JOURNAL OF NEUROTRAUMA 35:2554–2560 (November 1, 2018)

DOI: 10.1089/neu.2017.5535

Natural History, Predictors of Outcome, and Effects of Treatment in Thoracic Spinal Cord Injury: A Multi-Center Cohort Study from the North American Clinical Trials Network

Jefferson R. Wilson,[1] Blessing N.R. Jaja,[1,8] Brian K. Kwon,[2] James D. Guest,[3] James S. Harrop,[4] Bizhan Aarabi,[5] Christopher I. Shaffrey,[6] Jetan H. Badhiwala,[8] Elizabeth G. Toups,[7] Robert G. Grossman,[7] and Michael G. Fehlings[8]

Abstract

The course, treatment response, and recovery potential after acute traumatic spinal cord injury (SCI) have been shown to differ depending on the neurological level of injury. There are limited data focused on thoracic-level injuries, however. A cohort of 86 patients from the prospectively maintained North American Clinical Trials Network SCI registry were identified and studied to characterize the patterns of neurological recovery and to determine rates of acute hospital death and pulmonary complications. Regression analyses were used to examine the relationship between timing of surgery and administration of methylprednisolone on neurologic and clinical outcomes. Neurological conversion (≥1 American Spinal Injury Association Impairment Scale [AIS] grade improvement) was poorest for AIS grade A patients; 14.3% converted at last available follow-up (mean eight months). While rates of conversion were more optimistic for AIS-B patients (54.5%) and AIS C injuries (77.8%) at the same time point, none of the AIS grade D patients converted to AIS E. At last available follow-up (mean eight months), the magnitudes of lower motor extremity score (LEMS) change were highest for AIS C injuries (21.9 points), then AIS B (17.7 points), AIS D (16.4 points), and finally AIS A (2.5 points) ($p < 0.05$). Early surgical intervention (<24 h post-injury) was independently associated with an additional seven points in motor recovery and a 60% decreased incidence of pulmonary events ($p < 0.05$). Methylprednisolone administration was not an independent predictor of neurological outcome or pulmonary complications. Evaluation of this cohort obtained from a modern multi-center SCI registry provides an update on the natural history, acute death, and incidence of pulmonary complications after traumatic thoracic SCI. Although small sample size limited the extent of analyses possible, early surgical treatment was associated with significantly larger motor recovery and lower rates of pulmonary complications.

Keywords: complications; methylprednisolone; neurological recovery; North American Clinical Trials Network; thoracic; timing of surgery; traumatic spinal cord injury

Introduction

Globally, approximately half a million persons have a traumatic spinal cord injury (SCI) every year; their lives are altered permanently as a result of the associated physical disability, psychological trauma, and financial burden.[1] Multiple factors have been shown to influence the course, treatment response, and recovery potential, including: patient age, injury severity and level, comorbidities, treatment timing, and quality of care.[2,3] Of note, evaluations of neurological and functional outcome after SCI have been performed predominantly in patients with cervical SCI. Because very few series have focused on thoracic-level injuries, far

[1]Division of Neurosurgery, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada.
[2]Division of Spine Surgery, Vancouver General Hospital, University of British Columbia, Vancouver, British Columbia, Canada.
[3]Division of Neurosurgery, University of Miami, Miami, Florida.
[4]Division of Neurosurgery, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania.
[5]Division of Neurosurgery, Shock Trauma, University of Maryland, Baltimore, Maryland.
[6]Division of Neurosurgery, University of Virginia, Chalottesville, Virginia.
[7]Division of Neurosurgery, Methodist Hospital, Houston, Texas.
[8]Division of Neurosurgery, Toronto Western Hospital, University of Toronto, Toronto, Ontario, Canada.

less is known about the course, treatment response, and recovery potential of this patient group.[4–6]

Thoracic-level injuries account for about 35% of SCI, second in prevalence to cervical SCI.[7] These injuries have distinctive biomechanical and physiological characteristics because of the articulation of the rib cage to the upper thoracic vertebra and the added potential for pulmonary trauma, the relatively tenuous vascular supply of the region causing possibly less recovery potential, and the high energy impact needed for the injury occurrence.[8–10] In recent years, the preponderance of early phase clinical studies investigating the safety and feasibility of novel therapeutic agents have focused on patients with complete thoracic SCI, because of historical evidence suggesting negligible recovery among this patient group.[11–13]

There are few modern nontherapeutic studies, however, evaluating the recovery potential for a thoracic only cohort. Such studies are important to establish a baseline for future comparisons and to assess whether the results of historical series remain true today. Further to this point, because initial studies of novel therapeutics often depend on ''historical control'' data for comparison of neurologic recovery, it is important that such control data reflect recovery in the context of contemporary clinical practice. In addition, many of the studies investigating the impact of treatment variables, such as timing of surgery or acute administration of high dose methylprednisolone, have been performed in heterogeneous samples including all levels of injury or in cervical only samples.[14–18] As a result, there is an unmet need to understand the effects of these treatments in a thoracic only patient sample.

Apart from neurological outcomes, a critical component of SCI management is the prevention and treatment of pulmonary complications. In spite of improvements aimed at reducing their incidence, pulmonary complications still occur in 50% of patients, leading to prolonged hospital stay and higher rates of mortality and morbidity after SCI, and even potentially worse neurological outcome.[19,20] Understanding the incidence and predictors of pulmonary complication development is essential to developing improved strategies to combat their occurrence.

In this study, we investigated short- and long-term neurological recovery, as well as acute death and complications, after thoracic SCI using patient-level data from a large prospective SCI registry. In addition, we investigated the effects of patient characteristics as well as treatment variables—in particular the timing of surgery and acute methylprednisolone administration—on long-term neurological outcome as well as acute inpatient pulmonary complications.

Methods

The North American Clinical Trials Network (NACTN) for SCI is a consortium of 11 university affiliated North American neurosurgery departments dedicated to the study and advancement of care for patients with SCI (see Appendix). Over a 12-year period (2005–2017), adult patients with acute traumatic SCI presenting to one of these centers were enrolled into the NACTN registry after informed consent from the patient/next of kin. All patients are enrolled in NACTN at the time of arrival at acute hospital presentation.

This study included those patients presenting with SCI secondary to a blunt mechanism, a neurological level of injury (NLI) between T1 and L1 with a documented neurological assessment available within the first seven days after injury. Comprehensive patient and injury related details were collected within the NACTN registry, including the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) at acute hospital presentation, age, sex, race, socioeconomic status, and Glasgow Coma Scale (GCS) score. Treatment-related variables include the timing of surgical treatment and administration of methylprednisolone sodium succinate (MPSS). Surgical intervention was defined as ''early'' when performed within 24 h of injury, and ''late'' when performed at or after 24-h post-injury.

In this analysis, the outcomes of interest were the incidence of pulmonary complications, acute inpatient death, and neurological outcome. Neurological outcome was defined in two ways: (1) the change in ISNCSCI motor score from admission to follow-up, and (2) the change in American Spinal Injury Association Impairment Scale (AIS) grade from admission to follow-up. Timing of patient follow-up neurological examination was assessed at: one to three months; three to six months; six to 12 months, and more than 12 months. For the statistical analysis, patient last follow-up assessments were considered in aggregate after the ''last observation carried forward'' approach.

Statistical analysis

Baseline patient characteristics as well as outcomes were described using frequency tables and means with standard deviation as appropriate. Linear regression models were fitted to study the association between patient- and treatment-related variables and motor neurological recovery. Poisson regression analysis was used to investigate the relation between the treatment variables and the incidence of pulmonary complications. Predictor variables were included in multi-variable models if considered clinically important relative to the outcome of interest or if the variable had a p value <0.25 in bivariate analysis. The analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Descriptive analysis

Of the 783 patients enrolled in the NACTN SCI registry, 183 patients had an initial NLI between T1 and L1, with 86 of these patients having neurological examination data available within the first week post-injury and hence meeting eligibility for inclusion in

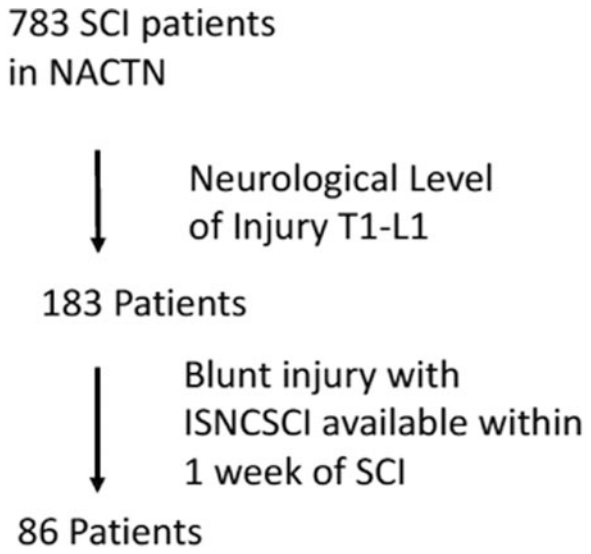

FIG. 1. Flowchart describing cohort derivation. SCI, spinal cord injury; NACTN, North American Clinical Trials Network; ISNCSCI, International Standards for Neurological Classification of Spinal Cord Injury.

Table 1. Characteristics of Patients with Thoracic Spinal Cord Injury

Characteristics	*No. patients (%)*
Sex[a]	
Female	21 (25.6)
Male	61 (74.4)
Age (mean ± SD)	40.4 ± 15.8
Mean GCS score	15
Initial injury severity:	
AIS A	55 (64.0)
AIS B	11 (12.8)
AIS C	13 (15.1)
AIS D	7 (8.1)
Neurological level of Injury:	
T1–4	20 (23.3)
T5–8	18 (20.9)
T9–L1	48 (55.8)
Injury mechanism:	
MVA	40 (46.2)
Fall	30 (35.5)
ATV accident	6 (7.5)
Assault	2 (2.2)
Pedestrian	3 (3.2)
Other	5 (5.4)
NASCIS II MPSS[b]	31 (36.5)
Time to surgical treatment (h)	52.0 ± 74.0
Surgery <24 h post-SCI[c]	25 (36.7)
Discharge disposition	
Inpatient rehab	77 (90.6)
Long-term care	3 (3.4)
Home	3 (3.5)
Other	2 (2.4)
Mean length of stay (days)	18.4 ± 33.8

SD, standard deviation; GCS Glasgow Coma Scale; AIS, American Spinal Injury Association Impairment Scale; MVA, motor vehicle accident; ATV, all terrain vehicle; NASCIS, National Acute Spinal Cord Injury Study; MPSS, methylprednisolone sodium succinate.

Long-term care includes discharge to nursing home.

[a]Value missing for four patients.

[b]Value missing for one patient.

[c]Value missing for 18 patients.

this study (Fig. 1). Table 1 outlines their injury and treatment characteristics. The patients were mostly men (74.4%). The majority (64.0%) had AIS grade A injury with most patients (55.8%) demonstrating a neurological level of injury between T9 and L1. With respect to treatment, 31 (36.5%) patients received MPSS at hospital presentation. The mean time to surgical treatment was 52.0 ± 74.0 h, with 25 (36.7%) patients undergoing surgery within 24 h of injury. The mean length of acute hospital stay was 18.4 ± 33.8 days. During the admission, no patient deaths were recorded.

Tables 2 and 3 show the pattern of neurological recovery across the follow-up time points. There was a decrease over time in the proportion of patients who remained at their baseline AIS grade. The rate of conversion was poorest for those with AIS A injuries, with 10.3% and 23.1% improving at least one grade at three months and greater than 12 months, respectively (overall 14.3% at last follow-up). For AIS B patients, six of 11 (54.5%) improved at least one grade, and two (18.1%) patients deteriorated to become AIS A at last follow-up; at greater than 12 months, 75% of patients improved at least one grade, with one patient converting to AIS E. The majority of patients with AIS C injuries experienced conversion over time, with three (33%) patients improving to AIS D and four (44%) patients improving to AIS grade E at last available follow-up. In contrast, the vast majority of patients with grade D injuries remained at D over time (100% at last available follow-up).

Table 2. American Spinal Injury Association Impairment Scale Conversion and Lower Motor Extremity Score Change within 12 Months Follow-Up

AIS grade at follow-up	*AIS A*	*AIS B*	*AIS C*	*AIS D*	*AIS E*	*LEMS change (%)*
At 1–3 months						
AIS A ($n=29$)	26	2	1	0	0	0.4 (1.9)
AIS B ($n=8$)	1	3	1	3	0	15.5(17.5)
AIS C ($n=5$)	0	0	1	2	2	21.6 (11.6)
AIS D ($n=3$)	0	0	0	2	1	13.5(2.1)
At 3–6 months						
AIS A ($n=25$)	21	1	3	0	0	1.3 (3.2)
AIS B ($n=6$)	1	2	2	1	0	14.8 (16.8)
AIS C ($n=3$)	0	0	0	1	2	27.0 (3.6)
AIS D ($n=3$)	0	0	0	2	1	18.0 (7.1)
At 6–12 months						
AIS A ($n=22$)	18	2	2	0	0	1.5 (3.3)
AIS B ($n=6$)	1	1	2	1	1	22.3 (22.2)
AIS C ($n=8$)	0	0	0	4	4	25.5(6.0)
AIS D ($n=3$)	0	0	0	2	1	24.5(3.5)

AIS, American Spinal Injury Association Impairment Scale.

At last available follow-up (mean eight months), rates of at least a one AIS grade improvement depending on baseline AIS grade were: AIS A,14%; AIS B, 64%; AIS C, 78%; AIS D, 0%. Rates of at least a two AIS grades of improvement were: AIS A, 10%; AIS B, 27%; AIS C, 44%. With respect to motor score improvement, at last available follow-up (mean eight months), the magnitude of LEMS changes was highest for AIS grade B and C patients (17.7 and 21.9 points, respectively), and sequentially less so for AIS D (16.4 points) and AIS A (2.5 points) patients ($p<0.05$).

There were a total of 50 pulmonary complications reported among 27 patients (range: 0–5/patient), making the incidence of

Table 3. American Spinal Injury Association Impairment Scale Conversion and Lower Motor Extremity Score Change at Greater than 12 Months and at Last Available Follow-Up

AIS grade at follow-up	*AIS A*	*AIS B*	*AIS C*	*AIS D*	*AIS E*	*LEMS change (%)*
>12 months						
AIS A ($n=13$)	10	1	1	1	0	5.1 (10.4)
AIS B ($n=4$)	0	1	2	0	1	25.3 (16.6)
AIS C ($n=5$)	0	0	1	1	3	25.4 (9.5)
AIS D ($n=5$)	0	0	0	4	0	19.0 (13.1)
At last follow-up (mean 8 months post SCI)						
AIS A (N=42)	36	2	3	1	0	2.5 (6.5)
AIS B (N=11)	2	3	3	2	1	17.7 (17.6)
AIS C (N=9)	0	0	2	3	4	21.9 (10.3)
AIS D (N=6)	0	0	0	6	0	16.4(9.9)

AIS, American Spinal Injury Association Impairment Scale; LEMS, lower motor extremity score.

pulmonary complications in this cohort 31.4%. Figure 2 shows the distribution of types of pulmonary complications encountered.

Outcome analysis and impact of therapeutic interventions

In a bivariate analysis to evaluate neurologic recovery (Table 4), AIS B, C, and D injuries at final follow-up were associated with an additional 15, 19, and 14 motor points of recovery, respectively, over AIS A injuries ($p < 0.01$ for all comparisons). There was a trend toward poorer motor recovery with T1–4 and T5–8 injuries compared with T9–L1 injuries. MPSS administration in this bivariate analysis was associated with nine fewer points in motor score recovery (PE −8.93, $p < 0.01$), and early surgery was associated with an additional eight points of motor recovery (PE 7.74, $p = 0.06$). Patient age was not significantly associated with motor recovery.

In a subsequent multi-variate analysis of neurologic recovery (Table 5), admission AIS grade remained a significant independent predictor of motor recovery. Early surgical treatment was associated with an additional seven points in motor recovery (PE 7.01, $p = 0.02$); there was no significant association between MPSS administration and motor recovery (PE: −1.90, $p = 0.55$).

In a bivariate analysis to evaluate pulmonary complications (Table 6), midthoracic (IRR 3.55, $p < 0.01$) and upper-thoracic injuries (IRR 2.40, $p = 0.02$) were associated with higher incidence of pulmonary events, compared with lower thoracic injuries. There was a trend toward increased incidence of pulmonary complications in patients who received MPSS (IRR 1.42, $p = 0.22$) and decreased incidence in those who underwent early surgical treatment (IRR 0.41, $p = 0.05$). In the subsequent multi-variate analysis (Table 7), midthoracic (IRR 7.55, $p < 0.01$) and upper-thoracic injuries (IRR 3.54, $p = 0.01$) were associated with a higher incidence of pulmonary events. Early surgical treatment was associated with a decreased incidence (IRR 0.39, $p = 0.05$). We noted a trend toward an increased incidence of pulmonary events with MPSS administration (IRR 1.97, $p = 0.07$).

Discussion

In this study, we employed a large modern prospectively maintained SCI registry to investigate patterns of neurological recovery as well as rates of acute inpatient death and pulmonary complications. We also identified several patient and treatment variables that were associated with neurological recovery and the incidence of pulmonary complications in this cohort. Our data on the course and recovery potential are comparable to the trends seen in more recent prospective series of thoracic SCI, although at variance with the findings of much older series.

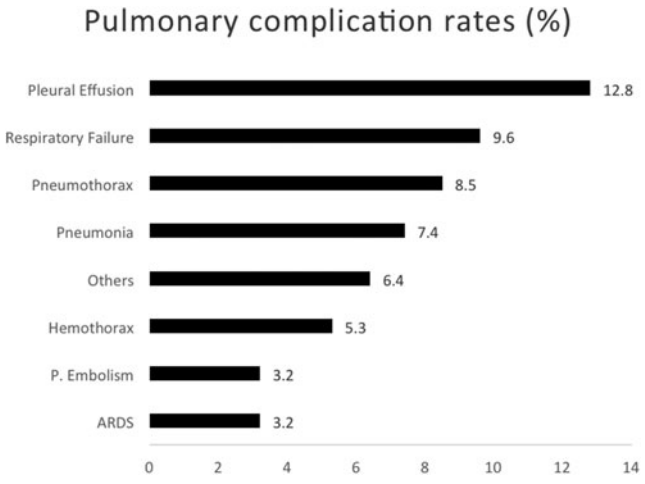

FIG. 2. The number of patients experiencing pulmonary complications and the calculated rate of complication. ARDS, acute respiratory distress syndrome.

TABLE 4. BIVARIATE LINEAR REGRESSION ANALYSIS EVALUATING THE IMPACT OF TREATMENT RELATED VARIABLES ON ASIA MOTOR SCORE RECOVERY

Predictor	*Parameter estimate (95% CI)*	p
AIS grade		
AIS A (ref)	–	
AIS B	15.28 (8.86,21.70)	<0.01
AIS C	19.44 (12.48,26.40)	<0.01
AIS D	13.95 (5.00,22.90)	<0.01
Age	0.01 (−0.19,0.21)	0.94
Neurological level		
T1–4	−3.02 (−10.31,4.27)	0.41
T5–8	−4.67 (−12.27,2.94)	0.23
T9–L1 (ref)	–	–
MPSS administration	−8.93(−15.01,−2.85)	<0.01
Surgery prior to 24 h	7.74 (0.58,14.88)	0.03

CI, confidence interval; AIS, American Spinal Injury Association Impairment Scale; MPSS, methylprednisolone sodium succinate.

In our study, patients with thoracic SCI who had complete injury (AIS grade A) had the poorest prognosis. Most (86%) experienced no change in AIS grade—their injury was still complete at last follow-up (mean eight months post-SCI). A few had a small increase in LEMS. Recovery for this set of patients, however, was superior to rates reported in several previous series but inferior to those reported in other series. In a study using the European Multicenter Spinal Cord Injury database, Zariffa and associates[21] reported approximately 20% of paraplegic thoracic AIS-A SCI improved at least one grade at one year follow-up. In the thoracic cohort from the US SCI model systems (SCIMS), Lee and colleagues[22] noted 15.5% of AIS A patients converted to higher grades, whereas Fawcett and coworkers[23] reported a 12.6% conversion rate when examining thoracic AIS A patients enrolled in the multicenter Sygen study.

A more pessimistic recovery course was noted in a Level-1 trauma center cohort by Harrop and colleagues,[4] who reported only

TABLE 5. MULTIVARIABLE LINEAR REGRESSION ANALYSIS EVALUATING THE IMPACT OF TREATMENT RELATED VARIABLES ON ASIA MOTOR SCORE RECOVERY

Predictor	*Parameter estimate (95% CI)*	p
AIS grade		
AIS A (ref)	–	
AIS B	14.20 (6.66,21.73)	<0.01
AIS C	17.14 (8.24,26.05)	<0.01
AIS D	16.37 (3.90,28.83)	0.01
MPSS administration	−1.90(−8.10,4.28)	0.55
Surgery prior to 24 h	7.01 (1.14,13.03)	0.02

CI, confidence interval; AIS, American Spinal Injury Association Impairment Scale; MPSS, methylprednisolone sodium succinate.

Table 6. Bivariate Poisson Regression Analysis Showing the Impact of Variables on Incidence of Pulmonary Complications

	Parameter est. 95% CI	*IRR*	p-
AIS grade:			
A(ref)	–		
B	−25.51 (−224283,224232.4)	0	1.0
C	−1.69(−3.11,−0.28)	0.18	0.02
D	−1.07 (−2.49,0.34)	0.34	0.14
age	0.01 (−0.01,0.03)	1.01	0.21
Level			
T1-4	0.88 (0.16,1.59)	2.40	0.02
T5-8	1.27 (0.60,1.94)	3.55	<0.01
T9-12 (ref)	–	–	–
MPSS administration			
Yes	0.35 (−0.21,0.91)	1.42	0.22
No(ref)	–		
Surgery prior to 24 h			
Yes	−0.88(−1.78,0.01)	0.41	0.05
No (ref)	–	–	

CI, confidence interval; AIS, American Spinal Injury Association Impairment Scale; MPSS, methylprednisolone sodium succinate.

3% (one of 31) of thoracic motor complete AIS A patients had any improvement in neurologic function at one-year follow-up, a rate that was similar to that reported by Waters and associates[24,25] in their series of 148 patients with complete thoracic injuries.

While not entirely clear, the explanation for the relatively favorable conversion rate observed in our series (14.3% at last follow-up) compared with these historical series could be related to several factors including: changes in vehicle design, improved triage/resuscitation, earlier surgery, and/or better hemodynamic management for patients included in this modern series. It is important to note, however, that while rates of conversion were somewhat higher than previous studies, motor recovery remained poor among thoracic AIS As (2.5 points at last follow-up), suggesting that many of the coversions occurring may not be associated with clinically meaningful functional recovery.

Not unexpectedly, neurological recovery was much better for patients with incomplete injuries, although the extent of recovery was expectedly less dramatic for AIS D patients. The very low conversion rates among grade D patients are likely related to the poor sensitivity and ceiling effects of the ISNCSCI measures, particularly for less severely injured patients.

Table 7. Multivariable Poisson Regression Model Investigating Impact of Variables on Incidence of Pulmonary Complications

	Parameter est. 95% CI	*IRR*	p
Level			
T1–4	1.27(0.26,2.27)	3.54	0.01
T5–8	2.02 (1.11,2.93)	7.55	<0.01
T9–12 (ref)	–	–	–
MPSS administration			
Yes	0.68 (−0.06,1.42)	1.97	0.07
No (ref)	–		
Surgery prior to 24 h			
Yes	−0.93 (−1.85,−0.01)	0.39	0.046
No (ref)	–		
Age	−0.002 (−0.02,0.03)	1.00	0.84

CI, confidence interval; MPSS, methylprednisolone sodium succinate.

Although increasingly studied in recent years, the impact of the timing of surgery on neurological outcome after acute traumatic SCI has remained the subject of considerable debate, particularly for complete (AIS A) injuries. Recently developed clinical guidelines suggest early surgical management (<24 h post-injury) for all patients with SCI when medically feasible based on the best available evidence on the topic (which we acknowledge to be limited).[26,27]

For thoracic SCI, data are sparse, and our study is among the very few to examine the influence of treatment variables on neurological recovery and secondary complications in this subset of SCI. Early surgical management had a positive effect on motor recovery and additionally reduced the incidence of adverse pulmonary events. In the multi-variate analysis, we noted a seven-point improvement in motor recovery with early surgery performed within 24 h post-injury. Our finding is consistent with the findings of Dvorak and coworkers[15] in a Canadian registry cohort that included patients with all levels of injury (cervical, thoracic, and lumbosacral SCI) from the Rick Hansen Spinal Cord Injury Registry (RHSCIR). In that study, a 6.3-point improvement in motor recovery was noted with early surgery (within 24 h of injury) compared with late surgery (after 24 h), with follow-up between three and six months of injury.

In a meta-analysis of studies reporting the effect of timing of surgical spinal decompression after traumatic SCI, Middendorp and associates[28] noted an overall motor score improvement of 5.94 points, 95% (confidence interval: 0.74–11.15) with early compared with late surgical decompression. Future studies evaluating the specific effects of surgical timing in thoracic SCI are needed to confirm these results.

While predictors of adverse pulmonary events after traumatic SCI have been studied before, we focused specifically on evaluating the incidence and predictors of these events in a thoracic cohort, noting a lower incidence of pulmonary complications with early surgery. In a series of 298 patients from the German National Trauma Database, Schinkel and colleagues[29] reported that patients who had early stabilization of the thoracic injury (defined as within 72 h post-trauma) also had a lesser dependence on mechanical ventilation, a shorter intensive care unit and hospital stay, and lower mortality rate and pulmonary failure. That series did not examine the impact of thoracic-injury level. In our cohort, higher level thoracic injuries were associated with more pulmonary complications than lower thoracic level injury (T9–L1). In a prior NACTN registry study, Aarabi and coworkers[30] also showed that patients with paraplegia at higher thoracic levels (T2–6) were at greater risk than those with paraplegia at the lower levels of T7–12.

Further support for this correlation was reported by Cotton and colleagues[31] who analyzed 596 patients with thoracic SCI from the Pennsylvania Trauma System Foundation registry, and demonstrated that higher thoracic injuries (T1–6) increased the risk of pneumonia, the need for intubation, and likelihood of death compared with T7–12 injuries. It will be of interest to determine whether this link is because of greater lung tissue injury or the impact of injury level on immune function.

We acknowledge that there is some controversy and variability in the literature surrounding the specific neurological levels of injury to be considered when studying thoracic SCI. While some authors have studied thoracic SCI cohorts including patients with

injury levels between T1–T12,[32] others have used T2–12[21] or T4–12[4] to define this group, with different rationales used to justify these eligibility criteria in each case. In this study, we chose to include patients with NLIs between T1 and L1. Our decision to include patients with L1 NLI was based on several considerations. Because there is no L1 myotome, often it can be difficult to differentiate a patient with a T12 NLI versus a L1 NLI based on sensory status alone. In general, patients with both levels of injury experience deficits that extend above the testable myotomes in the lower extremities and behave in a similar fashion clinically. Further, there is no evidence to suggest that the pattern of neurological recovery differs substantially for a T12 SCI and a L1 SCI of the same injury severity.

We do acknowledge that there is a concern that, by including patients with L1 injuries, the cauda equina/peripheral nerve injuries might be included, and with the greater potential for neurologic recovery, these may confound the results and interpretation of recovery from a central nervous system injury. It should be noted, however, that the motor recovery observed in the complete AIS A injuries was only 2.6 points. Therefore, it is not as though we observed an unusually high degree of motor recovery in the AIS A patients. Anatomically, the L1 segment of the spinal cord is in extremely close proximity to the T12 vertebral region above the conus medularis, often in the setting of a lower thoracic spine fracture. Given the relative scarcity of thoracic injuries, for purposes of maximizing sample size available for this study, our eligibility criteria were designed to be maximally inclusive.

We acknowledge limitations first because of the small size of the study population. Still, thoracic SCI is substantially less common than cervical SCI; the current study represents one of the largest modern thoracic SCI series. Second, because of the retrospective analysis, the potential for confounding and selection biases cannot be completely eliminated through the use of regression techniques. Regarding selection bias, it is possible that more critically ill, polytrauma patients never gained admission to the registry and are underrepresented here. Third, given the sample size available, it was possible to control for a limited number of variables, although likely the most important, when modeling predictors of neurological recovery and pulmonary complications. Moreover, the improvement in recovery and reduction in the incidence of pulmonary complications with early surgical treatment may reflect the natural history of the thoracic SCI; and because all patients had spinal stabilization, the impact of surgery itself on the course of recovery was not ruled out.

There is the potential for center specific effects in the multicenter NACTN cohort or variability in assessments because of the different study personnel. The heterogeneity that naturally accompanies multi-center data collection, however, might increase the generalizability of our conclusions. Finally, with respect to surgical decompression, we acknowledge that there was not radiographic confirmation of spinal cord decompression in all cases and that in certain situations, the primary goal of surgery may have been stabilization rather than decompression. As a result, we have used the terms ''surgical management'' or ''surgical treatment'' in lieu of surgical decompression in this article.

Conclusion

Through use of a modern multi-center SCI registry, this study provides an important update surrounding the natural history, acute death, and incidence of pulmonary complications in patients with thoracic SCI. While methylprednisolone administration did not significantly impact neurological recovery or rates of pulmonary complication, early surgical management within 24 h of trauma was associated with significantly larger motor recovery and lower rates of pulmonary complications. The strength of these conclusions, however, must be tempered by our relatively small sample size and potential for selection bias intrinsic in registry-based studies. Larger series with random treatment allocation would be needed to confirm these treatment effects.

Funding Information

This work was supported by the AOSpine Spinal Cord Injury Knowledge Forum. The Christopher Reeve Foundation provided funding for the NACTN registry. MGF would like to acknowledge support from the Halbert Chair in Neural Repair and Regeneration and the DeZwirek Family Foundation.

Author Disclosure Statement

No competing financial interests exist.

References

1. World-Heath-Organization. (2017). Spinal Cord Injury.
2. Bransford, R.J., Chapman, J.R., Skelly, A.C., and VanAlstyne, E.M. (2012). What do we currently know about thoracic spinal cord injury recovery and outcomes? A systematic review. J. Neurosurg. Spine 17, Suppl 1, 52–64.
3. Wilson, J.R., Cadotte, D.W., and Fehlings, M.G. (2012). Clinical predictors of neurological outcome, functional status, and survival after traumatic spinal cord injury: a systematic review. J. Neurosurg. Spine 17, Suppl 1, 11–26.
4. Harrop, J.S., Naroji, S., Maltenfort, M.G., Ratliff, J.K., Tjoumakaris, S.I., Frank, B., Anderson, D.G., Albert, T., and Vaccaro, A.R. (2011). Neurologic improvement after thoracic, thoracolumbar, and lumbar spinal cord (conus medullaris) injuries. Spine 36, 21–25.
5. Waters, R., Adkins, R., Yakura, J. and Sie, I. (1994). Motor and sensory recovery following incomplete paraplegia. Arch. Phys. Med. Rehabil. 75, 67–72.
6. Waters, R., Yakura, J., Adkins, R., and Sie, I. (1992). Recovery Following Complete Paraplegia. Arch. Phys. Med. Rehabil. 73, 784–789.
7. Ackery, A., Tator, C., and Krassioukov, A. (2004). A global perspective on spinal cord injury epidemiology. J. Neurotrauma 21, 1355–1370.
8. Koizumi, M., Ueda, Y., Iida, J., Matsuyama, E., Yoshikawa, T., Takakura, Y., Hirai, T., and Murakami, J. (2002). Upper thoracic spinal cord injury without vertebral bony lesion: a report of two cases. Spine 27, E467–E470.
9. Andriacchi, T., Schultz, A., Belytschko, T., and Galante, J. (1974). A model for studies of mechanical interactions between the human spine and rib cage. J. Biomech. 7, 497–507.
10. el-Khoury, G.Y. and Whitten, C.G. (1993). Trauma to the upper thoracic spine: anatomy, biomechanics, and unique imaging features. AJR. Am. J. Roentgenol. 160, 95–102.
11. InVivo-Therapeutics. (2017). Neuro-Spinal Scaffold. www.invivotherapeutics.com/research-clinical-development/pipeline/neuro-spinal-scaffold
12. Saberi, H., Moshayedi, P., Aghayan, H.R., Arjmand, B., Hosseini, S.K., Emami-Razavi, S.H., Rahimi-Movaghar, V., and Firouzi, M. (2008). Treatment of chronic thoracic spinal cord injury patients with autologous Schwann cell transplantation: an interim report on safety considerations and possible outcomes. Neurosci. Lett. 443, 46–50.
13. Wilson, J.R., Forgione, N., and Fehlings, M G. (2013). Emerging therapies for acute traumatic spinal cord injury. CMAJ 185, 485–492.
14. Fehlings, M.G., Vaccaro, A.R., Wilson, J.R., Singh, A., Cadotte, D.W., Harrop, J.S., Aarabi, B., Shaffrey, C., Dvorak, M., Fisher, C., Arnold, P., Massicotte, E.M., Lewis, S., and Rampersaud, R. (2012). Early versus delayed decompression for traumatic cervical spinal cord injury: results of the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS). PLoS One 7,e32037.
15. Dvorak, M.F., Noonan, V.K., Fallah, N., Fisher, C.G., Finkelstein, J., Kwon, B.K., Rivers, C.S., Ahn, H., Paquet, J., Tsai, E.C., Townson, A., Attabib, N., Bailey, C.S., Christie, S.D., Drew, B., Fourney, D.R., Fox, R.,

Hurlbert, R.J., Johnson, M.G., Linassi, A.G., Parent, S., Fehlings, M.G., and RHSCIR Network. (2015). The influence of time from injury to surgery on motor recovery and length of hospital stay in acute traumatic spinal cord injury: an observational Canadian cohort study. J. Neurotrauma 32, 645–654.
16. Wilson, J.R., Singh, A., Craven, C., Verrier, M.C., Drew, B., Ahn, H., Ford, M,. and Fehlings, M.G. (2012). Early versus late surgery for traumatic spinal cord injury: the results of a prospective Canadian cohort study. Spinal Cord 50, 840–843.
17. Bracken, M.B., Shepard, M.J., Collins, W.F., Holford, T.R., Young, W., Baskin, D.S., Eisenberg, H.M., Flamm, E., Leo-Summers, L., and Maroon, J., et al. (1990). A randomized, controlled trial of methylprednisolone or naloxone in the treatment of acute spinal-cord injury. Results of the Second National Acute Spinal Cord Injury Study. N. Engl. J. Med. 322, 1405–1411.
18. Bracken, M.B. (2012). Steroids for acute spinal cord injury. Cochrane Database Syst. Rev. 1, CD001046.
19. Jackson, A.B. and Groomes, T.E. (1994). Incidence of respiratory complications following spinal cord injury. Arch. Phys. Med. Rehabil. 75, 270–275.
20. Kopp, M.A., Watzlawick, R., MArtus, P., Failli, V., Finkenstaedt, F.W., Chen, Y., DeVivo, M.J., Dirnaqi, U., and Schwab, J.M. (2017). Long-term functional outcome in patients with acquired infections after acute spinal cord injury. Neurology 88, 892–900.
21. Zariffa, J., Kramer, J.L., Fawcett, J.W., Lammertse, D.P., Blight, A.R., Guest, J., Jones, L., Burns, S., Schubert, M., Bollinger, M., Curt, A., and Steeves, J.D. (2011). Characterization of neurological recovery following traumatic sensorimotor complete thoracic spinal cord injury. Spinal Cord 49, 463–471.
22. Lee, B.A., Leiby, B.E., and Marino, R.J. (2016). Neurological and functional recovery after thoracic spinal cord injury. J. Spinal Cord Med. 39, 67–76.
23. Fawcett, J.W., Curt, A., Steeves, J.D., Coleman, W.P., Tuszynski, M.H., Lammertse, D., Bartlett, P.F., Blight, A.R., Dietz, V., Ditunno, J., Dobkin, B.H., Hayton, L.A., Ellaway, P.H., Fehlings, M.G., Privat, A., Grossman, R., Guest, J.D., Kleitman, N., Nakamura, M, Gaviria, M., and Short, D. (2007). Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. Spinal Cord 45, 190–205.
24. Waters, R.L., Yakura, J.S., Adkins, R.H., and Sie, I. (1992). Recovery following complete paraplegia. Arch. Phys. Med. Rehabil. 73, 784–789. SAME AS #6
25. Waters, R.L., Adkins, R., Yakura, J., and Sie, I. (1998). Donal Munro Lecture: Functional and neurologic recovery following acute SCI. J. Spinal Cord Med. 21, 195–199.
26. Furlan, J.C., Noonan, V., Cadotte, D.W., and Fehlings, M.G. (2011). Timing of decompressive surgery of spinal cord after traumatic spinal cord injury: an evidence-based examination of pre-clinical and clinical studies. J. Neurotrauma 28, 1371–1399.
27. Wilson, J.R., Tetreault, L.A., Kwon, B.K., Arnold, P.M., Mroz, T.W., Shaffrey, C., Harrop, J.S., Chapman, J.R., Casha, S., Skelly, A.C., Holmer, H.K., Brodt, E.D., and Fehlings, M.G. (2017). Timing of decompression in patients with acute spinal cord injury: a systematic review. Global Spine J. 7, Suppl 3, 95S–115S.
28. van Middendorp, J.J., Hosman, A.J., Pouw, M H.; EM-SCI Study Group, Van de Meent, H. (2009). ASIA impairment scale conversion in traumatic SCI: is it related with the ability to walk? A descriptive comparison with functional ambulation outcome measures in 273 patients. Spinal Cord 47, 555–560.
29. Schinkel, C. and Anastasiadis, A.P. (2008). The timing of spinal stabilization in polytrauma and in patients with spinal cord injury. Curr. Opin. Crit. Care 14, 685–689.
30. Aarabi, B., Harrop, J.S., Tator, C.H., Alexander, M., Dettori, J.R., Grossman, R.G., Fehlings, M.G., Mirvis, S.E., Shanmuganathan, K., Zacheri, K.M., Burau, K.D., Frankowski, R.F., Toups, E., Shaffrey, C.I., Guest, J.D., Harkema, S.J., Habashi, N.M., Andrews, P., Johnson, M.M., and Rosner, M.K. (2012). Predictors of pulmonary complications in blunt traumatic spinal cord injury. J. Neurosurg. Spine 17, Suppl 1, 38–45.
31. Cotton, B.A., Pryor, J.P., Chinwalla, I., Wiebe, D.J., Reilly, P.M., and Schwab, C.W. (2005). Respiratory complications and mortality risk associated with thoracic spine injury. J. Trauma 59, 1400–1407.
32. Maung, A.A., Schuster, K.M., Kaplan, L.J., Maerz, L.L., and Davis, K.A. (2011). Risk of venous thromboembolism after spinal cord injury: not all levels are the same. J. Trauma 71, 1241–1245.

Address correspondence to:
Michael G. Fehlings, MD, PhD
Division of Neurosurgery
Toronto Western Hospital
399 Bathurst Street, Suite 4W-449
Toronto, Ontario M5T 2S8
Canada

E-mail: michael.fehlings@uhn.ca

Appendix. Centers Contributing Data to North American Clinical Trials Network

Houston Methodist Hospital, Houston, Texas
University of Texas Health Science Center, Houston, Texas
University of Toronto, Toronto, Virginia
University of Virginia, Charlottesville, Virginia
University of Louisville—Kentucky Spinal Cord Injury Research Center, Louisville, Kentucky
University of Maryland, Baltimore, Maryland
Walter Reed National Military Medical Center, Bethesda, Maryland
University of Miami, Miami, Florida
Thomas Jefferson University, Philadelphia, Pennsylvania
Brooke Army Medical Center, Fort Sam Houston, Texas
Louisiana State University Health Sciences Center, New Orleans, Louisiana