Predictors of intramedullary lesion expansion rate on MR images of patients with subaxial spinal cord injury

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OBJECT Studies of preclinical spinal cord injury (SCI) in rodents indicate that expansion of intramedullary lesions (IMLs) seen on MR images may be amenable to neuroprotection. In patients with subaxial SCI and motor-complete American Spinal Injury Association (ASIA) Impairment Scale (AIS) Grade A or B, IML expansion has been shown to be approximately 900 $\mu\text{m}/\text{hour}$. In this study, the authors investigated IML expansion in a cohort of patients with subaxial SCI and AIS Grade A, B, C, or D.

METHODS Seventy-eight patients who had at least 2 MRI scans within 6 days of SCI were enrolled. Data were analyzed by regression analysis.

RESULTS In this cohort, the mean age was 45.3 years (SD 18.3 years), 73 patients were injured in a motor vehicle crash, from a fall, or in sport activities, and 77% of them were men. The mean Injury Severity Score (ISS) was 26.7 (SD 16.7), and the AIS grade was A in 23 patients, B in 7, C in 7, and D in 41. The mechanism of injury was distraction in 26 patients, compression in 22, disc/osteophyte complex in 29, and Chance fracture in 1. The mean time between injury onset and the first MRI scan (Interval 1) was 10 hours (SD 8.7 hours), and the mean time to the second MRI scan (Interval 2) was 60 hours (SD 29.6 hours). The mean IML lengths of the first and second MR images were 38.8 mm (SD 20.4 mm) and 51 mm (SD 36.5 mm), respectively. The mean time from the first to the second MRI scan (Interval 3) was 49.9 hours (SD 28.4 hours), and the difference in IML lengths was 12.6 mm (SD 20.7 mm), reflecting an expansion rate of 366 $\mu\text{m}/\text{hour}$ (SD 710 $\mu\text{m}/\text{hour}$). IML expansion in patients with AIS Grades A and B was 918 $\mu\text{m}/\text{hour}$ (SD 828 $\mu\text{m}/\text{hour}$), and for those with AIS Grades C and D, it was 21 $\mu\text{m}/\text{hour}$ (SD 304 $\mu\text{m}/\text{hour}$). Univariate analysis indicated that AIS Grade A or B versus Grades C or D ($p < 0.0001$), traction ($p = 0.0005$), injury morphology ($p < 0.005$), the surgical approach ($p = 0.009$), vertebral artery injury ($p = 0.02$), age ($p < 0.05$), ISS ($p < 0.05$), ASIA motor score ($p < 0.05$), and time to decompression ($p < 0.05$) were all predictors of lesion expansion. In multiple regression analysis, however, the sole determinant of IML expansion was AIS grade ($p < 0.005$).

CONCLUSIONS After traumatic subaxial cervical spine or spinal cord injury, patients with motor-complete injury (AIS Grade A or B) had a significantly higher rate of IML expansion than those with motor-incomplete injury (AIS Grade C or D).

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KEY WORDS trauma; cervical spine; spinal cord injury; MRI

DESPITE significant advances in methods of improving quality of life for people with spinal cord injury (SCI), full characterization of SCI and therapies to alter its course remain elusive. The importance of this condition is evidenced by the fact that every year, 12,000 people in the United States suffer an SCI, with an incidence of 40 per million. The worldwide population of people liv-

ing with SCI is 2.5 million, resulting in immense personal burdens and societal costs.^{3,16,22,33,55,82} Although the means to reverse the initial damage to spinal cord tissues has yet to be discovered, halting the progression of the secondary injury at the molecular level seems promising.^{21,31,64,66,78,81}

The results of preclinical studies in animal models indicate that SCI is not the result of a single static insult. Rather,

ABBREVIATIONS AIS = American Spinal Injury Association (ASIA) Impairment Scale; AMS = ASIA motor score; IML = intramedullary lesion; ISS = Injury Severity Score; MABP = mean arterial blood pressure; MCC = maximum canal compromise; MSCC = maximum spinal cord compression; SCI = spinal cord injury.

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it is a dynamic process defined by a distinctive cascade of molecular events after the initial trauma that creates a graded yet expansive intramedullary lesion (IML) that destroys spinal cord tissues, including endothelial cells, axons, myelin, and cell bodies.^{8,10,13,17,27,30,31,35,40,49,51,65,68} Unlike with motor-complete SCI, hematomyelia is absent in those with motor-incomplete SCI. These patients have axonal swelling and disruption in conjunction with minimal coagulative necrosis of the spinal cord parenchyma.^{1,2,24,26,46,53,59,75}

As evident in experimental models of SCI,^{20,57,64} IML expansion in humans has yet to be fully validated.² At the microscopic level, histopathological studies have shown that IML expansion occurs primarily within the first 24 hours after trauma.^{42,45,48} At the clinical level, analyses of MR images acquired during the first 6 days of injury have shown that patients with motor-complete SCI have significantly longer IMLs than patients with motor-incomplete injury.^{1,2,34,54,61} An attempt to characterize the temporal evolution of these IMLs in motor-complete (American Spinal Injury Association [ASIA] impairment scale [AIS] Grades A and B) subaxial cervical SCI through examination of serial MR images revealed that the rate of rostrocaudal expansion of IML occurred at approximately 900 $\mu\text{m}/\text{hour}$.² Because of the differing clinical courses and outcomes in motor-incomplete SCI (AIS Grades C and D), we sought to verify the rate of IML expansion in this patient population and compare it to the rate found in patients with motor-complete SCI. To our knowledge, no study has examined serial MR images of humans with motor-incomplete SCI.

Because the final IML size seems to correlate with motor function, the ability to halt IML expansion and ultimately reduce the extent of injury can potentially lead to decreased morbidity from SCI. In vivo rodent models of SCI indicate that IML expansion can be mitigated by chemotherapeutic agents.^{50,56,57,64} Thus, full characterization of IML expansion and identification of factors influencing its progression may help identify medical and surgical interventions that could alter the course of SCI and result in improved clinical outcomes.^{2,64} Our hypothesis was that in patients with subaxial cervical spine trauma and SCI, IML expansion remains constant across all AIS grades.

Methods

Design

This was a retrospective analysis of prospectively collected data.

Primary Outcome

We studied the IML expansion rate on MR images of patients with subaxial cervical SCI.

Selection Criteria

Inclusion Criteria

To be included in the study, patients had to have had the following: 1) age older than 15 years, 2) a blunt trauma resulting in subaxial cervical spine fracture dislocations and SCI, 3) diagnosis of an AIS Grade A, B, C, or D injury, and 4) good-quality postresuscitation and postoperative

(up to 6 days postinjury) CT and MRI scans (with distinct IML borders) of the cervical spine available.

Exclusion Criteria

Excluded were patients who had the following: 1) a penetrating cervical spine and spinal cord injury, 2) AIS Grade E, 3) traumatic brain injury, 4) only 1 MRI scan or only CT myelograms, 5) a nontraumatic central cord syndrome, and 6) neurological worsening during the study period.

Institutional Review Board Approval

This study was approved by the institutional review board of the University of Maryland School of Medicine.

Management Process

Emergency Medical, Prehospital, Trauma Center, and Critical Care Management

Emergency medical, transportation, trauma resuscitation unit, and inpatient critical care management of patients with SCI was performed according to the guidelines of the Maryland Institute for Emergency Medical Services System and the Congress of Neurological Surgeons/American Association of Neurological Surgeons–approved guidelines for the management of cervical spine and spinal cord injury.^{4,9,41}

Clinical Evaluation and Imaging (CT and MRI) Studies

After patients were resuscitated by volume expansion and blood pressure augmentation⁷³ and considered stable, primary and secondary surveys were performed by medical and surgical staff of the trauma center. Each patient was examined by the neurosurgical staff (attending physician, senior resident, or nurse practitioners) to determine the ASIA motor score (AMS) and AIS grade.⁷⁶ Each patient was then transported to undergo CT scanning of the cervical spine and CT angiography.^{1,2} CT was used to assign a mechanistic phylogeny and stage for each patient according to Allen et al.⁷ After the CT scan, each patient underwent MRI studies of the cervical spine. Patients with electromagnetically activated implants or those with metallic foreign bodies near the spinal column incompatible with MRI underwent CT myelography to rule out the need for spinal cord decompression. Subjects with an intrinsic spinal cord lesion and no spinal cord compression underwent preoperative MRI only; however, those who underwent surgery for spinal cord decompression routinely had at least 1 postoperative MRI scan to verify spinal cord decompression.

Calculation of Maximum Canal Compromise, Maximum Spinal Cord Compression, and IML Expansion Rate

We used T2-weighted images or STIR sequences to determine maximum canal compromise (MCC) and maximum spinal cord compression (MSCC), as originally reported by Fehlings et al. and validated in several independent investigations.^{28,29,38,39,54} The mean interval from the injury to the time of acquisition of the first MRI scan was 10 hours (SD 8.7 hours; range 3–67.2 hours); this period was called Interval 1. The second MRI scan was per-

formed a mean of 60 hours (SD 29.6 hours; range 15–134 hours) after trauma; this time period was called Interval 2. The mean time between the first and second MRI studies was 49.9 hours (SD 28.4 hours; range 9–124 hours) and was called Interval 3. MRI after trauma was used to determine the following parameters: 1) the IML length at the end of Interval 1 (IML1, in millimeters); 2) the sagittal diameter of the spinal canal at the site of skeletal injury (Di , in millimeters); 3) the MCC at the site of injury (in percent); and 4) the MSCC at the site of injury (in percent). The MCC and MSCC were calculated as follows using previously validated formulas:^{29,39}

$$MCC = [(Da + Db)/2 - Di]/(Da + Db)/2 \times 100,$$

where Di is the subaxial cervical spine sagittal diameter at the level of injury, Da is the midsagittal diameter of the spinal canal 1 or 2 motion segments above the level of injury, and Db is the midsagittal diameter of the spinal canal 1 or 2 motion segments below the level of spinal injury. The MSCC was calculated according to the following formula:

$$MSCC = [(da + db)/2 - di]/(da + db)/2 \times 100,$$

where da is the diameter of the spinal cord at a normal segment above the level of SCI, db is the diameter of the spinal cord at a segment below the level of SCI, and di is the diameter of the spinal cord at the level of SCI (Fig. 1).

The second MRI scans were used to measure the rostral-caudal IML length at the end of Interval 2 (IML2, in millimeters). The rate of IML expansion was calculated according to the following formula:

$$\text{rate} = (IML2 - IML1)/(Interval\ 2 - Interval\ 1).$$

Medical Management

Each patient's postresuscitation mean arterial blood pressure (MABP) was kept at approximately 85 mm Hg for 7 days, as recommended, unless not medically advised because of comorbidities or age.^{14,52,73} Methylprednisolone for SCI was part of our medical management protocol from 2005 to 2010.^{44,63} Medical management was continued for each patient in the critical care or intermediate care facility until he or she was discharged to a rehabilitation center.

Closed Reduction

Patients with unilateral or bilateral facet dislocations (flexion distraction Stage 2 or 3) and those with significant compressive flexion injuries (teardrop fractures) underwent attempted closed reduction as a preliminary step before definitive spinal cord decompression. Closed reduction was not attempted for facet subluxations, Chance fractures, or extension injuries. In the majority of patients, closed reduction was performed after the admission CT and MRI studies. It is our practice to apply 5–7 lbs of traction per motion segment (counting from C-1) to complete closed reduction within a maximum interval of 1–2 hours.

Surgery

The surgical procedure prescribed for each individual

FIG. 1. Midsagittal reformatted STIR image obtained 8.5 hours after trauma in a 27-year-old man who was involved in an automobile accident and sustained a C-6 teardrop fracture that resulted in quadriplegia. On admission, his AMS was 27 and his AIS grade was A. He underwent circumferential realignment, decompression, and internal fixation 20 hours after the trauma. The image indicates the Da , Di , Db , da , di , and db , parameters that were used to calculate the MCC and MSCC. The patient continued to have an AMS of 28 and AIS grade of A 11 months after the trauma. See *Calculation of Maximum Canal Compromise, Maximum Spinal Cord Compression, and IML expansion Rate* for the full explanation.

patient was determined by the injury severity, morphology according to Allen's classification, and the presence of spinal instability.^{7,72} Overall, each patient with a facet dislocation, a teardrop fracture, or a vertical distraction

TABLE 1. Characteristics of 78 patients with motor-complete and motor-incomplete subaxial SCIs

Variable	All Patients	Patients w/ Motor-Complete SCI	Patients w/ Motor-Incomplete SCI
No. of patients	78	30	48
Male sex (no. [%])	60 (77)	26 (86.7)	34 (71)
Age (mean [SD]) (yrs)	45.3 (18.3)	33.1 (12.8)	52.8 (17.1)
Mechanism (no. [%])			
Motor vehicle crash	30 (38.5)	17 (56.7)	13 (27)
Fall	26 (33.3)	5 (16.7)	21 (43.8)
Sport	17 (21.8)	6 (20)	11 (23)
Other	5 (6.4)	2 (6.7)	3 (6.3)
Admitting ASIA motor score (mean [SD])	53.6 (35.2)	14.4 (11.5)	78.1 (18.8)
AIS grade (no. [%])			
A	23 (29.5)	23 (76.7)	0 (0.0)
B	7 (9)	7 (23.3)	0 (0.0)
C	7 (9)	0 (0.0)	7 (14.6)
D	41 (52.6)	0 (0.0)	41 (85.4)
Injury severity			
ISS (mean [SD])	26.7 (16.7)	41.5 (17.7)	17.3 (5.4)
Morphology of injury (no. [%])			
Distraction	26 (33.3)	16 (53.3)	10 (20.8)
Compression	22 (28.2)	12 (40.0)	10 (20.8)
Disc/osteophyte complex	29 (37.2)	2 (6.7)	27 (56.3)
Other	1 (1.3)	0 (0)	1 (2.1)
Subaxial sagittal diameter (mean [SD]) (mm ³)	6.8 (2)	7.1 (2.4)	6.7 (1.7)
MCC (mean [SD]) (%)	42.2 (14)	45.9 (16.4)	39.9 (12.3)
MSCC (mean [SD]) (%)	7.5 (22)	5.7 (30.6)	8.6 (15.1)
IML length (mean [SD]) (mm)			
During Interval 1	38.8 (20.4)	59.0 (15.3)	26.3 (10.8)
During Interval 2	51 (36.5)	87.4 (33.5)	28.2 (11.3)
IML expansion rate (mean [SD]) (mm/hr)	366 (712)	920 (820)	20 (340)
Management (no. [%])			
Surgical approach			
Anterior	24 (30.7)	4 (13.3)	20 (41.7)
Posterior	10 (12.8)	1 (3.3)	9 (18.8)
Circumferential	44 (56.5)	25 (83.3)	19 (39.6)
Steroids	47 (60)	25 (83.3)	22 (45.8)
Outcome			
AMS at follow-up (mean [SD])	69.1 (37)	22 (17.5)	94.6 (8.5)
AIS grade at follow-up* (no. [%])			
A	22 (28.2)	22 (81.5)	0 (0)
B	5 (6.5)	5 (18.5)	0 (0.0)
C	2 (2.5)	0 (0.0)	2 (3.9)
D	40 (51.3)	0 (0)	40 (78.4)
E	9 (11.5)	0 (0)	9 (17.7)
Mean follow-up (mos)	21.4	15	31

* Because of their improved conditions, some patients' grades were different at follow-up (motor-complete SCI, n = 27; motor-incomplete SCI, n = 51).

injury underwent surgery via a circumferential approach to ensure that the construct being placed did not fail over time. Any patient with an extension-distraction injury associated with disc/osteophyte complexes or spinal stenosis underwent decompression and fusion via either an anterior

or posterior approach alone, because there were usually no associated facet subluxations or dislocations.^{25,30,50,79}

Follow-Up

After acute care and discharge, each patient was fol-

lowed up to record the full degree of his or her neurosurgical recovery. The majority of the patients were followed up at institutions affiliated with the University of Maryland School of Medicine.

Safeguard for Bias

Selection bias was prevented by controlling for the following variables: MRI and surgical intervention intervals, age, sex, mechanism of injury, Injury Severity Score (ISS), admission and follow-up AMS and AIS grade, Allen et al. morphology phylogenies, vertebral artery injury, MCC, MSCC, closed reduction, steroid protocol, and surgical technique.⁷⁴

Statistical Analysis

We report descriptive statistics as the mean and SD for continuous variables and frequencies and proportions for categorical variables. First, a univariate analysis was conducted to assess the association between any independent variable and the IML expansion rate. Because of the small sample sizes and nonnormal distribution of the outcome variable, a Mann-Whitney U-test or Kruskal-Wallis test was used to examine the association between the IML expansion rate and the categorical independent variables. In addition, a Spearman correlation was used to assess the correlation between the IML expansion rate and the other continuous variables. Finally, we performed a multiple regression analysis to assess the relationships between the IML expansion rate and the independent variables that were significant in the univariate analysis. We used the statistical program Stata SE/12.1 (release 12; Stata Corp LP) for analysis.

Results

From January 2005 to December 2012, 984 patients were admitted to the University of Maryland R Adams Cowley Shock Trauma Center with traumatic subaxial cervical SCI, of whom 78 consecutive subjects were eligible for our study. Table 1 lists the baseline characteristics of these patients along with the injury classifications and management variables. Under the mechanisms of injury in Table 1, the "other" category includes assault and battery in 3 patients and fall of heavy object on the head in 2 patients. On the basis of their AIS grade, we categorized the patients as having motor-complete SCI or motor-incomplete SCI.

Volume Expansion and Blood Pressure Augmentation

Of our 78 patients, 73 had detailed vital signs recorded for the entirety of the period between arrival and the second MRI scan. Of these 73 patients, 22 (30%) had at least 1 episode of an MABP of < 60 mm Hg for at least 15 minutes. Fifty-one patients (70%) had a stable MABP (≥ 60 mm Hg) for the time interval of interest. The average IML expansion was 340 $\mu\text{m}/\text{hour}$ (SD 710 $\mu\text{m}/\text{hour}$) in patients with evidence of assumed ischemic episodes and 410 $\mu\text{m}/\text{hour}$ (SD 737 $\mu\text{m}/\text{hour}$) in patients without evidence of ischemic episodes. This difference was not statistically significant ($p = 0.41$).

CT Scanning and CT Angiography

Fourteen (18%) of 78 patients did not undergo vascular studies. Of the remaining 64 patients, 19 (30%) showed evidence of vertebral artery injury. Vertebral artery injury was on the left side in 7, on the right side in 6, and bilateral in 6 patients. Injury was Grade IV in 14, Grade III in 1, Grade II in 2, and Grade I in 2 patients. The average IML expansion rate was 560 $\mu\text{m}/\text{hour}$ (SD 802 $\mu\text{m}/\text{hour}$) in patients with vertebral artery injury and 390 $\mu\text{m}/\text{hour}$ (SD 743 $\mu\text{m}/\text{hour}$) in patients without vertebral artery injury. Univariate statistical analysis indicated that this difference was significant ($p = 0.02$); however, this difference lost its statistical value in multivariate regression analysis.

MRI Studies

In this investigation, 2 patients underwent CT myelography and 49 patients had an intrinsic spinal cord lesion without spinal cord compression. These patients did not undergo postoperative MRI studies and were excluded from the study. When the IML expansion rate was plotted against the timing of the first MRI acquisition, it was evident that the rate of expansion was faster closer to the time of trauma. The exact time of onset of IML expansion could not be determined from our retrospective data (Fig. 2).

Steroid Protocol

Of the 78 patients in our study, 31 did not receive the steroid protocol, whereas 47 did (30 mg/kg/hour for 15 minutes and 5.4 mg/kg/hour for 24 hours).¹⁵ The average rate of IML expansion was 300 $\mu\text{m}/\text{hour}$ in patients treated with steroids and 409 $\mu\text{m}/\text{hour}$ in patients not treated with steroids. This difference did not achieve statistical significance ($p = 0.198$).

Closed Reduction

Of our 78 patients, traction was not applicable in the 29 patients with SCI because of extension injuries with disc/osteophyte complexes or in the 1 patient with a Chance fracture. Of the 26 patients with distraction injuries, 14 underwent closed reduction, which was successful in 8 patients. Of the 22 patients with compression fractures,

FIG. 2. Scatter plot demonstrating the relationship between the IML expansion rate and the time past injury to the first MRI scan (Interval 1). The expansion rate increases as the MR image acquisition approaches the time of trauma.

FIG. 3. Midsagittal reformatted CT and MR images of the cervical spine of a 20-year-old woman admitted to the trauma resuscitation unit after an automobile accident with an AMS of 89 (AIS Grade D). Forty-two months after decompression and circumferential internal fixation, her AMS was 99 and her AIS grade was D. **A:** Teardrop compression fracture of C-6 (white arrow). **B:** A lesion 32 mm long with high signal intensity 14.4 hours after the trauma (bracket 1). **C:** At 64.8 hours after the injury and after decompression, realignment, and internal fixation, her MR image showed a high-intensity signal that was 35.9 mm long (bracket 2). The IML expansion rate in this patient was 80 $\mu\text{m}/\text{hour}$.

3 underwent closed reduction, all of which were successful. The average IML expansion rate was 880 $\mu\text{m}/\text{hour}$ (SD 900 $\mu\text{m}/\text{hour}$) in patients who had traction and 220 $\mu\text{m}/\text{hour}$ (SD 580 $\mu\text{m}/\text{hour}$) in patients who did not have traction. Univariate statistical analysis indicated that this difference was significant ($p = 0.0005$). The significance, however, was lost in multivariate regression analysis.

Surgical Decompression

Of our 78 patients, the exact time interval between the injury and surgery was unknown for 6 patients. In the remaining 72 patients, 45 (62.5%) underwent surgical intervention less than 24 hours after the trauma, and 27 (37.5%) underwent surgical intervention 24 hours or more after injury. The mean IML rates of expansion in the first and second groups were 500 $\mu\text{m}/\text{hour}$ and 190 $\mu\text{m}/\text{hour}$, respectively. Although this difference seems considerable ($p < 0.05$, univariate analysis), in the multivariate regression analysis, the interval between injury and surgery did not have a statistically significant effect on the rate of lesion expansion.

In this study, anterior, posterior, and circumferential surgical approaches were used in 24, 10, and 44 patients, respectively. The mean IML expansion rates were 152 $\mu\text{m}/\text{hour}$ (SD 345 $\mu\text{m}/\text{hour}$) in patients who underwent either the anterior or posterior surgical approach and 532 $\mu\text{m}/\text{hour}$ (SD 867 $\mu\text{m}/\text{hour}$) in those who underwent the circumferential surgical approach. Univariate statistical analysis indicated that this difference was significant ($p = 0.009$); however, the significance was lost in the multivariate regression statistical analysis.

AIS Grade

The mean rostrocaudal IML lengths seen on the first and second MRI scans were 38.8 mm (SD 20.4 mm) and 51 mm (SD 36.5 mm), resulting in a difference in lesion length of 12.6 mm (SD 20.7 mm) between the 2 scans. As a result, the mean IML expansion rate was found to be 366 $\mu\text{m}/\text{hour}$ (SD 710 $\mu\text{m}/\text{hour}$) for the entire cohort. When lesion expansion was analyzed separately for patients with motor-complete (AIS Grade A or B) and motor-incomplete (AIS Grade C or D) SCI, the rate was significantly different. The mean rate of lesion expansion in patients with AIS Grade A or B was found to be 918 $\mu\text{m}/\text{hour}$ (SD 828 $\mu\text{m}/\text{hour}$), whereas that in those with AIS Grade C or D was much lower (21 $\mu\text{m}/\text{hour}$ [SD 304 $\mu\text{m}/\text{hour}$]). In comparison with the rapid rate of expansion seen in patients with motor-complete SCI, the rate in patients with motor-incomplete SCI was nearly static and even showed regression in some patients.

Case 1

A 20-year-old woman sustained injury in a motor vehicle crash and was admitted to our center with an AMS of 89 and AIS grade of D. CT scanning revealed a C-6 compressive flexion Stage 3 injury. The IML length on the admission MR images, acquired 14.4 hours after the accident, was 32.0 mm, and the IML length in the second MR images, acquired 64.8 hours after injury, was 35.9 mm. The rate of IML expansion was 80 $\mu\text{m}/\text{hour}$. Forty-two months after the trauma, her AMS was 99 and AIS grade was D (Fig. 3).

FIG. 4. Midsagittal preoperative (**A** and **B**) and postoperative (**C** and **D**) CT and MR images of a 25-year-old man who sustained a traumatic C-5 compression fracture. At the time of admission, his AMS was 12 and his AIS grade was A. Ten months after injury, he remained quadriplegic. Shown are a C-5 teardrop fracture (**A**) (white arrow), a preoperative MR image 4.5 hours after injury with an intramedullary high-intensity signal measuring 76.2 mm in length (**B**) (bracket E), a postoperative CT image (**C**), and a postoperative MR image 44 hours after injury demonstrating an IML measuring 259 mm in length (**D**) (bracket F). The IML expansion rate was 3200 $\mu\text{m}/\text{hour}$.

Case 2

While trimming a tree branch, a 25-year-old man sustained a C-5 teardrop (compressive flexion Allen Stage 4)⁷ fracture and became quadriplegic. His admission AMS was 12 and AIS grade was A. The IML length on the admission MR images, acquired 4.5 hours after injury, was 76.2 mm, and the IML length on the postoperative MR images acquired 44 hours after admission was 205.9 mm. The rate of expansion was 3200 $\mu\text{m}/\text{hour}$ (Fig. 4).

Statistical Findings

Univariate analysis of 9 prognostic indicators revealed that age ($p = 0.05$; Fig. 5), ISS ($p = 0.05$), admission AMS ($p = 0.05$; Fig. 6), time between injury and surgery ($p = 0.05$; Fig. 7), injury morphology ($p = 0.005$; Fig. 8), and SCI severity (AIS Grade A or B vs AIS Grade C or D, $p < 0.0001$; Fig. 9) affected the IML expansion rate. When analyzed by regression analysis, however, only AIS grade significantly influenced the IML expansion rate ($p = 0.005$) (Table 2).

Discussion

Analyses of the data from this investigation indicate that AIS grade significantly influences the lesion expansion rate after traumatic SCI.

Light and electron microscopic studies in animal models of traumatic SCI by Dohrmann et al. and Wagner et al.^{23,24,75} indicated that within 5 minutes of a compressive and contusive SCI, congestion of venules in the capillary-rich central gray matter was followed by a break in endothelial integrity and extravasation of red blood cells, producing hematomyelia. Microangiographic studies by

Fairholm and Turnbull²⁶ revealed a fluffy extravasation of contrast material in the central part of the spinal cord within 10 minutes.^{5,6,23,24,26,69,70,75} From 4 to 7 days after SCI, capillary perfusion in the central gray matter was disrupted permanently and replaced by myelomalacia and coagulative necrosis.²⁵ Numerous preclinical studies have indicated that immediately after SCI, the disruption of endothelial cells, axons, and the cytoskeleton, in association with molecular cascades and ionic imbalances, results in cytotoxic and vasogenic spinal cord edema, collectively labeled “secondary injury.”^{11–13,17–19,26,35,36,43,62,65,67,68}

The results of combined MRI and necropsy investigations by Quencer et al.,⁵⁹ Jimenez et al.,⁴⁶ and Martin et al.⁵³ of patients who died within a few days after acute traumatic central cord syndrome indicated that axonal swelling and disruption in association with minimal co-

FIG. 5. Scatter plot illustrating a progressive decline in IML expansion with increased patient age.

FIG. 6. Scatter plot demonstrating the relationship between the IML expansion rate and AMS at admission. Lower AMSs tended to have faster IML expansion rates.

agulative necrosis of gray matter are visualized as a high-intensity signal IML on T2-weighted MR images. These patients with partial SCI did not show hematomyelia in histological sections. Similarly, none of the patients with AIS Grade C or D in our investigation had hematomyelia on MRI. In contrast, studies of patients with complete subaxial SCI since the 1990s have clearly depicted associated intramedullary hematomyelia and swelling, as seen in our investigation in the patients with motor-complete SCI.^{1,2,34,54,60,61} Hematomyelia was often seen in complete SCI in association with an IML length that exceeded a single motion segment in the studies of Flanders et al.,³⁴ Schaefer et al.,⁶¹ and Miyanji et al.,⁵⁴ who demonstrated a relationship between injury severity and IML length.² In 2007, Miyanji et al.⁵⁴ reported on the IML length in patients with complete versus those with incomplete SCI. In their study, IML length was approximately 20 mm in incomplete injuries and reached up to 40 mm in complete injuries. Further expansion of this concept was seen in 2012, when Aarabi et al.² reported that IML length on MR images is a dynamic phenomenon with an expansion rate of 900 $\mu\text{m}/\text{hour}$. In the present investigation, applying a regression model to control for age, ISS, inpatient hypotensive episodes, injury morphology, vertebral artery injuries,

FIG. 7. Scatter plot depicting the relationship between time to surgery and the IML expansion rate.

FIG. 8. Histogram showing the relationship between injury morphology and the IML expansion rate. DISC/OST = disc/osteophyte complex.

performance of closed reduction, steroid protocol, operative technique, and the timing of decompression, the expansive character of the IML in patients with motor-complete SCI was validated to be close to 920 $\mu\text{m}/\text{hour}$. To our surprise, however, in patients with motor-incomplete SCI (AIS Grades C and D), the IML length-expansion rate was almost static (20 $\mu\text{m}/\text{hour}$; Fig. 9) without the aggressive expansive character observed in patients with motor-complete SCI (AIS A and B).

In vivo preclinical MRI studies by Nout et al.,⁵⁷ Chou et al.,²⁰ and Simard et al.⁶⁴ indicated that not only is an IML clearly demonstrated in experimental animals, but expansion of the lesion may also respond to neuroprotection.³⁷ In those investigations, hypertonic saline, S-nitrosoglutathione, and glibenclamide slowed the progression of the molecular cascades seen in secondary injury, thereby shortening the final IML length. Our present investigation supports the notion that secondary injury may be much more intense in patients with motor-complete SCI than in those with incomplete SCI and may require the initiation of more aggressive neuroprotection at an earlier time to attenuate IML expansion.

Considering the nearly static nature of the IML in motor-incomplete subaxial cervical SCI, one possible implication of this study is the potential difference between patients with motor-incomplete and those with motor-complete

FIG. 9. Histogram illustrating the relationship between AIS grade and the IML expansion rate.

TABLE 2. Multiple regression model indicating significance of multiple independent variables as predictors of the IML rate of expansion

Independent Variable	Coefficient (95% CI)	p Value
Age	0.0056 (−0.0065 to 0.0179)	0.93
ISS	−0.0022 (−0.0148 to 0.0102)	0.718
AMS	−0.0002 (−0.0095 to 0.0090)	0.956
TPI to surgery	0.0022 (−0.0051 to 0.0096)	0.546
Accidental fall	−0.1303 (−0.5231 to 0.2625)	0.510
Sport injury	0.0239 (−0.3471 to 0.3949)	0.898
Compression injury	0.631 (−0.3765 to 0.5029)	0.775
Disc-osteophyte injury	−0.0045 (−0.4252 to 0.4161)	0.983
Traction	0.1932 (−0.1572 to 0.5436)	0.275
AIS Grades A & B vs Grades C & D	1.0452 (0.3244 to 1.769)	0.005*
Constant	−0.2618 (−1.2950 to 0.7714)	0.614

CI = confidence interval; TPI = time past injury.

* Statistically significant.

SCI in terms of level of urgency for neuroprotection and timing of decompression. Many of the exigencies considered vital for the management of motor-complete SCIs, such as early initiation of therapy for neuroprotection and the timing of decompression, may not apply to motor-incomplete SCI as well as to acute traumatic central cord syndrome.^{1,58,71,73} In addition, the seemingly significant effects manifested by traction, the timing of decompression, and surgical technique may simply reflect increased injury severity contributing to greater spinal cord swelling and a faster IML expansion rate.^{32,47,77,79,80}

There are limitations to this study. Because the study was retrospective, the allocation of Intervals 1, 2, and 3 to patients was inherently heterogeneous. Also, considering the small number of patients and their uneven distribution in each category, statistical findings should be interpreted with caution. The findings of this investigation should be validated by a prospective multicenter study.

Conclusions

The results of previous MRI studies of patients with SCI suggest that those with incomplete SCI do not harbor hematomyelia; instead, the high-intensity signal seen on MR images is indicative of swollen and interrupted axons, primarily in the dorsolateral funiculi of the involved spinal cord segments. In addition, IML length has been reported to be longer in patients with motor-complete SCI. Further expanding on these previous findings, results of the present investigation indicate that the IML in motor-complete SCI expands aggressively in association with significant swelling, whereas the IML in patients with motor-incomplete SCI is almost static with little expansion, and in some cases regression, over time. One potential implication of these findings is that the pursuit of neuroprotection should be more aggressive and earlier to interrupt the expansion of the molecular cascades forming the foundation of secondary injury.

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