Acute Adverse Events After Spinal Cord Injury and Their Relationship to Long-term Neurologic and Functional Outcomes: Analysis From the North American Clinical Trials Network for Spinal Cord Injury

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Objectives: There are few contemporary, prospective multicenter series on the spectrum of acute adverse events and their relationship to long-term outcomes after traumatic spinal cord injury. The goal of this study is to assess the prevalence of adverse events after traumatic spinal cord injury and to evaluate the effects on long-term clinical outcome.

Design: Multicenter prospective registry.

Setting: Consortium of 11 university-affiliated medical centers in the North American Clinical Trials Network.

Patients: Eight-hundred one spinal cord injury patients enrolled by participating centers.

Interventions: Appropriate spinal cord injury treatment at individual centers.

Measurements and Main Results: A total of 2,303 adverse events were recorded for 502 patients (63%). Penalized maximum logistic regression models were fitted to estimate the likelihood of neurologic recovery (ASIA Impairment Scale improvement ≥ 1 grade point) and functional outcomes in subjects who developed adverse events at 6 months postinjury. After accounting for potential confounders, the group that developed adverse events showed less neurologic recovery (odds ratio, 0.55; 95% CI, 0.32–0.96) and was more likely to require assisted breathing (odds ratio, 6.55; 95% CI, 1.17–36.67); dependent ambulation (odds ratio, 7.38; 95% CI, 4.35–13.06) and have impaired bladder (odds ratio, 9.63; 95% CI, 5.19–17.87) or bowel function (odds ratio, 7.86; 95% CI, 4.31–14.32) measured using the Spinal Cord Independence Measure subscores.

Conclusions: Results from this contemporary series demonstrate that acute adverse events are common and are associated with worsened long-term outcomes after traumatic spinal cord injury. (*Crit Care Med* 2019; 47:e854–e862)

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Traumatic spinal cord injuries (SCIs) have devastating consequences for individuals and impose a significant burden on the healthcare system (1–6). Although the prevalence of SCI seems to have stabilized in the young, there is an increasing prevalence of fall-related SCI among the elderly population (7–10). It has been recognized that the severe primary and secondary injuries resulting from trauma translate into an increased risk of secondary adverse events (AEs) in these patients during the critical postinjury state. The quoted prevalence rates in the literature vary from 38% to 79% (1, 10–14). Furthermore, SCI-associated AEs remain the primary causes of premature mortality and prolonged morbidity in affected individuals (1, 9–12, 15–26). As a result, there is increasing acknowledgment of the need for vigilant postinjury management for traumatic SCI patients in the critical care setting (27, 28).

Despite advances in management, literature reviews suggest the current evidence base is not robust enough to dictate preventative and treatment strategies to target the most severe secondary AEs affecting individuals with SCI (29). Furthermore, recent studies suggest secondary AEs could have long-term impact on outcomes and survival (30, 31). Therefore, the need for effective strategies and tools to improve patient quality of life in the long-term has added relevance.

Although it is recognized that the time period of acute admission represents the period of greatest vulnerability to life-threatening AEs, most studies on the spectrum, prevalence, and risk factors for SCI-associated AEs have focused on the subacute or rehabilitation phases of injury. Furthermore, many other studies have focused on specific events (1, 4, 9, 11, 12, 17, 19, 22–25, 32), thus providing an incomplete picture of the overall burden of secondary AEs.

Previously, Grossman et al (10) analyzed data from 315 SCI patients who were prospectively enrolled from nine clinical centers of the North American Clinical Trials Network (NACTN), to address the prevalence and characteristics of AEs following acute admission for SCI. This preliminary study focused on the crude distribution of AEs, but provided limited insight on the likely association between these secondary events and SCI outcomes. Since then, NACTN has enrolled more patients and expanded to 11 centers. Our goal in the present study was to provide more granular insight into the spectrum, prevalence, and risk factors for SCI-associated AEs in the updated NACTN registry. In addition, we aimed to ascertain the relationship between acute AEs and long-term neurologic and functional outcomes using multivariable analysis.

MATERIALS AND METHODS

The study protocol was approved by the Human Research Protection Office, Office of Research Protections, and the United States Army Medical Research and Material Command.

Study Population

The present study included 801 patients who were enrolled from 11 acute SCI units at university-affiliated medical centers (**Supplemental Digital Content Table 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/E839) between June 2005 and March 2017. The eligibility criteria included: 1) subject had a neurologic assessment according to the International Standards for Neurologic Classification of Spinal Cord Injury (ISNCSCI) during acute hospital admission (Revised 2011); 2) age greater than or equal to 18 years; and 3) subject or legally authorized representative provided informed consent. Patient clinical care is standardized among the NACTN centers and is consistent with recommendations in the "Guidelines for the Management of Acute Cervical Spine and Spinal Cord Injuries." (33)

Data Collection and Management

Following informed consent, clinical coordinators collected patient data for each participating subject during the time from admission to a NACTN hospital to discharge. Data elements were collected for demographic characteristics, past medical history, current medications, mechanism of injury, time of arrival to center, patient's medical and neurologic status at presentation including vital signs, level of consciousness assessed according to the Glasgow Coma Scale (GCS), ISNCSCI examination details, extent of polytrauma measured using the Abbreviated Injury Scale, and complications. Treatment data on nonoperative and surgical treatments were also collected. The data were centrally stored and processed in a standard fashion.

Definition and Coding of AEs

In NACTN, AEs are defined as a change in a patient's physiologic state or anatomical integrity that required medical or surgical treatment and/or that prolonged the patient's hospitalization (10). AEs were categorized by organ system and according to specific diagnosis made during the acute admission, as determined by each center's principal investigator or treating physician (**Table 1**). Data on AEs were collected during the period of acute admission, mostly within 14 days of the injury.

Predictor Variables

The following patient and treatment characteristics were considered in multivariable analysis for association with acute AEs: age, baseline ASIA Impairment Scale (AIS) grade, baseline GCS score, injury neurologic level, type of injury (penetrating vs non penetrating), use of steroids, and time from injury to surgery (dichotomized as ≤ 24 hr vs > 24 hr).

Outcome Measures

Follow-up data were collected at acute discharge, rehabilitation discharge, and at 6 and 12 months. These included ISNCSCI examinations, Functional Independence Measure (FIM), Spinal Cord Independence Measure (SCIM) Version 2, and the Walking Index for SCI measures. For the present study, we included patients who had the initial AIS grade evaluation

TABLE 1. Adverse Events by Organ Specific Diagnosis

System	Specific Diagnosis
Respiratory	Acute lung injury, acute respiratory distress syndrome, respiratory failure, pulmonary embolus, pleural effusion, lobar collapse, mucus plug, pneumothorax, and hemothorax
Hematologic	Deep vein thrombosis, anemia, thrombocytopenia, and coagulopathy
Cardiac	Arrhythmias, bradycardia, cardiac arrest, myocardial infarction, systolic blood pressure ≤ 90 mm Hg, congestive heart failure, and cardiogenic pulmonary edema
Skin	Heel, trochanteric, sacral, scapular, occipital scalp or decubiti pressure sores, and operative wound issues
Infectious	Pneumonia, urinary tract infection, empyema, wound infection, sepsis, abscess, infectious diarrhea, and CNS infection
Gastrointestinal	Hemorrhage, ileus, pancreatitis, and cholecystitis
Renal	Hematuria and acute renal failure
Neuropsychiatric	Depression, psychosis, seizure, and cognitive deterioration

within 7 days of the injury. Neurologic recovery was defined as an AIS greater than or equal to 1 grade point improvement at 6 months follow-up. For functional outcome, we dichotomized the SCIM subscores for respiration, bladder, and bowel sphincter management; ambulation for a short distance indoors at 6 months postinjury (34). The two categories for each subscore are shown in **Supplemental Digital Content Table 2** (Supplemental Digital Content 1, http://links.lww.com/CCM/E839). Respiratory subscore was dichotomized as assisted breathing versus independent breathing. Bladder subscore was dichotomized as requires catheterization versus needs no catheterization. Bowel motion subscore was dichotomized as irregular motion versus regular motion. Ambulation was dichotomized as dependent versus independent ambulation.

Statistical Analysis

Descriptive statistics were applied including Mann-Whitney *U* test for continuous variables and chi-square test for dichotomous variables. A multivariable negative binomial regression model was used to study the factors that were predictive of a higher prevalence of AEs, with CIs obtained by bootstrap resampling (50 replicates). The effect size was reported as incidence rate ratios (IRRs). Penalized maximum logistic regression models were fitted to estimate the effect of AEs (dichotomized as present vs absent) on neurologic recovery (AIS ≥ 1 grade point improvement) or functional outcomes according to the dichotomized SCIM subscores as dependent variables. Logistic regression models were adjusted for age, baseline AIS grade, and injury level. In subanalysis, we investigated the effect of systolic blood pressure (SBP) on functional outcomes and the effect of time on the incidence of AEs. The effect size was reported as odds ratios (OR) with 95% CIs. Statistical significance was set at the 5% level.

RESULTS

Baseline Characteristics

The analysis included 801 subjects, among whom 614 (77%) had baseline AIS assessment within seven days of the injury. Functional outcomes data were complete for 402 subjects (50%) (**Supplemental Digital Content Fig. 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/E839). The cohort had a median age of 46 years (interquartile range [IQR], 29–59 yr) and were predominately men (78%) (**Table 2**). Among the subjects, AIS grade A injuries were diagnosed in 231 patients (37.6%). Grade B injuries were noted in 72 subjects (11.7%), grade C in 90 subjects (14.7%), and grade D in 175 subjects (28.5%). Regarding the neurologic level of injury, 528 subjects (70.9%) sustained a cervical level injury, followed by thoracic and lumbar/sacral levels with 166 subjects (22.3%) and 50 subjects (6.7%), respectively. As shown in Table 2, the patients who were lost to follow-up had lower frequencies of severe injuries (AIS grade A) or injuries from motor vehicular accidents. Among patients who completed follow-up, those who experienced one or more AEs during admission had double the length of stay compared with those who did not have any AEs (18 vs 9 d; $p < 0.001$). We found a higher incidence of acute AEs with more severe injury (**Supplemental Digital Content Fig. 2**, Supplemental Digital Content 1, http://links.lww.com/CCM/E839), with the incidence of AEs stratified by AIS as follows: grade A: 85.3% (95% CI, 80.0–89.6%); grade B: 65.3% (53.1–76.1%); grade C: 48.9% (38.2–59.7%); and grade D: 33.7% (26.8–41.2%). Among those with cervical SCI, the incidence rates were as follows: grade A: 91.6% (77.0–100%); grade B: 75.0% (53.3–100%); grade C: 47.0% (31.9–66.7%); and grade D: 31.0% (22.5–41.6%).

Prevalence and Predictors of AEs

There were 2,303 recorded acute AEs. The most common being pulmonary cause ($n = 577$; 25.1%), followed by infectious (442; 19.2%), hematological (402; 17.5%), cardiac (335; 14.5%), gastro-urinary (220; 9.6%), skin (178; 7.7%), and neuropsychiatric (149; 6.5%). Classified according to organ system, the most prevalent AEs were pneumonia (218 occurrences, 9.5% of all recorded AEs), respiratory failure (207; 9.0%), anemia (197; 8.6%), urinary tract infection (139; 6.0%), pleural effusion (92; 4.0%), bradycardia (93; 4.0%), depression (89; 3.9%), and sacral ulcers (72; 3.1%) (**Supplemental Digital Content Fig. 3**, Supplemental Digital Content

TABLE 2. Clinical Characteristics of the Study Cohort

Characteristics	*n* (%)	Loss to Follow-Up (*n* = 399)	Follow-Up Completed (*n* = 402)	*p*
Median age, yr, median (interquartile range)	46 (29–59)	49 (32–59)	44 (29–59)	0.09
Sex				
Male	609 (78)	304 (78.6)	305 (77.6)	0.75
College				
Yes	290 (44.8)	166 (58.0)	122 (41.2)	< 0.001
Cause of injury				
Fall	316 (39.8)	182 (45.6)	134 (33.8)	< 0.001
Motor vehicle accidents	298 (37.5)	124 (31.1)	174 (43.9)	
Others	49 (6.1)	93 (23.3)	88 (22.2)	
Injury type				
Penetrating	41 (5.3)	18 (4.6)	23 (5.9)	0.42
Nonpenetrating	736 (94.7)	371 (95.4)	365 (94.1)	
ASIA Impairment Scale grade				
A	231 (37.6)	108 (32.2)	123 (44.1)	< 0.001
B	72 (11.7)	41 (12.2)	31 (11.1)	
C	90 (14.7)	47 (14.0)	43 (15.4)	
D	175 (28.5)	118 (35.2)	57 (20.4)	
E	46 (7.5)	21 (6.3)	25 (9.0)	
Level				
Cervical	528 (70.9)	282 (72.3)	246 (69.3)	0.62
Thoracic	166 (22.3)	82 (21.0)	85 (23.9)	
Lumbar/sacral	50 (6.7)	26 (6.7)	24 (6.7)	
Glasgow Coma Scale				
15	623 (79.3)	327 (83.2)	296 (75.3)	0.02
9–14	123 (15.7)	51 (13.0)	72 (18.3)	
3–8	40 (5.1)	15 (3.8)	25 (6.4)	
Preinjury comorbidities	311 (39.2)	159 (40.1)	152 (38.4)	0.63
Steroid administration	307 (38.7)	131 (32.8)	176 (44.4)	0.001
Surgery within 24 hr	258 (41.2)	147 (43.4)	111 (38.7)	0.24

1, http://links.lww.com/CCM/E839). Among the 801 subjects, 502 (63%) experienced at least one AE, and 352 (44.4%) experienced more than one AE. As shown in **Table 3**, subjects with AEs were on average younger (45 vs 48 yr), had higher frequencies of ASIA grade A injuries (56.8%, $n = 197$ vs 15.4%, $n = 34$), severe head injuries (6.9%, $n = 34$ vs 2.0%, $n = 6$) or penetrating injuries (6.2%, $n = 30$ vs 3.8%, $n = 11$) than those without acute AEs. The average time from injury to surgery was comparable between the two groups (AEs group: 31 hr [IQR, 14–77 hr] vs No AEs group: 35 hr [IQR, 18–71 hr]). In the multivariable negative binomial regression model, the identified significant predictors for acute AEs were as follows: SCI injury severity (initial AIS grade: IRR, grade A, 4.70, 95% CI, 3.52–6.27; grade B, 3.25, 95% CI, 2.18–4.85; grade C, 2.13, 95% CI, 1.40–3.24; and grade D = base category) and age (IRR, 1.01; 95% CI, 1.00–1.02) (Table 3). No significant association was found for the GCS score, injury neurologic level, mechanism, premorbid conditions, steroid use, and time to surgery. In a model including the above variables and time period from admission to last year of recruitment, we found on average a 4% drop in the incidence of AEs per year (IRR, 1.04; 95% CI, 1.01–1.08; $p = 0.03$).

TABLE 3. Predictive Factors of a Higher Incidence of Secondary Adverse Events in Multivariable Analysis

Variable	Crude Distribution of Adverse Events		Multivariable Analysis	
	Absent, $n = 299$, n (%)	Present, $n = 502$, n (%)	Incidence Rate Ratio (95% CI)	p
ASIA Impairment Scale grade				
D	116 (52.5)	59 (17.0)	Reference	< 0.001
C	46 (20.8)	44 (12.7)	2.13 (1.40–3.24)	
B	25 (11.3)	47 (13.5)	3.25 (2.18–4.85)	
A	34 (15.4)	197 (56.8)	4.70 (3.52–6.27)	
Age, yr, median (interquartile range)	48 (33–60)	45 (28–59)	1.01 (1.00–1.02)	0.01
Glasgow Coma Scale				
3–8	6 (2.0)	34 (6.9)	Reference	0.39
9–14	6 (2.0)	43 (8.7)	0.75 (0.35–1.60)	
15	280 (95.9)	417 (84.4)	0.66 (0.32–1.37)	
Highest injury level				
Cervical	193 (69.7)	335 (71.6)	Reference	0.33
Thoracic	59 (21.3)	108 (23.1)	0.81 (0.61–1.08)	
Lumbar/sacral	25 (9.0)	25 (5.3)	0.95 (0.43–2.18)	
Penetrating injury				
No	280 (96.2)	456 (93.8)	Reference	0.12
Yes	11 (3.8)	30 (6.2)	1.81 (0.81–4.02)	
Steroid use				
No	185 (62.1)	303 (61.0)	Reference	0.85
Yes	113 (37.9)	194 (39.0)	0.98 (0.76–1.25)	
Surgery ≤ 24 hr				
No	140 (63.1)	228 (56.4)	Reference	0.28
Yes	82 (36.9)	176 (43.6)	0.90 (0.73–1.09)	

Effect of Secondary Events on Neurologic Recovery and Functional Outcome

The group of subjects who had acute AEs had a lower AIS conversion rate at 6 months compared with the group without AEs (41.9% vs 55.3%). This inverse relationship was present at each grade of the AIS (**Table 4**). In unadjusted analysis, the group with AEs was less likely to have AIS greater than or equal to 1 grade point improvement at 6 months (**Table 5**), and the association was maintained when adjusting for age, baseline AIS and injury neurologic level (OR, 0.55; 95% CI, 0.32–0.96). Among the 402 subjects with SCIM data at greater than or equal to 6 months, 23 patients (12%) required some form of mechanical assistance with breathing, 280 (61%) required some aid to walk indoors, 206 (51%) required catheterization for complete bladder emptying, and 195 (49%) had irregular bowel motion or needed suppositories to achieve regular motion. In adjusted analysis accounting for age, injury severity and level, acute AEs were found to be an independent predictor for assisted breathing (OR, 6.55; 95% CI, 1.17–36.67), decreased capacity for ambulation (OR, 7.38; 95% CI, 4.35–13.06) and poor bladder (OR, 9.63; 95% CI, 5.19–17.87) or rectal sphincter function (OR, 7.86; 95% CI, 4.31–14.32) at 6 months postinjury (Table 5).

In a subanalysis, we focused on the effect of hypotension at admission into acute care on functional outcomes. We noted lower mean SBP among subjects with AEs as compared to those without (120 ± 29 vs 136 ± 56 mm Hg; $p < 0.001$). When we dichotomized SBP as low (≤ 90 mm Hg: $n = 69$; 8.7%), within normal range (91–140 mm Hg: $n = 492$; 61.6%) or elevated (> 140 mm Hg: $n = 237$; 29.7%), there was no association with functional outcomes in adjusted analysis accounting for age, injury severity and levels (**Supplemental Digital Content Table 3**, Supplemental Digital Content 1, http://links.lww.com/CCM/E839). We repeated the analysis for the cohort

TABLE 4. ASIA Impairment Scale Conversion Rates at 6 Months

ASIA Impairment Scale Grade	Nil Adverse Events, *n* = 141, *n* (%)	Adverse Events, *n* = 203, *n* (%)
A	9 (40.9)	36 (32.4)
B	12 (75.0)	20 (71.4)
C	24 (88.9)	21 (75.0)
D	33 (43.4)	8 (22.2)
Total	78 (55.3)	85 (41.9)

TABLE 5. Effect of Adverse Events on Neurologic Recovery and Functional Outcomes

Outcomes	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	*p*
ASIA Impairment Scale improvement ≥ 1 point			
No	Reference	Reference	
Yes	0.59 (0.38–0.91)	0.55 (0.32–0.96)	0.04
Assisted breathing			
No	Reference	Reference	
Yes	6.52 (1.74–24.47)	6.55 (1.17–36.67)	0.03
Supported ambulation			
No	Reference	Reference	
Yes	5.71 (3.80–8.58)	7.38 (4.35–13.06)	< 0.001
Need catheterization			
No	Reference	Reference	
Yes	8.89 (5.59–14.13)	9.63 (5.19–17.87)	< 0.001
Irregular bowel motion			
No	Reference	Reference	
Yes	7.07 (4.48–11.17)	7.86 (4.31–14.32)	< 0.001

OR = odds ratio.

Models adjusted for age, baseline ASIA Impairment Scale grade, and injury level; *p* is derived from the adjusted analysis.

with cervical SCI using mean arterial blood pressure (MAP) as predictor variable. In this analysis, 3.4% of subjects ($n = 18$) with cervical SCI were hypotensive (MAP < 65 mm Hg) at initial blood pressure measurement at admission. In unadjusted analysis, we noted poorer functional outcomes among subjects with MAP less than 85 mm Hg than those with MAP greater than or equal to 85 mm Hg (breathing support: OR, 3.09, 95 CI, 1.23–7.80; difficulties with walking indoors: OR, 2.51, 95% CI, 1.55–4.07; need for catheterization for complete bladder emptying: OR, 2.84, 95 CI, 1.73–4.67; and irregular bowel motion or needed suppositories to achieve regular motion: OR, 3.21, 95 CI, 1.94–5.32). The association was lost in adjusted analysis accounting for baseline AIS (**Supplemental Digital Content Table 4**, Supplemental Digital Content 1, http://links.lww.com/CCM/E839).

DISCUSSION

To our knowledge, this study represents the largest series investigating secondary AEs and its impact on long-term outcomes in SCI patients. Importantly, our analysis used a multicenter, prospective cohort that was treated in accord with contemporary protocol. Our results demonstrate reduced prospects for neurologic improvement and functional independence among patients who experience secondary AEs during acute hospitalization and reflects the importance of clinical vigilance in the critical immediate postinjury period.

Spectrum and Incidence of AEs

This study has shown that despite modern SCI management, the rate of secondary AEs remains high in the postinjury period encompassing every organ system. Our results support high occurrence rates of SCI-associated AEs, especially pneumonia, reported in high frequency during acute admission (1, 11–14). Of note, the spectrum and incidence from the updated NACTN registry remained relatively consistent with the earlier study by Grossman et al (10) who reported a 58% incidence of SCI-associated AEs, with the most frequent types being respiratory failure, pneumonia, pleural effusion, anemia, cardiac dysrhythmia, and severe bradycardia. Interestingly, the study also showed that approximately three-quarters of AEs occur within 14 days of injury. In the Surgical Timing for Spinal Cord Injury Study (STASCIS), 38.9% of enrolled subjects experienced 240 AEs during the acute admission. Similar to our study, the majority were cardiopulmonary, including pneumonia (39%), infection (36%), surgical (12%), thrombotic (9%), and decubitus ulcers (5%) (35). Most likely, the lower incidence of acute events in the STASCIS study compared with our present study reflects the exclusion of subjects with life-threatening injury from that trial.

Risk Factors for Acute Secondary Events

The management of AEs in the setting of SCI is still challenging. Pneumonia—one of the leading causes of death in the postinjury setting (30, 36–39)—can be easily misdiagnosed due to the atypical presentation in this population (29, 40). In the high-paced postinjury acute care setting, less attention is given to neuropsychiatric conditions, which we have identified in the present study to be not uncommon. Recent reviews suggest strategies to optimize the management of acute AEs have a weak evidence base, highlighting the need to expand knowledge in the area (29). Our study contributes to the evidence for risk factors for secondary AEs, which could potentially be useful for tailoring management among high-risk SCI patients. We found that initial injury severity (AIS grade) and older age were the primary risk factors among our cohort. This finding is consistent with those of previous studies (10, 11, 14, 26, 32, 35, 41, 42) and likely reflects the impact of the initial trauma, age-related changes in neuroplasticity or the effect of comorbidity. SCI patients with concomitant severe head injuries might be at high risk for secondary events (43–45), although our study did not find the GCS score to be predictive of AEs. Most likely, this is because patients presenting with severe impairment of GCS were excluded from the NACTN registry since it precludes obtaining an accurate ASIA. Hence, 80% of the SCI patients in this study cohort had a GCS score of 15 and the majority with reduced GCS had only minor transient changes. Other risk factors that were previously identified in the literature include penetrating trauma, concomitant injuries and comorbidities, surgical invasiveness score, cigarette smoking, cervical level injury, timing from injury to surgical decompression, and steroid use (10, 11, 26, 35, 46).

Considering the importance of identifying at-risk patients early, Wilson et al (35) used the STASCIS trial dataset to develop a clinical prediction model for secondary AEs during acute admission that was based on a combination of five predictive factors including initial injury severity, a high energy injury mechanism, older age, absence of steroid administration, and comorbid illness. Despite satisfactory accuracy, the prediction model has yet to be studied in a validation cohort, which potentially limits its utility in clinical care.

Currently, the relationship between secondary AEs and steroid use (47–49) or timing of surgery (22–25) remains controversial. Recently published systematic reviews and guidelines have found evidence for a beneficial effect for steroid use in acute SCI presenting within 8 hours of injury while noting no significant difference in complication rates between patients who were treated with or without the 24-hour regimen (50, 51). Additionally, AOSpine review and treatment guidelines noted no significant difference in complication rates when comparing early to late surgical decompression (52, 53). The studies found early surgery, preferably within 24 hours of the injury, could improve neurologic recovery.

Secondary Events and Long-term Outcomes After SCI

In a preliminary analysis of 109 patients from the NACTN study (2005–2009), Aarabi et al (32) found no association between the development of moderate or severe pulmonary AEs and long-term neurologic recovery. In our more comprehensive analysis, which factored other AE types in the expanded NACTN registry, long-term neurologic recovery was noted to be poorer among subjects who sustained AEs in the acute inpatient setting. Also, this group was more likely to have worse functional outcomes across multiple functional domains including ambulation, respiration, bladder, and bowel functioning. Our finding is corroborated by those of two studies from the prospective multicenter National Spinal Cord Injury Database (NSCID, Birmingham, AL) that demonstrated significantly lower long-term neurologic recovery and functional independence among SCI patients who develop pneumonia and postoperative wound infections in acute care or rehabilitation settings (30, 31). In the NSCID studies, subjects who had pneumonia and/or wound infections improved less than controls when assessed at 1 year on the motor and sensory components of the AIS and at 5 years postinjury in the motor component of the FIM.

It is difficult to infer causality considering the cross-sectional design of our present study. Nonetheless, the results and those of previous studies underscore the need for clinical vigilance and careful attention to the management of acute AEs. Although SCI subjects represent a heterogeneous population in terms of AEs and injury profile, those with high cervical injuries, complete injury, advanced age, history of cardiopulmonary disease, diaphragmatic dysfunction, or tachypnea at admission are particularly high risk for cardiovascular instability and respiratory insufficiency (54). Hence, they are better managed in the ICU setting with round-the-clock monitoring and comprehensive cardiovascular and ventilatory support. Hypoperfusion from systemic hypotension resulting from hypovolemia or neurogenic shock remains a crucial management dilemma since it has been associated with poorer outcomes, and considering that the evidence is weak that blood pressure augmentation could improve outcome (54–56). Current recommendation that MAP should be routinely maintained between 85 and 90 mm Hg within the first 7 days is debatable in view of the weak evidence base and the fact that not all SCI patients are routinely monitored in the ICU. From the results of our study, which are based on a single blood pressure measurement, it would appear that the injury severity is critical to understanding the effect of hypotension on outcomes, and as such may need to be factored in the triage of cervical SCI subjects for aggressive blood pressure augmentation. Furthermore, since secondary acute events are preventable, we emphasize adherence to clinical guidelines on their prevention during acute care, especially for pneumonia. Also, close attention is required for early screening for neuropsychiatric conditions, as these are not uncommon and might be missed in the busy acute care setting. Generally, SCI patients should be afforded early surgical intervention, close postinjury monitoring as well as the early implementation of rehabilitation measures to reduce the incidence or severity of secondary AEs.

Study Limitations

The challenge with multicenter prospective studies of SCI remains maintaining long-term follow-up of the patients. In this study, 50% of participants were lost to follow-up, and these were found to be subjects with less severe injury profiles, suggesting we might have overestimated the incidence of AEs and the effect on outcomes. Similar studies to ours have also reported comparable loss to follow-up rates. For instance, in NSCID studies examining the effect of infectious AEs on SCI outcome, the proportion of incomplete follow-up was 44% at 1 year and 69% at 5 years (30). In as much as we tried to be rigorous in capturing AEs using well-defined protocols, it is possible that case ascertainment was incomplete. Earlier studies from 2 or more decades ago have reported very high rates of urinary or skin-related AEs (6, 57). Of note, these studies included patients at the subacute or rehabilitation phases of care. Therefore, as the spectrum and incidence of AEs change with time postinjury, chronic complications may predominate in the subacute and rehabilitation periods (58–60). Furthermore, the improvements in awareness, prevention and treatment of urinary and skin-related events over the decades might have impacted reported rates in more recent studies (10, 11, 13, 14, 46, 59, 61, 62). In the present study, we noted the prevalence of AEs dropped over time, on average 4% per year; a finding that might be attributed to advances in prevention for AEs and acute critical care for SCI, among other reasons. Finally, our primary goal in the present study was to analyze the overall effect rather than to focus on the effect of specific AEs types. Detailed analysis of specific AEs will be considered in future studies.

CONCLUSIONS

This study has provided strong evidence that acute secondary AEs can impact long-term neurologic and functional outcomes following a traumatic SCI. It is therefore vital that efforts be placed on the development of systems to implement preventive measures, vigilant screening, and early treatment. In particular, we emphasize the importance of postinjury care in the intensive care setting for those with severe injuries to reduce the occurrence of secondary AE.

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