voluntarily extend the elbow, nor do they experience involuntary activation of the muscle such as from spasms. Presumably, the cumulative effect of lost voluntary and involuntary muscle activation manifests in reduced joint mobility. Our analysis of triceps functional denervation did not replicate this finding. Despite differences in how the elbow extension range of motion values are distributed in our sample, the median values do not appear to vary significantly across the three groups. This is potentially due to differences in subject populations. The previous study included only subjects with motor complete C5 and C6 tetraplegia, whereas our sample includes individuals with incomplete injury as well. There may be unobserved characteristics of these individuals that are not represented by muscle strength and response to electrical stimulation alone. Further analysis of a larger sample of individuals with incomplete injury may help to better clarify the mechanism between voluntary function, muscle excitability and joint contracture.

Study limitations

Limitations should be noted in the interpretation of these results. First, our sample was a convenience sample disproportionately comprised of male veteran participants from a single geographical region of the United States, limiting generalizability of the results. A second limitation of the study is the cross-sectional design. While such a design is useful in developing an overall view of how this population is affected by contractures, it limits inferences about causation. As with most studies of passive range, there is variability in the measurement techniques and variability between assessors. Ideally, each joint would be examined by multiple independent assessors. A third limitation is that surface electrical stimulation is a measurement of functional denervation, as true denervation determination requires electrodiagnostic testing. A fourth limitation may also be a study bias due to the possibility that individuals developing the most severe contractures after many years post-injury are, in some manner, lost to regular clinical follow-up or are otherwise unavailable for recruitment in our study. It is also

possible that it is the other way around in that those with most severe contractures are who are seen the most. These contradictions deserve further study. A fifth limitation is that we did not examine hypermobility, which may lead to non-functional hand patterns when combined with joint contractures in adjacent joints. Finally, our sample size was limited to 38 subjects and a broader assessment is warranted, without sacrificing the thorough assessment of all joint movements.

Conclusion

Joint contractures were found to be a common problem after cervical level SCI based on our convenience sample of 38 subjects. Joint contractures are negatively correlated to functional ability, as measured by the SCIM III. This pilot study points to the need for larger studies that follow a large group of participants longitudinally are needed to elucidate the contributing factors to joint contractures, including pain and spasticity, so that better preventive interventions can be developed.

The information obtained from this study highlights the need for detailed evaluation of the arm and hand early after injury as well as continued monitoring of joint characteristics throughout the life course of the individual with tetraplegia.

Disclaimer statements

Conflict of interest Authors have no conflicts of interest and no financial interest or benefit has arisen from the direct application of this research.

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