Clinical Predictors of Recovery after Blunt Spinal Cord Trauma: Systematic Review

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Abstract

Several clinical, imaging, and therapeutic factors affecting recovery following spinal cord injury (SCI) have been described. A systematic review of the topic is still lacking. Our primary aim was to systematically review clinical factors that may predict neurological and functional recovery following blunt traumatic SCI in adults. Such work would help guide clinical care and direct future research. Both Medline and Embase (to April 2008) were searched using index terms for various forms of SCI, paraplegia, or quadri/tetraplegia, and functional and neurological recovery. The search was limited to published articles that were in English and included human subjects. Article selection included class I and II evidence, blunt traumatic SCI, injury level above L1-2, baseline assessment within 72 h of injury, use of American Spinal Injury Association (ASIA) scoring system for clinical assessment, and functional and neurological outcome. A total of 1526 and 1912 citations were located from Medline and Embase, respectively. Two surgeons reviewed the titles, abstracts, and full text articles for each database. Ten articles were identified, only one of which was level 1 evidence. Age and gender were identified as two patient-related predictors. While motor and functional recovery decreased with advancing age for complete SCI, there was no correlation considering incomplete ones. Therefore, treatment should not be restructured based on age in incomplete SCI. Among injury-related predictors, severity of SCI was the most significant. Complete injuries correlated with increased mortality and worse neurological and functional outcomes. Other predictors included SCI level, energy transmitted by the injury, and baseline electrophysiological testing.

Key words: American Spinal Injury Association (ASIA); blunt spinal cord injury; Spinal Cord Independence Measure (SCIM); traumatic spinal cord injury

Introduction

THE ABILITY TO PREDICT RECOVERY following spinal cord injury (SCI) is integral to the physician's role in providing the best care and guidance to patients and families during the illness. Recovery prediction helps physicians answer the first questions the patient and family ask regarding ability to walk, control over bowel and bladder, or even independence again. In addition, it is essential for future planning of rehabilitation programs, setting functional goals, and organizing financial requirements, including insurance coverage (Saboe et al., 1997; Scivoletto et al., 2004). Furthermore, it helps to improve medical strategies to achieve the best outcome, plan and de-

sign appropriate research, and test new drugs efficacy (Scivoletto et al., 2004).

For the purpose of this review, we have classified the potential predictors of neurological or functional outcome following SCI into clinical factors, imaging factors, and therapeutic factors. Clinical predictors could be further divided into factors related to the patient and those that are injury related. Table 1 was created based on the Medline search using broad criteria of prediction, outcome, SCI, and recovery.

The primary objective of the current article was to review the clinical factors that may predict neurological and functional outcome following blunt traumatic spinal cord injury in adults.

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TABLE 1. POTENTIAL PREDICTING FACTORS IN SCI PATIENTS

Category	Factors
Patient related	<ol style="list-style-type: none"> 1. Age 2. Sex/gender 3. Race/ethnicity 4. Marital status (for quality of life outcomes) 5. Educational level 6. Pre-existing co-morbidities (e.g., diabetes mellitus, heart disease, mental disorder) 7. Smoking 8. Alcohol 9. Income (for quality of life outcome) 10. Insurance 11. Occupational status
Injury related	<ol style="list-style-type: none"> 1. Level of injury 2. Severity of injury: ASIA (on admission and at 72 h), completeness 3. Time from injury to resuscitation 4. Initial blood pressure 5. Hypoxia 6. Associated injuries 7. GCS 8. Tendon reflex on examination 9. Injury Severity Score 10. Mechanism of injury: MVA, fall 11. Energy associated with the injury 12. Need/dependence on mechanical ventilation 13. WCIB 14. Central cord syndrome clinical pattern 15. Electrophysiological testing
Imaging features on MRI	<ol style="list-style-type: none"> 1. Number of levels involved with edema/signal change 2. Presence of intramedullary hematoma 3. Canal compromise 4. Value of diffusion weighted images
Intervention related	<ol style="list-style-type: none"> 1. Timing between injury and resuscitation 2. Timing of surgical intervention 3. Medications: minocyclin, steroids 4. Stem cells and future research application 5. ICU admission 6. In-hospital complications 7. Post injury pain

Based on Medline search using broad criteria of prediction, outcome, SCI, and any form of recovery.

Methods

Literature search

Computerized search of Medline and Embase databases (1966–2008) using Ovid search engine was performed by two board certified surgeons (an orthopedic surgeon and a neurosurgeon). Both had fellowship training in spine surgery and academic training in epidemiology. A standard format for prognosis was utilized for Medline that has a sensitivity of 90% and a specificity of 80% (Supplementary table 1) (Haynes, 2006). Similar steps were followed in the Embase data search using a standard Embase prognostic format (Supplementary table 2; see online supplementary material at www.liebertonline.com). It was further modified by adding a search for randomized controlled trials (Wilczynski and Haynes, 2005). Only class I and II evidence was included. Both search strategies were reviewed by a librarian who made minimal modifications.

Article selection

Inclusion criteria encompassed class I or II evidence articles that are in English, human studies, published work, spinal

cord injury (level of injury above L1-2), used ASIA classification for their primary method of neurological assessment (to assure uniform patient population), and baseline examination following the injury was from time of admission to the hospital or within 72 h. Exclusion criteria included articles that focused on SCI without radiological abnormality (SCI-WORA), penetrating spinal cord injury, peripheral nervous system injury, pregnancy, pediatric population, studies that focused on specific rehabilitation function (e.g., sexual and erectile dysfunction, urinary bladder dysfunction, diaphragmatic function, spasticity, pain, depression), SCI of non-traumatic etiology (e.g., electricity, burns, ischemia), case reports, and small case series. In addition, articles focusing solely on central cord syndrome were excluded, given the condition's characteristic injury pattern, mechanism, age of predisposition, and prognosis. We believed this syndrome deserved its own systematic review.

Outcome measures

Assessment of outcome of SCI has gone through several refinements during the past several decades. Outcome can be looked at from three different domains: neurological, which

was assessed mainly using the American Spinal Injury Association scale (ASIA); functional for daily living, using the Functional Independence Measure (FIM) or Spinal Cord Independence Measure (SCIM); and overall quality of life as determined by the Short Form-36 (SF-36).

ASIA provides a scoring system to assess the extent of neurological damage. A patient with ASIA A has a complete loss of motor and sensory functions below the level of the injury. ASIA B indicates complete motor injury but intact sensory function at S4-5 level. ASIA C has some motor function below the level of the injury with strength of more than half of the key muscles being <3 . ASIA D is similar to grade C but the strength of more than half of the key muscles below the level of the injury are ≥ 3 . ASIA E patients have normal motor and sensory examinations (Fawcett et al., 2007). The initial neurological exam, as assessed by ASIA scoring system, is considered key in deciding the management and predictor prognosis of motor recovery (Brown et al., 1991; Clinical assessment, 2002; Fawcett et al., 2007; Miyanji et al., 2007; Waters et al., 1998). ASIA was also found to predict function in the rehabilitation period, more so in quadriplegic than in paraplegic patients (Clinical assessment, 2002; Lazar et al., 1989). It also correlated with walking ability as tested from the biomechanical aspects of walking to predict ambulation (Clinical assessment, 2002; Waters et al., 1994). The motor assessment was considered more reliable than the sensory component in correlating with functional outcome (Steeves et al., 2007). The timing of an acceptable baseline ASIA score is estimated to be within the first 72 h, given the often associated multiple co-morbidities that could take place at the time of the initial assessment (Brown et al., 1991; Fawcett et al., 2007).

Functional Independence Measure tests the burden of care for a disabled person to effectively perform basic activities of life, such as eating, bathing, ability to transfer, and self-care (Cohen and Marino, 2000). It consists of cognitive and motor subscales (5 and 13, respectively). Each item is scored from 1 to 7, depending on the level of required help in basic daily life activities. Independent function is given a score of 6 or 7 and dependent function is assigned a lower score. FIM was found to have a high internal consistency, discriminative ability, and a good interobserver reliability among trained rehabilitation clinicians (Clinical assessment, 2002; Dodds et al., 1993; Hamilton et al., 1994). It is the standard measure for functional assessment in most rehabilitation programs concerned with disabled persons (Clinical assessment, 2002; Cohen and Marino, 2000). Furthermore, FIM was suggested by both the guidelines of acute spinal cord injury management (Clinical assessment, 2002) and the guidelines for conducting clinical trials in SCI by the International Campaign for Cures of SCI Paralysis panel (ICCP) in their recent recommendations (Steeves et al., 2007).

Spinal Cord Independence Measure was developed specifically to assess the function of SCI patients (Itzkovich et al., 2002, 2007; Steeves et al., 2007; van Hedel and Curt, 2006) with good reliability and validity when tested in an international multi-center trial (Itzkovich et al., 2007). Its three basic components—self care, respiration and sphincter management, and mobility—are of prime importance to the patient's function (Itzkovich et al., 2007).

Predictors presented in the current review were level 1 or 2 evidence and met our inclusion criteria.

Results

A total of 1526 and 1912 citations were located from both Medline and Embase, respectively. Each database was reviewed separately by two board certified neurosurgeons with a fellowship in spinal surgery. The review involved titles, abstracts, and full text for selected articles. Any disagreement was resolved through discussion. A total of 10 articles addressing clinical predictors and satisfying our inclusion criteria were included.

Patient-related predictors

Age. Three articles meeting our inclusion criteria examined the relationship between age and outcome from SCI (Table 2). Fisher and colleagues (2005) studied the outcome of 70 ASIA A tetraplegic and paraplegic patients to determine the pattern of their motor recovery. In a secondary analysis, they found a non-significant trend ($p = 0.052$) toward lesser rates of motor recovery in individuals 24 years or older with complete tetraplegia. A retrospective review by van Hedel and Curt (2006) looked at the influence of segmental recovery on the clinical outcome. They found that functional outcome, as measured by SCIM, decreased significantly with increasing age in 98 motor complete (ASIA A and B) paraplegic and tetraplegic patients.

On the other hand, age was not found to be a significant predictor of marked recovery (MR) in a retrospective analysis of data from the multi-center prospective trial of Gm-1 (Coleman and Geisler, 2004). MR was defined as a 2 point improvement from baseline ASIA Impairment Scale (AIS) to Modified Benzel Scale at the 26th week. It was used as the outcome measure because it was thought to reflect more meaningful clinical recovery for the patient and family (Coleman and Geisler, 2004).

Gender. Gender was not found to correlate with motor recovery in patients with complete tetraplegia in the retrospective review by Fisher and colleagues (2005). A study by McKinley and colleagues (2003) compared early surgical intervention, late surgery, and no surgery following SCI. There was no difference between the three groups regarding AIS grade, neurological level, or FIM motor efficiency score. Their early surgical group (within 72 h) included more women in addition to more paraplegics, and more motor vehicle accidents. In our review, there was no class I or II study that matched our inclusion criteria that specifically looked at gender for prediction of neurologic and functional recovery following SCI.

Discussion. Increasing age may affect an individual and may contribute to one's response to various conditions. In our review, level 2 evidence studies showed decreasing neurological and functional outcome with advancing age in patients with complete SCI (Fisher et al., 2005; van Hedel and Curt, 2006). When incomplete injuries were included, age was not found to be a significant predictor (Coleman and Geisler, 2004). However, this finding may be inaccurate given the possible inclusion of central cord patients as a form of incomplete injury, which was separately found to correlate with outcome ($p = 0.001$) (Coleman and Geisler, 2004). We excluded studies that looked primarily at central cord, given their characteristic age association, mechanism of injury, and

TABLE 2. ARTICLES CONCERNED WITH PATIENT-RELATED PREDICTORS IN SPINAL CORD INJURY

<i>Reference, country, score, research design, total sample size</i>	<i>Method</i>	<i>Outcome</i>
van Hedel and Curt, 2006 Switzerland and Canada Retrospective cohort n = 98 Downs & Black Score = 12	Population: age 38 +/- 16.8 yr (avg.), male 77 pts. ASIA A = 78 and B = 20 (motor complete). Tetraplegics = 39, paraplegics = 54. Treatment: N/A (observational) Outcome measures: ASIA and SCIM	<ol style="list-style-type: none"> 1. For each segment in tetraplegic pts, there was 9 point difference on ASIA motor and 4 points on SCIM. This was not found in paraplegics. 2. No significant difference between contributing centers on the outcome. 3. For tetraplegics, there was a high correlation between ASIA motor score and the SCIM-mot ($r = 0.73$, $p < 0.001$). While patients with thoracic lesions showed poor relationship between ASIA motor score and SCIM-tot and SCIM-mot. 4. Both in paraplegic and tetraplegic pts, the functional outcome decreased significantly with increasing age.
Fisher et al., 2005; Canada; Downs & Black; score = 17; retrospective cohort; n = 70	Population: age 31.6 +/- 11.5 years (avg.), male 58, female 12 pts. C0-C7 = 30, T1-T12 = 39, L1-2 = 1. All ASIA A. In tetraplegic pts, average admission ASIA motor score 11.8 (+/- 10.7). In paraplegics, average admission ASIA motor was 49.3 (+/- 2.4). Treatment: N/A (observational) Outcome measures: ASIA, FIM, SF-36	<ol style="list-style-type: none"> 1. Avg. ASIA score at follow-up was 20.1 (+/- 10.8) for tetraplegic pts and 50.6 (+/- 1.7) for paraplegic pts. None of tetraplegic pts recovered motor function in the lower extremities. 2. The energy by which the energy associated with the mechanism of injury was a strong predictor with local recovery. Low-energy injuries were associated with 5.5-fold improvement in functional recovery than high-energy mechanisms. 3. There was a non-significant trend ($p = 0.052$) toward lesser rates of recovery in those 24 years or older. 4. Gender was not found to correlate with motor recovery. 5. Functional recovery using FIM revealed a FIM score of 73 (+/- 21.9) for tetraplegics and 116.3 (+/- 7.8) for paraplegics. 6. FIM score before and after 33 mo (median follow-up) was not different in paraplegics or tetraplegics for PCS or MCS. 7. SF-36 physical component score (PCS) in tetraplegics was 26.2 (+/- 5.4) compared with 29.2 (+/- 8.3) in paraplegics. Mental component score (MCS) was 40.9 (+/- 18) in tetraplegics, 40 (+/- 17.3) in paraplegics.

<p>Coleman and Geisler, 2004; United States; Downs & Black; score = 22; retrospective analysis of RCT data; n = 760</p>	<p>Population: age <30 yr = 367, age ≥30 yr = 393. Total cervical (C) cases = 579 (76.2%), thoracic (T) cases = 181. AIS A = 482 (C = 332, T = 150), AIS B = 131 (C = 113, T = 18), AIS C&D = 147 (C = 134, T = 13). Complete injuries = 63.4%.</p> <p>Treatment: data included came from Sygen SCI RCT</p> <p>Outcome measures: MR defined as increase of at least 2 grades from AIS (at baseline) to modified Benzel scale (at wk 26). Others include changes in ASIA motor, light touch, and pin-prick score.</p>	<p>1. Two factors were dominant in determining MR at wk 8 and 26:</p> <ol style="list-style-type: none"> Injury severity (AIS C&D did better than B, which did better than A). Injury region: cervical did better than thoracic (given less complete pts in the cervical group and cervical complete did better than thoracic complete pts). However, this factor was confounded by the effect of severity of the lesion. <p>2. GM-1 drug effect was significant at wk 8 but not at wk 26.</p> <p>3. Other variables were not significant (spinal surgery, surgical timing, MFSS timing, age, or direct admission to tertiary care).</p> <p>4. Cervical had less AIS A and more AIS B compared to thoracic. Within AIS A, cervical did better. However, B and C&D groups were the same.</p> <p>5. New variable consisting of injury/severity can predict marked recovery and distinguish C+T regions within AIS A, but not AIS B or C/D; also a significant predictor of MR.</p>
<p>McKinley et al., 2004; United States; Downs & Black; score = 16; observational; n = 123</p>	<p>Population: mean age 37.65 (+/- 15.83) years, male 78.8%, white 76.7%, African American 18.1%, Asian 2.9%, other 2.3%. MVC 52.9%, falls 28.2%, sports 9.1%. Tetraplegia: incomplete 32.9%, complete 22.1%. Paraplegia: incomplete 17.8%, complete 27.2%.</p> <p>Treatment: N/A (observational)</p> <p>Outcome measures: ASIA motor index total score, AIS, neurological, motor, and sensory levels, FIM motor score, length of stay, hospital charge, medical complications, re-hospitalizations</p>	<ol style="list-style-type: none"> 1. Early surgical group included more women ($p = 0.05$), paraplegics, and MVC-related injuries. 2. Non-surgical group was significantly older ($p = 0.05$) and included more incomplete injuries. 3. At 1 yr, change in ASIA motor score was more likely in the non-surgical groups compared to the surgical. 4. Late surgical group had more acute care, hospital charges, length of stay, pneumonia, and atelectasis. 5. No difference found in neurological levels, AIS grade, or FIM motor efficiency between groups.

AIS, ASIA Impairment Scale; FIM, Function Independence Measure; MR, marked recovery; pts, patients; RCT, randomized controlled trial; SCIM, Spinal Cord Independence Measure.

outcome. It was thought they should be examined in a dedicated systematic review.

Several other studies in the literature considered age at the time of SCI as one of the predictors for functional outcome during rehabilitation (Cifu et al., 1999; Committee on Trauma, 1999; DeVivo et al., 1990; Krassioukov et al., 2003; Noreau et al., 2000; Pentland et al., 1995). Many of these studies did not meet our selection criteria. Some proposed that younger individuals tend to have greater potential for recovery given better spinal cord plasticity, which diminishes after 65–70 years of age (Tuszynski et al., 2007). Others suggested that accompanying pre-morbid conditions in older patients, such as like diabetes and hypertension, would adversely affect recovery of the injured spinal cord and pose a challenge to the medical management (Tuszynski et al., 2007).

Studies from Virginia Commonwealth University showed a lower functional outcome on FIM for older individuals following SCI (McKinley et al., 2003). Compared to matched controls of younger age, older individuals had lower FIM scores, lower change in FIM scores, and lower efficiency of FIM scores at discharge from rehabilitation (McKinley et al., 2003). Other reports have also found a higher mortality rate following SCI in older patients (18%) compared to that of younger individuals (8%) (Pickett et al., 2006).

In studies of older SCI patients, the length of hospital or rehabilitation admission was found to be longer for paraplegic injuries than for tetraplegic injuries (Cifu et al., 1999; McKinley et al., 2003; Outcomes of early surgical management, 2004). This relationship has not been consistent however in the literature, with some reports showing shorter stays in older individuals (McKinley et al., 2003).

Notions of ageism may affect the management of the older individuals, and many clinicians may not consider older patients appropriate candidates for rehabilitation given perceptions of less favorable recovery (McKinley et al., 2003). Future studies of age and SCI may need to consider separating complete from incomplete injuries and investigating special consideration to central cord injuries.

In our review, gender was not found to correlate with motor recovery in complete tetraplegic patients (Fisher et al., 2005). Other studies have suggested that men may function better at the time of discharge from rehabilitation for a matched level and degree of neurological injury (Sipski et al., 2004). Others have not found any gender differences in neurological (measured by ASIA) or functional (measured by FIM) outcomes after acute rehabilitation for SCI (Greenwald et al., 2001). However, these articles were excluded from our review because they included levels of injury below the spinal cord (low lumbar) or penetrating injuries. Future prospective trials are required to further look at gender in a more uniform sample of traumatic, non-penetrating injuries that excludes levels below the spinal cord.

Several other patient-related predictors were included in the literature (Supplementary table 1) but did not meet our selection criteria. Our exclusion of penetrating injuries also ruled out the available studies analyzing race and ethnicity. We recommend that inclusion criteria should be suitable to the factor studied or the question under review.

Conclusions. There is level 2 evidence that motor recovery (as measured by ASIA) and functional recovery (as mea-

sured by SCIM) decreases with advancing age for complete SCI patients. There is level 2 evidence that age is not a significant predictor when incomplete SCI were included in the analysis. There is level 2 evidence that there is no difference between males and females in local motor recovery for complete tetraplegic SCI patients.

Injury-related predictors

Level of SCI. Neurological recovery was different depending on the level of SCI (Table 3). While cervical injury is more incapacitating than thoracic ones, the rate of recovery within each group was different. In the retrospective analysis of the data from the multicenter trial of GM-1, level of injury was a strong predictor for marked recovery but was confounded by injury severity (Coleman and Geisler, 2004). Their cervical patients did better than did thoracic ones (MR, 37.2% vs. 15.9%, respectively; $p = 0.0001$). This finding was not significant for the incomplete group (AIS ASIA B and combined C and D groups) (Coleman and Geisler, 2004). Although their data were prospectively collected and randomized, there was an uneven recruitment where cervical patients comprised more than three quarters (76.2%) of the patients and two third of the patients were complete (AIS ASIA A, 63.4%), with few thoracic incomplete injuries (Coleman and Geisler, 2004).

Similar findings were reported by Vale and colleagues (1997) in the prospective pilot study of volume expansion and maintenance of blood pressure of SCI patients. Their cervical injury patients had a better neurological outcome compared to the thoracic group at 12 months post-injury (Vale et al., 1997). There was an improvement of at least one Frankel or ASIA grade in 60% of patients with complete cervical injury, and, at 1 year post-injury, 30% regained ability to walk and 20% experienced bladder function return (Vale et al., 1997). On the other hand, only 33% of complete thoracic SCI patients had an improvement of one Frankel or ASIA grade and 10% regained the ability to walk and the return of bladder function (Vale et al., 1997).

van Hedel and Curt (2006) looked at the difference in neurological function per segment of involvement. In their retrospective review of motor complete SCI (ASIA A and B), they described the loss of 9 points on ASIA motor score for one level drop from C6 to C5. This was also reflected on the functional scale where there was a loss of 4 SCIM-total and SCIM-motor score for the same level loss (van Hedel and Curt, 2006). This was less pronounced in the complete paraplegic patients where ASIA score remained at 50 in patients with lesions from T2-T8 and the functional scores for SCIM-total and SCIM-motor did not correlate significantly with the level of injury (van Hedel and Curt, 2006). The correlation between the three categories of SCIM—self-care, mobility, and respiration and sphincter management—was variable depending on the level of complete injury. While tetraplegic injuries showed moderate correlation for self-care ($r = 0.45$, $p = 0.004$) and mobility ($r = 0.43$, $p = 0.006$), the correlation with respiration and sphincter management was poor ($r = 0.15$, $p = 0.36$) (van Hedel and Curt, 2006). For complete thoracic SCI, there was low to absent correlation with all SCIM categories: self-care ($r = -0.01$, $p = 0.48$), mobility ($r = 0.07$, $p = 0.63$), and respiratory and sphincter management ($r = -0.30$, $p = 0.03$) (van Hedel and Curt, 2006). Furthermore, within patients with complete tetraplegia and

TABLE 3. ARTICLES CONCERNED WITH INJURY-RELATED PREDICTORS IN SPINAL CORD INJURY

Reference, country, score, research design, total sample size	Method	Outcome
Vazques et al., 2008; Spain; Downs & Black; score = 10; observational cohort study; n = 173	Population: ASIA A = 39.3%, ASIA B = 15.6%, ASIA C = 29.47, ASIA D = 15.6%. Pts admitted to a spinal cord injury center with traumatic etiology (1995–2000) Treatment: N/A (observational) Outcome measures: ASIA Impairment scale (AIS)	1. Neurological improvement in 35.83%, more in incomplete injury: a. ASIA A = 6%, 94% remained complete, any improvement occurred early, no case reached functional level. b. ASIA B = 63%, 1/3 of ASIA B showed improvement, of whom 33% were functional. c. ASIA C = 76.4%, 76% of ASIA C showed neurological improvement; all were functional. d. All ASIA D were functional. 2. No cases of neurological deterioration recorded. 3. With the exception of two ASIA C pts, all cases were unchanged after 1st year. 4. No statistical difference from 1st to 5th yr after discharge. 14.45 of those who improved did so within 1st year.
Spieess et al., 2008; Spain; Downs & Black; score = 12; observational cohort study; n = 297	Population: age 44 +/–19 yr, mean height 175.1 +/–9.6 cm, male 77.1%. ASIA A = 36.7%, ASIA B-D = 45.1%. AIS not determined in 18.2%. Tetraplegic = 67.3%. Retrospective cohort from EM-SCI (2003–2006). Pts were assessed at 5 stages after injury: 1 = within first 15 d, 2 = 16–40 d, 3 = 70–98 d, 4 = 150–186 days, 5 = 300–400 d. Treatment: N/A (observational) Outcome measures: AIS, tSSEP, ASIA LT, 10 MWT for functional outcome.	1. 60% did not show recordable tSSEP during 1st year after injury. 20% had recordable potentials at assessment stages and improved over time. 2. tSSEP latencies showed improvement over time. 10% potential recovered during 1st year. Remaining cases, potentials inconsistently recordable. 3. All groups had similar neurological and functional improvement. 4. Initial absence of tSSEP is associated with poor neurological and functional outcome in about 75% of pts. In remaining 25%, initially absent tSSEP recovers and is accompanied by favorable neurological and functional outcome.
van Hedel and Curt, 2006; Switzerland and Canada; Downs & Black; score = 12; retrospective cohort; n = 98	Population: age 38 +/–16.8 yr (avg.), male 77 pts. ASIA A = 78, B = 20 (motor complete). Tetraplegics = 39, paraplegics = 54 Treatment: N/A (observational) Outcome measures: ASIA and SCIM	1. For each segment in tetraplegic pt, there was 9 point difference on ASIA-motor and 4 points on SCIM. This was not found in paraplegics. 2. No significant difference between contributing centers on the outcome. 3. For tetraplegics, there was high correlation between ASIA-motor score and SCIM-mot ($r = 0.73$, $p < 0.001$), while pts with thoracic lesions showed poor relationship between ASIA motor score and SCIM-tot and SCIM-mot. 4. In paraplegic and tetraplegic pts, the functional outcome decreased significantly with increasing age.

(Continued)

TABLE 3. (Continued)

Reference, country, score, research design, total sample size	Method	Outcome
Fisher et al., 2005; Canada; Downs & Black; score = 17; retrospective cohort; n = 70	Population: age 31.6 $\pm$ 11.5 yr (avg.), male 58, female 12 pts. C0-C7 = 30, T1-T12 = 39, L1-2 = 1. All ASIA A. In tetraplegic pts, avg. admission, ASIA motor score was 11.8 ($\pm$ 10.7). In paraplegics, avg. admission ASIA motor was 49.3 ($\pm$ 2.4). Treatment: N/A (observational) Outcome measures: ASIA, FIM, SF-36 (PCS, MCS)	<ol style="list-style-type: none"> 1. Average ASIA score at follow-up was 20.1 ($\pm$ 10.8) for tetraplegic pts and 50.6 ($\pm$ 1.7) for paraplegics. No tetraplegic pts recovered motor function in the lower extremities. 2. Energy associated with mechanism of injury was strong predictor with local recovery. Low-energy injuries were associated with 5.5-fold more improvement in functional recovery than high-energy mechanisms. 3. Age was on edge of significance ($p = 0.052$); those ≥ 24 yr were less likely to recover. 4. Gender was not found to correlate with motor recovery. 5. Functional recovery using FIM, 73 ($\pm$ 21.9) in tetraplegics and 116.3 ($\pm$ 7.8) in paraplegics. 6. FIM score before and after 33 mo (median follow-up) was not different in pts for PCS or MCS. 7. SF-36 PCS in tetraplegics was 26.2 ($\pm$ 5.4) compared with 29.2 ($\pm$ 8.3) in paraplegics. MCS score was 40.9 ($\pm$ 18) for tetraplegics and 40 ($\pm$ 17.3) in paraplegics.
Coleman & Geisler, 2004; United States; Downs & Black; score = 22; retrospective analysis of RCT data; n = 760	Population: age < 30 yr = 367, age ≥ 30 yr = 393. Total cervical (C) cases = 579 (76.2%) and thoracic (T) cases = 181. AIS A = 482 (C = 332, T = 150), AIS B = 131 (C = 113, T = 18), AIS C&D = 147 (C = 134, T = 13). Complete injuries = 63.4%. Treatment: data included came from Sygen SCI RCT Outcome measures: MR defined as increase of at least 2 grades from AIS (at baseline) to modified Benzel scale (at wk 26). Others include changes in ASIA motor, light touch, and pin-prick score	<ol style="list-style-type: none"> 1. Two factors were dominant in determining marked recovery at wk 8 and 26: <ol style="list-style-type: none"> a. Injury severity (AIS C&D did better than B, which did better in the cervical group, and cervical complete did better than thoracic complete patients). However, this factor was confounded by the effect of severity of the lesion. 2. GM-1 drug effect was significant at wk 8 but not at wk 26. 3. Other variables were not significant (spinal surgery, surgical timing, MPSS timing, age, or direct admission to tertiary care). 4. Cervical had less AIS A and more AIS B compared to thoracic. Within AIS-A, cervical did better. However, B and C&D groups were the same. 5. New variable consisting of injury/severity can predict MR and distinguish C+T regions within AIS A but not AIS B or C/D. This variable is significant predictor of MR.
McKinley et al., 2004; United States; Down & Black; score = 16; observational; n = 123	Population: mean age 37.65 ($\pm$ 15.83) yr, male 78.8%, white 76.7%, African Americans 18.1%, Asian 2.9%, other 2.3%. MVC 52.9%, falls 28.2%, sports 9.1%. Tetraplegia: incomplete 32.9%, complete 22.1%; paraplegia: incomplete 17.8%, complete 27.2%	<ol style="list-style-type: none"> 1. Early surgical group included more women ($p = 0.05$), pts with paraplegia, and MVC-related injury. 2. Non-surgical group was significantly older ($p = 0.05$) and incomplete. 3. At 1 yr, change in ASIA motor score was more likely in non-surgical groups than in surgical group. 4. Late surgical group had more acute care, hospital charges, length of stay, and pneumonia and atelectasis.

Geisler et al., 2001; United States; PEDro = 9; RCT; n = 760	<p>Treatment: N/A (observational)</p> <p>Outcome measures: ASIA motor index total score, AIS, neurological, motor, and sensory levels, FIM motor score, length of stay, hospital charge, medical complications, re-hospitalizations</p> <p>Population: age <30 yr = 367, age ≥30 yr = 393 yr. Total cervical (C) case s = 579 (76.2%) and thoracic (T) cases = 181. AIS A = 482 (C = 332, T = 150), AIS B = 131 (C = 113, T = 18), AIS C&D = 147 (C = 134, T = 13). Total C = 579, T = 181. Complete injuries = 63.4%; cause: MVA = 411, fall s = 123, water-related = 83, gunshot wounds = 35, other (pedestrian, sport, asault, heavy object) = 108. Gunshot injuries were allowed if they did not penetrate the cord.</p> <p>Treatment: double-blinded study to Sygen, placebo</p> <p>Outcome measures: ASIA and modified Benzel classification (motor and sensory) were performed 4, 8, 16, 26, and 2 wk after injury. MR defined as increase of at least 2 grades from AIS (at baseline) to modified Benzel scale (at wk 26). Others include changes in ASIA motor, light touch, and pin-prick score.</p>	<p>5. No difference found in neurological levels, AIS grade, or FIM motor efficiency between groups.</p>
Geisler et al., 2001; United States; PEDro = 9; RCT; n = 760	<p>Population: age <30 yr = 367, age ≥30 yr = 393 yr. Total cervical (C) case s = 579 (76.2%) and thoracic (T) cases = 181. AIS A = 482 (C = 332, T = 150), AIS B = 131 (C = 113, T = 18), AIS C&D = 147 (C = 134, T = 13). Total C = 579, T = 181. Complete injuries = 63.4%; cause: MVA = 411, fall s = 123, water-related = 83, gunshot wounds = 35, other (pedestrian, sport, asault, heavy object) = 108. Gunshot injuries were allowed if they did not penetrate the cord.</p> <p>Treatment: double-blinded study to Sygen, placebo</p> <p>Outcome measures: ASIA and modified Benzel classification (motor and sensory) were performed 4, 8, 16, 26, and 2 wk after injury. MR defined as increase of at least 2 grades from AIS (at baseline) to modified Benzel scale (at wk 26). Others include changes in ASIA motor, light touch, and pin-prick score.</p>	<ol style="list-style-type: none"> 43 pts died, deaths were greater in complete group (AIS = A), comparing A with B+C+D ($p = 0.017$). MR at 26 wk was better with better AIS score and not different comparing methylprednisone before or after 3 h. Light touch and bladder improved with time. For light touch, improvement was greater in those with better baseline.
Geisler et al., 2001; United States; PEDro = 9; RCT; n = 760	<p>Population: age <30 yr = 367, age ≥30 yr = 393 yr. Total cervical (C) case s = 579 (76.2%) and thoracic (T) cases = 181. AIS A = 482 (C = 332, T = 150), AIS B = 131 (C = 113, T = 18), AIS C&D = 147 (C = 134, T = 13). Total C = 579, T = 181. Complete injuries = 63.4%; cause: MVA = 411, fall s = 123, water-related = 83, gunshot wounds = 35, other (pedestrian, sport, asault, heavy object) = 108. Gunshot injuries were allowed if they did not penetrate the cord.</p> <p>Treatment: double-blinded study to Sygen, placebo</p> <p>Outcome measures: ASIA and modified Benzel classification (motor and sensory) were performed 4, 8, 16, 26, and 2 wk after injury. MR defined as increase of at least 2 grades from AIS (at baseline) to modified Benzel scale (at wk 26). Others include changes in ASIA motor, light touch, and pin-prick score.</p>	<ol style="list-style-type: none"> 43 pts died (18 of 330 in placebo group [5.5%], and 25 of 430 in Sygen arms [5.8%]), difference was not significant. There was no difference between Sygen and placebo at wk 26 (negative result). However, there was significant effect at wk 8. There was a continuous trend toward Sygen in the ASIA (motor and sensory) scores. Less-injured individuals had better benefit from drug. Minimal evidence against Sygen.

(Continued)

TABLE 3. (Continued)

Reference, country, score, research design, total sample size	Method	Outcome
Pointillart et al., 2000; France; PEDro = 8; RCT; n = 106	<p>Population: mean age 25 yr for no medication group, 32 for nimodipine group, 32 for methylprednisolone group, 28 for combined methylprednisolone and nimodipine. Male 90%. Complete spinal cord lesions, 48 pts. MVA 46%, falls 29%, sports accidents (incl. diving) 25%.</p> <p>Treatment: four groups; methylprednisolone, nimodipine, combined, and neither. Early spinal decompression and stabilization was done ASAP in all patients. Doses include: methylprednisolone 30 mg/kg over 1 h, followed by 5.4 mg/kg/h for 23 h. Nimodipine 0.15 mg/kg/h for 2 h followed by 0.03 mg/kg/h for 7 d.</p> <p>Outcome measures: ASIA, AIS, complications, ISS</p>	<ol style="list-style-type: none"> 1. All groups improved neurologically ($p < 0.0001$). 2. No additional neurological benefit from treatment. 3. Methylprednisolone group had more complications. 4. Extent (complete or incomplete) of spinal injury was the only predictor of outcome; early surgery did not make a difference.
Vaccaro et al., 1997; United States; PEDro = 6; RCT; n = 64	<p>Population: early group: avg. age 37.79 yr (15–75 yr), male 24, female 10. Avg. 1.8 days before surgery; avg. motor score on admission, 32.8 (SD 30.5). Avg. motor score on admission to rehab, 38.6 (SD 32.4); on discharge from rehab, 46.2 (SD 33.7); on most recent follow-up, 64 (SD 35.3). LOS in the hospital: 17.7 d, Rehab 51.1 d. Late group: avg. age 39 yr (16–75 yr), male 22, female 6. Avg. 16.8 d before surgery, avg. motor score on admission 28.4 (SD 23). Avg. motor score on admission to rehab, 38.2 (SD 28.4); on discharge from rehab, 50 (SD 31.1); on most recent follow-up, 54.2 (SD 37.4). LOS in the hospital: 18.5 d, rehab 51.5 d</p> <p>Treatment: All pts were immobilized pre-op and received methylprednisolone according to NASCIS II. Pts were randomized to early (<72 h) vs. late (>5 d) surgery, including surgical decompression and/or stabilization.</p> <p>Outcome measures: ASIA, length of ICU stay, length of hospital stay</p>	<ol style="list-style-type: none"> 1. No statistical difference between 2 groups—early vs. late surgery: no significant difference in length of stay, length of inpatient rehab, ASIA grade, or motor score. 2. Late group had more costs (probably due to longer hospital stay).

AIS, ASIA impairment scale; EM-SCL, European Multi-center Study on Human Spinal Cord Injury; FIM, Functional Impairment Measure; ISS, Injury Severity Score; LT, light touch; MCS, mental component score; MR, marked recovery; 10 MWT, 10 m walking test; PCS, physical component score; RCT, randomized controlled trial; SCIM, Spinal Cord Independence Measure; SF-36, Short Form-36; tSSEP, tibial somatosensory evoked potentials.

paraplegia, Fisher and colleagues (2005) did not find a difference in FIM score before and after 33 months median follow-up. However, both groups were significantly different in their FIM score at final follow-up (tetraplegics, 73 ± 21.9 , compared to paraplegics, 116.3 ± 7.8 , $p < 0.0001$) (Fisher et al., 2005).

Severity of SCI. Severity of the injury was considered as the primary predictor for neurological recovery in multiple studies (Coleman and Geisler, 2004; Fisher et al., 2005). In the prospective randomized trial of Sygen in acute SCI, post-hoc analysis showed more patients from the complete SCI group (AIS A, 7.1% vs. AIS B+C+D, 3.2%; $p = 0.017$) among the 43 patients who died in the first year (Geisler et al., 2001).

Better recovery at 26 weeks was noticed with better AIS scores and was not different comparing methylprednisone before or after 3 h (Geisler et al., 2001). Later, a retrospective analysis on the same data showed that complete SCI (AIS A) had the least recovery (12.8%) (Coleman and Geisler, 2004). The best recovery was seen in the motor incomplete group (AIS C and D, 84%), which was significantly different ($p = 0.0001$) compared to the motor complete group (AIS B, 46.6%). When both injury severity and anatomical level were considered in a logistic model, neither the term for level of injury ($p = 0.37$) nor its interaction with severity ($p = 0.33$) was significant (Coleman and Geisler, 2004). Fisher and colleagues' (2005) findings supported the premise of poor recovery of complete SCI as they found none of their complete tetraplegic patients experienced motor recovery in their lower limbs. They defined local recovery as a gain of an additional 1 to 3 motor levels. The change in ASIA motor score for their complete SCI patients from admission to follow-up (avg. 20.1 ± 10.8 months, from 11.9 ± 10.7 to 20.1 ± 10.8) was a reflection of local recovery (Fisher et al., 2005). This local recovery was found for 1 level in 67%, 2 levels in 16%, and 3 levels in 3% (Fisher et al., 2005). In addition, they defined the rate of change in ASIA motor score from baseline as the percent deficit improvement ($PDI = (\text{score at follow-up} - \text{score at admission}) / (\text{maximum score} - \text{baseline}) \times 100$). PDI was significantly higher in complete paraplegics compared to complete tetraplegics ($p < 0.0001$) (Fisher et al., 2005). Strict inclusion criteria were used in their study. They identified patients with spinal shock on presentation (7%) and avoided classifying them as complete injuries. In addition, they differentiated between improvement of one motor level and improvement in the zone of partial preservation (Fisher et al., 2005).

Vazquez and colleagues (2008) performed a retrospective study for 173 blunt traumatic SCI patients with 5-year follow-up. The rate of improvement was least in ASIA A patients; 94% of them remained complete upon discharge and none of them was functional. In contrast, incomplete injury patients experienced better recovery; one third of ASIA B had neurological recovery and 33.3% of them were functional, 76.4% of ASIA C improved neurologically, with all of them functional, and all ASIA D were functional upon discharge (Vazquez et al., 2008). However, no standard functional outcome measure was used in their assessment. Stability of neurological outcome was reached within a year from the time of the injury, and even less for complete injuries (Vazquez et al., 2008).

Similarly, other studies showed that the severity of injury was reflected on the functional performance of the patient. van Hedel and Curt (2006) described a high correlation be-

tween AIS A motor score and SCIM total score ($r = 0.63$, $p < 0.001$) in tetraplegics patients but much lower in paraplegics ($r = 0.26$, $p = 0.06$). In a prospective randomized trial studying the effect of methylprednisone, nimodipine, both medications combined, or none following SCI, injury severity (complete or incomplete) was the only factor that correlated with recovery (Pointillart et al., 2000).

Energy transmitted by the injury. Fisher and colleagues (2005) found that within individuals with complete tetraplegia who improved one level below their original motor level, those who sustained low energy were 5.5 times better in their functional recovery compared to those with high mechanism of energy. Low energy was defined according to the classification of the American College of Surgeons (Committee on Trauma, 1999). No other article falling within the inclusion criteria looked at this predictor.

Electrophysiological testing. Spiess and colleagues (2008) studied the prognostic value of tibial-somatosensory evoked potentials (tSSEP) in 297 patients from the European Multi-center Study on Human Spinal Cord Injury (EM-SCI) between 2003 and 2006. They utilized ASIA light touch (ASIA LT) for neurological assessment and 10 m walking test (10MWT) for functional outcome. Initial absence of tSSEP was associated with a poor neurological and functional outcome in about 75% of patients. In the remaining 25%, initially absent tSSEP recovered and was accompanied by a favorable neurological and functional outcome. However, there were difficulties; 60% did not show any recordable tSSEP throughout the first year after injury, 20% had recordable potentials at all assessment stages and showed improvement over time, and 10% of potentials recovered during the first year. For the remaining cases, potentials were inconsistently recordable. In addition, differences between neurological status and outcome could not be differentiated based on differences in tSSEP latencies (Spiess et al., 2008).

Discussion. Injury severity was the most significant predictor of neurological outcome compared to other variables. Injury region was also significant. The variability in neurological recovery between complete cervical and thoracic injuries could be related to methodological and sample issues, such as recruiting less complete injuries in the cervical group (Coleman and Geisler, 2004). In addition, thoracic injury patients tend to have more associated cardiac and pulmonary injuries with the potential for less blood supply to the injured spinal area due to the watershed phenomenon (Vale et al., 1997). Subsequently, they tend to experience less recovery compared to cervical injury patients (Vale et al., 1997). Therefore, a new variable that combines both region and severity has been suggested for patients with complete injuries (Coleman and Geisler, 2004). This variable was found to be a significant predictor for marked recovery within the complete injury group ($p = 0.0001$) (Coleman and Geisler, 2004).

Other factors may also be related to the measuring instrument. The assessment of motor changes using ASIA in patients with thoracic SCI has limitations. There are no motor segments included in the ASIA score for muscles supplied by the thoracic region. Therefore, while the ASIA score could be 50 for different patients, their functional level could vary significantly (van Hedel and Curt, 2006).

There are multiple additional predictors that are discussed in the literature but did not meet our inclusion criteria, including the presence of multiple associated injuries, hypoxia, hypotension on presentation, and many others. Some of the difficulties providing level 1 or 2 evidence for some of these (especially hypoxia and hypotension) are due to ethical or logistical considerations. Not providing such evidence does not prove that they are not significant or that they are not helpful in managing SCI patients. Most of them make intuitive sense and already constitute the standard of practice in most of the centers treating SCI patients.

Conclusion. There is level 2 evidence that cervical complete SCI had better recovery compared to thoracic complete injuries. This was not significant for incomplete injuries.

There is level 2 evidence that losing a segment in the cervical spinal cord is reflected by a loss of about 9 points on ASIA and 4 points on SCIM. This was not found in thoracic spinal cord injury patients.

There is level 1 evidence that there is more mortality among complete injuries compared to incomplete ones.

There is level 2 evidence that both neurological and functional recovery correlate with the severity of injury, the least recovery being found in complete injuries.

There is level 2 evidence that none of the motor tetraplegics regained motor recovery in the lower limbs.

There is level 2 evidence that stability of neurological outcome was reached within a year from the time of injury.

There is level 2 evidence that low energy mechanism injury was better than high injury by 5.5 times in the functional outcome.

There is level 2 evidence that initial absence of tibial-SSEP is associated with a poor neurological and functional outcome in 75% and a more favorable outcome in 25%; 60% did not have recordable tSSEP.

Author Disclosure Statement

No competing financial interests exist.

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