Article published online: 2022-06-03

Original Article

Predicting the Role of Preoperative Intramedullary Lesion Length and Early Decompressive Surgery in ASIA Impairment Scale Grade Improvement Following Subaxial Traumatic Cervical Spinal Cord Injury

Raj Kamal[1] Himanshu Verma[1] Sunil Narasimhaiah[1] Suruchi Chopra[2]

[1] Department of Neurosurgery, Escorts Hospital, Amritsar, Punjab, India
[2] Department of Radiology, Escorts Hospital, Amritsar, Punjab, India

Address for correspondence Raj Kamal, MS, MCh, Department of Neurosurgery, Escorts Hospital, Sehaj Enclave, Amritsar, Punjab 143001, India (e-mail: dr_rkamal@yahoo.com).

J Neurol Surg A Cent Eur Neurosurg 2023;84:144–156.

Abstract

Background Traumatic cervical spinal cord injury (TCSCI) is a disabling condition with uncertain neurologic recovery. Clinical and preclinical studies have suggested early surgical decompression and other measures of neuroprotection improve neurologic outcome. We investigated the role of intramedullary lesion length (IMLL) on preoperative magnetic resonance imaging (MRI) and the effect of early cervical decompressive surgery on ASIA impairment scale (AIS) grade improvement following TCSCI.

Methods In this retrospective study, we investigated 34 TCSCI patients who were admitted over a 12-year period, from January 1, 2008 to January 31, 2020. We studied the patient demographics, mode of injury, IMLL and timing of surgical decompression. The IMLL is defined as the total length of edema and contusion/hemorrhage within the cord. Short tau inversion recovery (STIR) sequences or T2-weighted MR imaging with fat saturation increases the clarity of edema and depicts abnormalities in the spinal cord. All patients included had confirmed adequate spinal cord decompression with cervical fixation and a follow-up of at least 6 months.

Results Of the 34 patients, 16 patients were operated on within 24 hours (early surgery group) and 18 patients were operated on more than 24 hours after trauma (delayed surgery group). In the early surgery group, 13 (81.3%) patients had improvement of at least one AIS grade, whereas in the delayed surgery group, AIS grade improvement was seen in only in 8 (44.5%) patients (early vs. late surgery; odds ratio [OR] = 1.828; 95% confidence interval [CI]: 1.036–3.225). In multivariate regression analysis coefficients, the timing of surgery and intramedullary edema length on MRI were the most significant factors in improving the AIS grade following cervical SCI. Timing of surgery as a unique variance predicted AIS grade improvement significantly

Keywords
- ► spinal cord injury
- ► intramedullary length lesion (IMLL)
- ► neuroprotection
- ► MRI
- ► early cervical decompressive surgery

received September 13, 2020
accepted after revision September 15, 2021
article published online June 3, 2022

DOI https://doi.org/10.1055/s-0041-1740379.
ISSN 2193-6315.

($p < 0.001$). The mean IMLL was 41.47 mm (standard deviation [SD]: 18.35; range: 20–87 mm). IMLL was a predictor of AIS grade improvement on long-term outcome in bivariate analysis ($p < 0.001$). This study suggests that patients who had IMLL of less than 30 mm had a better chance of grade conversion irrespective of the timing of surgery. Patients with an IMLL of 31 to 60 mm had chances of better grade conversion after early surgery. A longer IMLL predicts lack of improvement ($p < 0.05$). If the IMLL is greater than 61 mm, the probability of nonconversion of AIS grade is higher, even if the patient is operated on within 24 hours of trauma.

Conclusion Surgical decompression within 24 hours of trauma and shorter preoperative IMLL are significantly associated with improved neurologic outcome, reflected by better AIS grade improvement at 6 months' follow-up. The IMLL on preoperative MRI can reliably predict outcome after 6 months. The present study suggests that patients have lesser chances of AIS grade improvement when the IMLL is ≥61 mm.

Introduction

Spinal cord injury (SCI) is a disabling neurologic condition with a significant socioeconomic impact on injured patients and their families. Global prevalence rates of traumatic SCI varied from approximately 250 per million to 906 per million and data on incidence varied from approximately 8 to 49.1 per million.[1,2] The major cause of injury in the developed world is motor vehicle accidents as compared with two-wheeler accidents in Southeast Asia.[3]

Traumatic cervical spinal cord injury (TCSCI) affects the subaxial cervical spine with or without fracture and dislocations. TCSCI clinically can present as an incomplete injury with tetraparesis and sensory loss,[4] whereas more severe injury results in tetraplegia with complete sensory loss below the level of injury. The American Spinal Injury Association (ASIA) Impairment Scale (AIS) is used commonly in grading the degree of sensory and motor impairment.[5]

The initial injury to the spinal cord at the time of an accident is known as a primary injury. Spinal cord injury is caused by fractured vertebrae, herniated ruptured disk, and ligaments.[5–9] The force of impact directly damages both ascending and descending pathways in the spinal cord and disrupts blood vessels and cell membranes[10–13] causing spinal shock, hypotension, cord ischemia, ionic imbalance, and accumulation of neurotransmitter at the injured site.[14,15] The secondary injury to the cord follows primary damage, causing further loss of remaining viable neurons in the vicinity. Secondary injury can be divided into acute, subacute, intermediate, and chronic phases.[14] Within a few minutes of primary injury, the secondary injury begins causing local ischemia, vasospasm, and hypoperfusion.[16–21] Ischemia increases local vascular permeability, compromising the integrity of the blood–spinal cord barrier (BSCB).[21] This disruption of BSCB initiates a rapid influx of inflammatory cells like neutrophils, macrophages that release proinflammatory cytokines.[22] The most common proinflammatory cytokines are tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-1β (IL-1β).[23–25] The release of proinflammatory cytokines, chemokines, nitric oxide, ions, and proteases, results in cell death through apoptosis and necrosis.

The intramedullary lesion on MRI represents the injury resulting from the molecular cascade, as a result of the trigger from primary injury. The intramedullary lesion includes the spinal cord edema and contusion/hemorrhage.[26–29] The spinal cord edema rapidly increases in the first 48 hours after SCI, followed by a gradual decrease in the following 3 weeks.[26,27] It collaborates with acute inflammatory changes in the first 48 hours.[27] MRI can reliably show the extent of cord compression and signs of cord injury.[28] Hematoma in the spinal cord has been associated with a poor neurologic prognosis and is one of the important predictors for neurologic outcome. The intramedullary blood itself leads to necrosis, apoptosis, and impaired regeneration.[29,30]

The primary injury cannot be influenced through treatment, but timely optimum management can reduce or limit secondary damage. early surgical decompression of the spinal cord is neuroprotective.[12,31–36] This neuroprotective effect seems to vary inversely with the time elapsed from injury to decompression.[37–39] In this study, we analyzed the impact of preoperative intramedullary lesion length (IMLL), early surgical decompression, and other factors on AIS grade improvement after 6 months of follow-up. The null hypothesis was that in subaxial TCSCI preoperative IMLL on MRI and early surgical decompression do not affect long-term improvement in AIS grade.

Methods

This study is a retrospective analysis of over 12 years, from January 1, 2008 to January 31, 2020. We selected 34 TCSCI patients who were admitted to a level I trauma center. The inclusion criteria were older than 16 years and younger than 80 years, Glasgow Coma Scale (GCS) score greater than 14, patients with subaxial cervical spine fracture-dislocations, and MRI studies indicating adequate spinal cord

Table 1 Morphology of injury based on AO classification (for detailed classification, see Vaccaro et al[40])

A0: insignificant Injury	B1: posterior tension band injury (Bony)	C: translational injury in any axis displacement
A1: wedge compression fracture	B2: posterior tension band injury (Ligamentous)	
A2: split fracture	B3: anterior tension band injury	
A3: incomplete burst fracture		
A4: complete burst fracture		

Table 2 American Spinal Injury Association scale (ASIA) Impairment Scale (AIS) grade according to International Standards for Neurological Classification-1 (ISNC-1)

A	Complete. No sensory or motor function is preserved below the level of injury
B	Sensory incomplete. Sensory but no motor function is preserved below the motor level on either side of the body
C	Motor incomplete. Motor function is preserved, but less than half of key muscle functions below the single neurologic level of injury (NLI) have a muscle grade <3
D	Motor incomplete. Motor incomplete status as defined above, with at least half (or more) of key muscle functions below the single NLI having a muscle grade ≥ 3
E	Normal

decompression following surgery and follow-up of at least 6 months after the trauma. Patients who had upper cervical SCI, inadequate spinal cord decompression on MRI, and patients on conservative treatment were excluded. We studied patient demographics, mode of injury, MRI findings, and time between trauma and surgical decompression. The IMLL is defined as the total length of edema and contusion/hemorrhage within the cervical cord. The morphology of injury was based on AO Spine classification. The injuries were classified into A0, A1–A4, B1–B3, and C (►**Table 1**).[40] After admission, the clinical parameters studied were ASIA motor score (AMS), ASIA sensory score (ASS), and the overall AIS grade.[5] The improvement of AIS grade was defined as an improvement of at least one grade (►**Table 2**).

MRI was performed using a 1.5-T MRI. The study included T1-weighted, T2-weighted, and short tau inversion recovery (STIR) sequences in sagittal and axial planes. Using STIR or T2-weighted imaging with fat saturation increases the clarity of edema in the bones and ligaments and depicts abnormalities in the spinal cord, disks, and epidural space (►**Figs. 1** and **2**). Preoperative MRI was made in all the cases to delineate the degree of spinal cord compression, the extent of cord edema, presence of hematoma, and spinal stenosis. IMLL was measured in preoperative MRI for reference. Postoperative and follow-up MRI scans were obtained to evaluate the extent of spinal cord decompression and the course of the spinal cord lesion over time (►**Figs. 1** and **2**). We divided IMLL into three groups[41–43]: (1) less than 30 mm, (2). 31 to 60 mm, and (3) greater than 61 mm. The rationale behind this grouping is that by dividing continuous data into three categories, it is more effective to correlate data without sacrificing the interpretability.[43]

All patients were medically stabilized before surgery,[37,44] intubated, and put on a ventilator if necessary. Preoperative cervical traction was used in 18 patients using Gardner-Wells tongs under fluoroscopy. We used 2.25 kg of weight per segment, not exceeding 20 kg. In most cases, a closed reduction of facet dislocation was achieved. Methylprednisolone was given if trauma was within 8 hours as per recommendations of the second National Acute Spinal Cord Injury Study (NASCIS-2) study.[44]

Patients who underwent decompressive surgery with fixation had either early surgery ($\leq$24 hours after trauma) or late surgery ($\geq$24 hours after trauma). We operated as soon as possible after medical stabilization, but we classified our patients as per the Surgical Timing in Acute Spinal Cord Injury (STASCIS) study into early surgery and late surgery.[37] The timimg of surgery depended on patient arrival at a hospital emergency ward, the time required for medical stabilization, and the time required for necessary diagnostic investigation and documentation.[37] Cervical cord decompression was done from either the anterior or the posterior approach. In a few cases, both approaches were used. Spinal fixation was done in all cases whether it was an anterior or posterior approach.[45,46] The neurologic status was recorded at the 6-month follow-up. The 6 months of follow-up was based on recommendations used in the STASCIS, NASCIS, and Sygen trials.[37–52] The AIS improvement of one grade represented grade conversion.[13,27,45]

Statistical analysis was performed using the IBM SPSS classic version. The descriptive analysis was done as a mean and standard deviation (SD) for continuous variables and frequencies for categorical variables. The correlation was analyzed using bivariate analysis calculating the Pearson coefficient and its significance (►**Figs. S1**, **S2**, available online only). Multiregression analysis was done using grade improvement as a dependent variable, and grades on admission, mechanism of injury, IMLL, presence of hemorrhage/contusion, timing of surgery were independent variables.

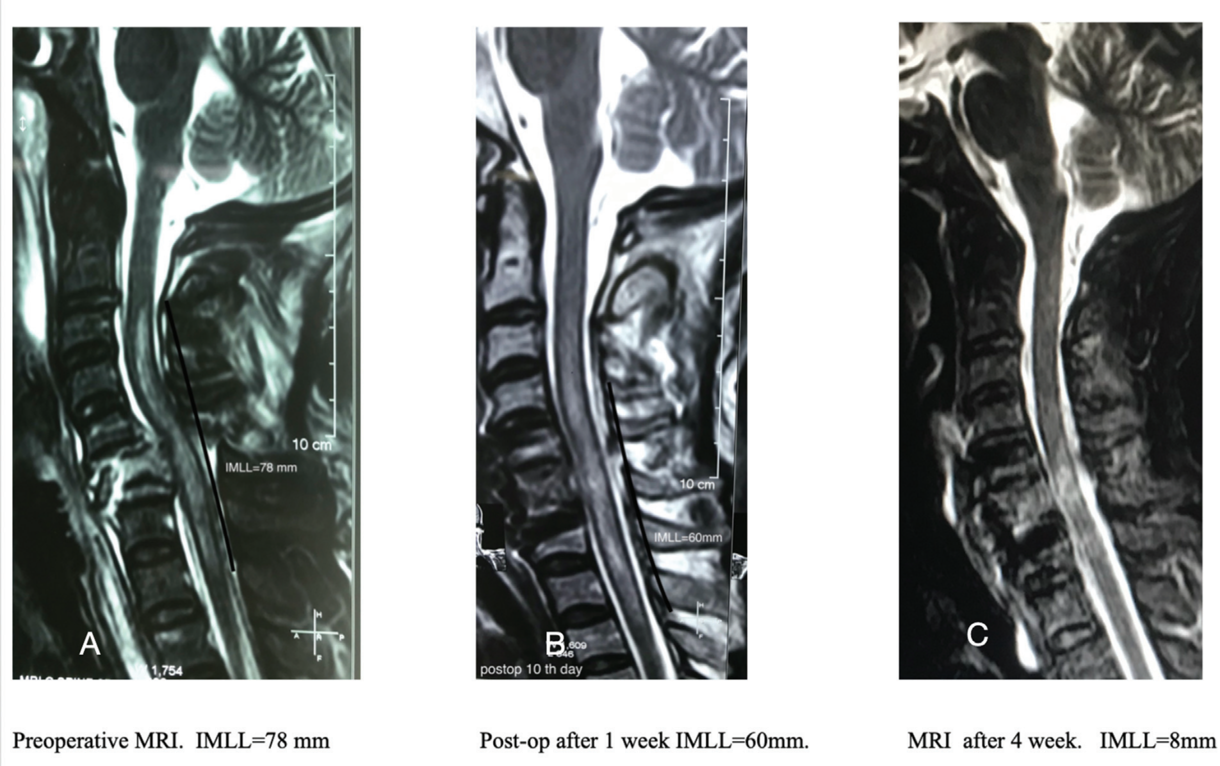

Fig. 1 A 55-year-old woman sustained a fall and was brought to the emergency room 6 hours after trauma. At the time of admission, she was hypotensive and on a ventilator. Her American Spinal Injury Association scale (ASIA) Impairment Scale (AIS) grade was B. (**A**) Preoperative magnetic resonance imaging (MRI) of the cervical spine showed C6 vertebral body fracture with retropulsed fragment causing significant cervical cord compressive injury with bleeding at the epicenter and spinal cord edema extending from C3 to C8. It also shows a bright T2-weighted signal in the surrounding ligaments that is suggestive of disruption. The intramedullary lesion length (IMLL) was 78 mm. She underwent anterior cervical fusion within 24 hours resulting in proper realignment of the spinal column. (**B**) Postoperative MRI taken after 1 week of surgery indicated good decompression with significant improvement of intramedullary edema (IMLL = 60 mm). (**C**) MRI after 4 weeks showed a further decrease in IMLL to 8 mm. Six months later, her AIS grade was D.

Results

A total of 34 patients were included in this study. The mean age was 54.06 ± 15.44 years (range: 18–80 years). Twenty-nine (85.3%) patients were males and 5 (14.7%) were females (►**Table 3**). Of the 34 patients, 16 patients were operated on within 24 hours after SCI and were considered the early surgery group (►**Table 3**). Eighteen patients were operated on more than 24 hours after SCI and they were designated as the delayed surgery group. In the early surgery cohort, the mean age was 50.6 ± 19.6 with 13 males (81.3%) and 3 females (18.7%). In the late surgery cohort, the mean age was 57 ± 11.0 years with 16 males (88.9%) and 2 females (11.1%). Overall TCSCI was caused by a fall in 19 (55.9%) patients, motor vehicular accidents in 13 (38.2%) patients, and sports injury in 2 patients (►**Table 3**).

Among the patients, 30.8% of AIS grade A, 80.0% of AIS grade B, and 81.8% of AIS grade C at admission improved to a better AIS grade during 6 months of follow-up ($p < 0.05$; ►**Table 4**). The mean age of patients who improved to a better AIS grade was 52.48 ± 17.26 years, whereas the mean age of patients who did not show improvement was 56.62 ± 12.16 years. In the early surgery group, 13 (81.3%) patients had an AIS grade improvement of at least one grade, whereas 3 (18.7%) patients did not improve (►**Table 3**). In the delayed group (≥24 hours after trauma), AIS grade improvement was seen in 8 (44.5%) patients (early vs. late surgery: odds ratio [OR] = 1.828; 95% confidence interval [CI]: 1.036–3.225).

We performed multiregression analysis using grade improvement as a dependent variable, and timing of surgery, IMLL, presence of hemorrhage/contusion, mechanism of injury, grade on admission as independent variables. In the model summary (►**Fig. S1**, available online only) of multiregression analysis, R^2 is 0.55. This means that the contribution of these factors was 55% in grade improvement. Analysis of variance (ANOVA) of the regression model suggests the overall contribution being significant ($p < 0.001$; $R^2 = 0.55$). In the final step of regression analysis coefficients, IMLL and timing of surgery were the most significant factors related to AIS grade improvement (►**Fig. S1**, available online only). The timing of surgery as a unique variance predicted AIS grade improvement better ($p < 0.001$).

In our study, the mean IMLL was 41.47 mm (SD: 18.35; range: 20–87 mm). IMLL on preoperative MRI was a significant predictor of grade conversion in bivariate analysis ($p < 0.001$) (►**Fig. S2**, available online only). Longer IMLL

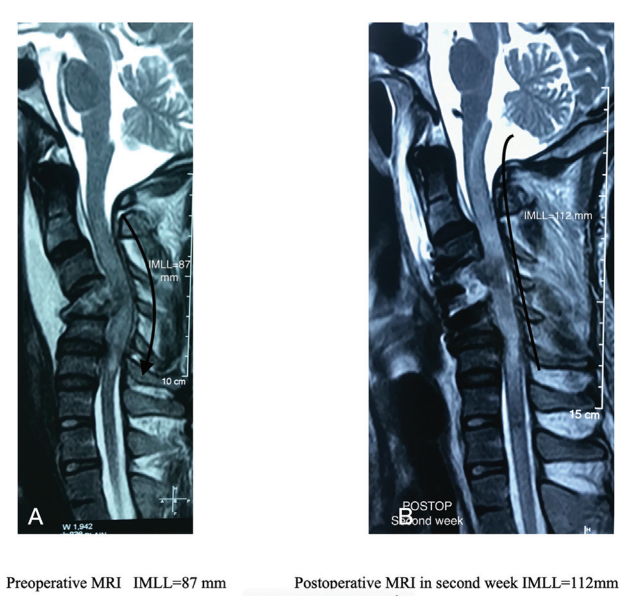

Fig. 2 A 24-year-old man who suffered an automobile accident and was transferred to our hospital with acute cervical spinal cord injury resulting in respiratory distress and quadriplegia. His American Spinal Injury Association scale (ASIA) Impairment Scale (AIS) grade was A. He was intubated and put on ventilator support. (**A**) Magnetic resonance imaging (MRI) of the cervical spine was done, which showed a C4 vertebral body fracture with retropulsed segment causing severe cord compression and significant contusion with long-segment cord edema (intramedullary lesion length [IMLL] = 87 mm). He underwent early C4 anterior corpectomy and fusion. (**B**) Postoperative MRI done after 1 week showed severe cord swelling and an increase of the IMLLto112 mm, now extending from the craniocervical junction to D1. Moderate cord compression was still present at the C5/C6 level, which was one level below the injury level. This was probably related to a preexisting degenerative change at the C5/C6 level. Postoperatively, his AIS grade did not improve and remained grade A.

on preoperative MRI predicted poor AIS grade conversion after 6 months as depicted in ►**Figs. 3** and **4**. AIS grade A patients had a mean IMLL of 57.54 ± 19.4 mm, AIS grade B of 35.2 ± 8.30 mm, and AIS grade C of 28.2 ± 5.25 mm.

There were 12 patients in whom IMLL was ≤30 mm, 15 patients had IMLL of 31 to 60 mm, and 7 patients had IMLL ≥61 mm. In the first group (IMLL ≤ 30 mm), AIS grade improvement of at least one grade was seen in 10 patients (83.3%). Four patients had early surgery and all four patients improved (►**Table 5**). Eight patients underwent late surgery, out of which six patients (75%) improved ($p = 0.317$; 95% CI: −0.778 – 0.278). In the second group (IMLL: 31–60 mm), 10 patients (66.6%) showed grade improvement ($p < 0.05$). Out of nine patients who had early surgery (≤24 hours of admission), eight patients improved, whereas two patients who had late surgery improved. In the third group with IMLL ≥61 mm, three patients had early surgery and four patients underwent late surgery. Only one patient who was operated on within 24 hours had agrade conversion ($p = 0.236$).

The probability of grade improvement is higher with shorter IMLL (►**Fig. S1**, available online only). A longer IMLL predicts lack of improvement ($p < 0.05$). If the IMLL is more than 61 mm, the probability of nonconversion of AIS grade is higher, irrespective of the timing of surgery. These findings rejected our null hypothesis.

The AMS on admission was 28.32 ± 15 for the whole cohort. The AMS of patients who converted to a better AIS grade was 33.67 ± 12.48 ($p < 0.05$). Patients who did not show any grade improvement had a mean AMS score of 19.69 ± 15.14. The ASS of the patients on admission was 56.7 ± 27.27. The ASS of patients who had grade conversion was 61.43 ± 23.6 and the ASS of those who did not convert to a better grade was 49 ± 31.9 ($p > 0.05$).

An intramedullary hemorrhage was present on preoperative MRI at the epicenter of injury in 13 (38.2%) patients. Nine (69.2%) patients with intramedullary hemorrhage did not improve after 6 months of follow-up. This was significant on univariate analysis ($p = 0.005$), but not on multiregression analysis (►**Table 3**).

Discussion

This study analyzed factors such as admission AMS, AIS grade, injury morphology, the timing of surgery, surgical approach, presence of intramedullary hemorrhage, and IMLL on AIS grade conversion at 6 months after TCSCI. On multiregression analysis, using grade improvement as a dependent variable, preoperative IMLL and early surgery were the two most significant factors that predicted AIS grade improvement.

In this series, there was a significant association between preoperative IMLL and AIS grade conversion ($p = 0.03$). Our AIS grade conversion rates were similar to results reported by Marino et al[46] and Aarabi et al[42] (►**Table 4**).

Patients who had a mean preoperative IMLL of 33.71 ± 9.96 mm had grade conversion, whereas patients who had no grade conversion had a mean IMLL of 54 ± 22.05 mm ($p < 0.001$). In the present study, patients with IMLL less than 30 mm showed better grade improvement irrespective of the timing of surgery. This is because shorter IMLL indicated less severe SCI (►**Figs. 3** and **4**). Patients with IMLL between 31 and 60 mm had more often grade conversion with early surgery. Probably, the observed effect was related to a prevention of secondary cord damage by early adequate decompressive surgery. Patients with IMLL greater than 61 mm had a lesser probability of AIS grade improvement irrespective of early or late surgery (►**Fig. 2**). In these patients, delayed surgical decompression is justified.

The IMLL on MRI is proportional to the severity of the primary and secondary injuries.[13,15,27,36,53–59]

Parashari et al[41] studied the prognostic role of MRI and its association with the clinical outcome and concluded that chances of improvement were more in patients with cord edema involving less than 3 cm of the spinal cord than patients with cord edema involving greater than 3 cm of the spinal cord.

According to Aarabi et al,[42] patients who had IMLL close to 62.4 mm and adequate decompression had a better chance of conversion ($p = 0.001$) than patients with inadequate decompression and an IMLL of 100.3 mm.

Is there an association between preoperative IMLL on MRI and the severity of SCI? In our study, longer IMLL was

Table 3 Patient characteristics and relationship with AIS grade conversion

Characteristics	Frequency	AIS grade conversion: yes	AIS grade conversion: no	Comments
Age (y)	54.06 ± 15.44			
Gender (%)				
Male	29 (85.3)			
Female	5 (14.7)			
Mode of accident (%)				
MVC	13 (38.2)	8 (38.1)	5 (38.5)	$p = 0.904$
Fall	19 (55.9)	12 (57.1)	7 (53.8)	
Others	2 (5.9)	1 (4.8)	1 (7.7)	
AIS at admission (%)				
AIS grade A	13 (38.2)	4 (30.8)	9 (69.2)	$p = 0.08$
AIS grade B	10 (29.4)	8 (80)	2 (20)	
AIS grade C	11 (32.4)	9 (81.8)	2 (18.2)	
ASIA Motor Score (AMS)	28.32 ± 15.0	33.67 ± 12.48	19.69 ± 15.14	$p = 0.011$
ASIA Sensory Score (ASS)	56.68 ± 27.2	61.43 ± 23.6	49.0 ± 31.85	$p > 0.05$
Injury morphology (%)				
A0	10 (23.5)	8 (80)	2 (20)	$p = 0.14$
A1–A4	19 (55.9)	12 (63.2)	7 (36.8)	
B1–B3	2 (8.8)	1 (50)	1 (50)	
C	3 (11.8)	0	3 (100)	
Timing of surgery (%)				
Early surgery (≤24 h)	16 (47.1)	13 (81.2)	3 (18.8)	$p = 0.027$
Delayed surgery (≥24 h)	18 (52.9)	8 (44.4)	10 (55.6)	OR: 1.83; 95% CI: 1.036–3.225
Surgical approach (%)				
Anterior	15 (44.1)	11 (73.3)	4 (26.7)	$p = 0.578$
Posterior	17 (50)	8(47)	9 (53)	
Combined	2 (5.9)	2 (100)	[ndash]	
Preoperative IMLL (%)				
group 1; <30 mm	12 (35.3)	10 (83.3)	2 (16.7)	$p = 0.317$; OR: 0.6; 95% CI: 0.36–0.99
Group 2; 31–60 mm	15 (44.1)	10 (66.7)	5 (33.3)	$p < 0.05$; OR: 16; 95% CI: 1.093–234.2
Group 3; >61 mm	7 (20.6)	1 (14.2)	6 (85.8)	$p = 0.236$; OR: 3; 95% CI: 0.968–9.302
Presence of hemorrhage (%)				
Yes	13 (38.2)	4 (30.8)	9 (69.2)	$p = 0.005$; 95% CI: 0.190–0.813
No	21 (61.8)	17 (81)	4 (19)	

Abbreviations: AIS: American Spinal Injury Association impairment scale; ASIA, American Spinal Injury Association scale; ACI, confidence interval; IMLL, intramedullary lesion length; MVC, motor vehicle collision; OR, odds ratio.

associated with more severe AIS grade on admission. Edema and necrosis on MRI represent the injury resulting from molecular cascade as suggested by a preclinical high-field (9.4 T) MRI study on rats.[53,54] This hyperintense signal and lesion length on high-field MRI were the most valuable parameters and were highly correlated to histopathologic changes.[53,54] Several studies have indicated a significant relationship between the severity of SCI, neurologic outcome, and the finding of contusion hemorrhage on MRI.[55–63] In this study, IMLL was delineated in both STIR and T2 images pre- and postoperatively (►**Figs. 1** and **2**).[64,65] Our study infers that preoperative IMLL was a significant predictor of long-term outcome after TCSCI.

The other aspect of IMLL is its expansion after trauma. According to Aarabi et al[27] and Le et al,[66] the rate of expansion of the IMLL differs with the severity of subaxial cervical injury. The speed of expansion measures from 200 µm/h in AIS grade C patients to 900 µm/h in AIS grade

Table 4 Correlation between IMLL and AIS grade conversion

IMLL	No. of patients	Early surgery	AIS grade conversion (%) after early surgery	Delayed surgery	AIS grade conversion (%) after delayed surgery	Significance of early surgery vs. delayed surgery and 1 grade improvement
≤30 mm	12	4	4 (100)	8	6 (75)	$p = 0.317$ OR: 0.6; 95% CI: 0.362–0.995 Not significant
31–60 mm	15	9	8 (88.9)	6	2 (33.3)	$p < 0.05$ OR: 16; 95% CI: 1.093–234.2 Significant
≥61 mm	7	3	None	4	1 (25)	$p = 0.286$ OR: 3; 95% CI: 0.968–9.302 Not significant

Abbreviations: **AIS:** American Spinal Injury Association **impairment** scale; CI, confidence interval; IMLL, intramedullary lesion length; OR, odds ratio.

A and B patients. After a cervical injury, progressive edema and hemorrhage cause severe progressive compression of the cervical cord circumferentially against the dura and the bony structures at multiple levels.[67–69] The spinal cord edema can be reduced through timely and adequate surgical decompression and restoration of alignment[69,70] as shown in ►**Figs. 1**, **2**, **5**, and **6**. Interestingly, it was found that adequate decompression was done in only 66% of AIS grade A and B patients,[71] which resulted in a poor outcome.

In our series, the presence of intramedullary hemorrhage on preoperative MRI was a bad sign for AIS grade conversion. AIS grade conversion occurred only in 30.8% of patients with intramedullary blood (►**Fig. 7**). On multivariate analysis, the IMLL was a stronger predictor of AIS grade conversion than the presence of intramedullary hemorrhage. The possible explanation could be that IMLL includes intramedullary hematoma.[72] Flanders et al[62] reported that hemorrhage is almost always present concurrently with edema, and on MRI it is surrounded by a hyperintensity normally associated with edema.

The greatest lengths of spinal cord edema and hematoma were found in those with the most severe (AIS grades A and B) injuries.[26] Hematoma in the spinal cord was seen in all AIS A and B patients and in 50% of the AIS C patients.[26] The presence of intramedullary hemorrhage was predictive of worse neurologic recovery. The extent of hemorrhage

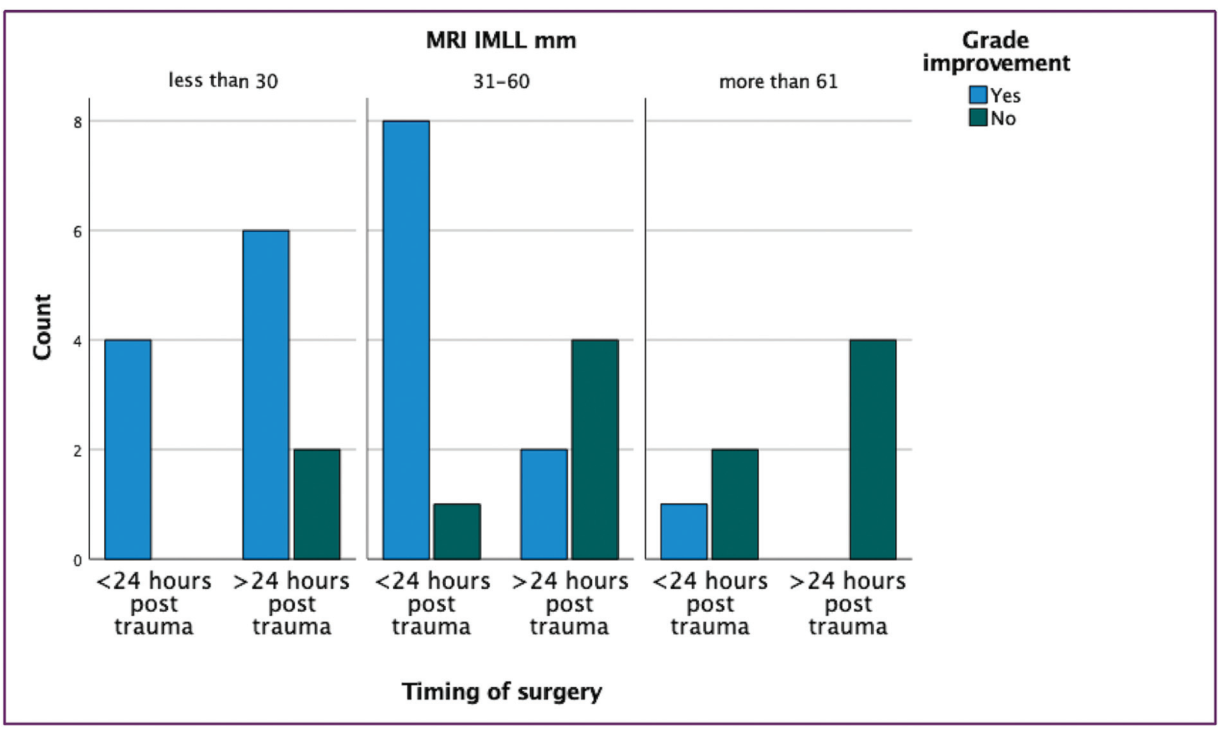

Fig. 3 Bar graph showing the relation between the three groups of intramedullary lesion length (IMLL), grade improvement and timing of surgery.

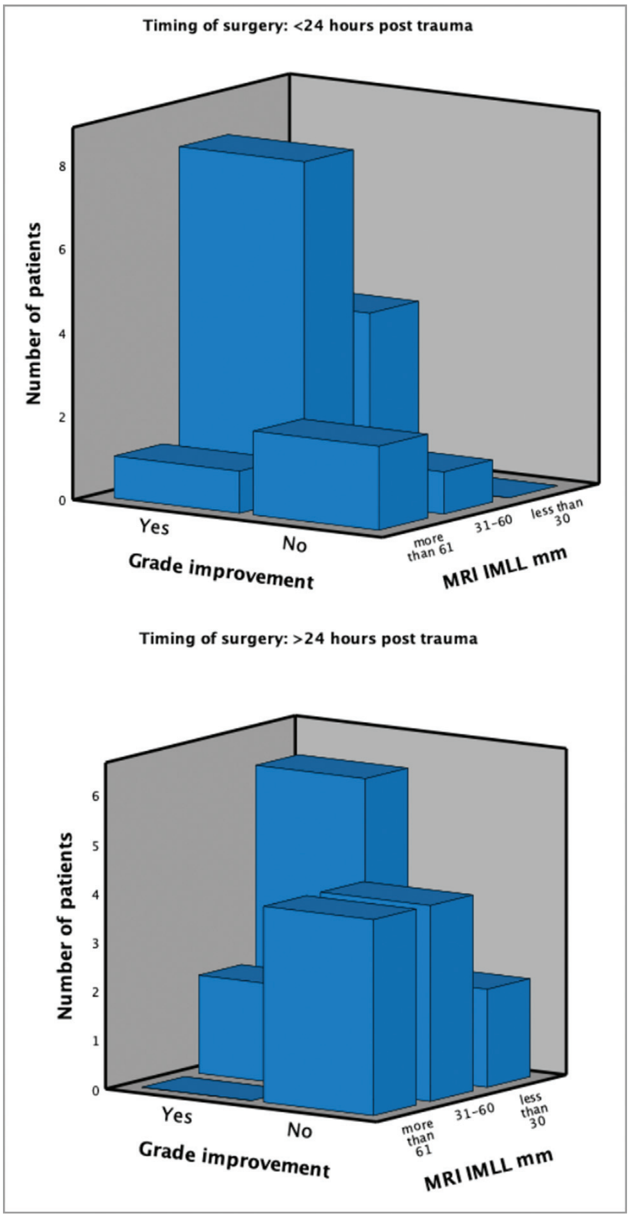

Fig. 4 3D bar graph showing the relation between the three groups of intramedullary lesion length (IMLL),grade improvement and timing of surgery.

within the cord has been correlated with outcome, with a small focus on hemorrhage of less than 4 mm more likely to be associated with radiologic and clinical improvement on follow-up , compared with a larger spinal cord hematoma.[20]

The cervical compression should be relieved early, but the question is how early? In our study, early decompression (≤24 hours) has shown a significant impact on improvement in the AIS scale of at least one grade (►**Fig. 3**). In the early surgery group, 81.3% of patients had an AIS grade improvement, whereas in the delayed group, AIS grade improvement was seen in 44.5% patients only ($p = 0.027$). Early surgical decompression relieves cord compression, preventing further secondary injury.[73–76] The STASCIS trial, published in 2012, was a prospective study of 222 patients undergoing early (<24 hours) versus late (>24 hours) decompression. Patients receiving early surgical intervention were twice as likely to improve by 2 or more AIS grades at 6 months.[37] A prospective Canadian cohort study by Wilson et al[71] suggested that a significant number of patients who underwent early decompression improved by two or more AIS grades. Dvorak et al[77] reported shorter hospital stay after early decompression for patients with ASIA A or B injuries. Studies that performed postoperative MRI indicate that up to 25% of patients may need expansive dura plasty for adequate spinal cord decompression to improve functional outcome.[78–82] Early decompression is recommended in clinical management guidelines by the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons.[83] The recent AO Spine guideline also recommends decompression within 24 hours of SCI.[84] There are advocates of surgery within 12 hours (ultra-early) with better outcome after cervical SCI.[85,86]

There are studies that suggest there is no benefit of early decompression.[75,76,87–94] Aarabi et al[87] concluded that complete decompression of cervical cord, confirmed by postoperative MRI, determines the long-term neurologic outcome and not the timing of surgery. In their study, decompression had been performed either ultra-early (<12 hours) or early (12-24 hours). A study by Vaccaro et al[89] revealed no significant neurologic benefit when cervical spinal cord decompression was performed less than 72 hours after injury as compared with waiting longer than 5 days, whereas a systematic review suggested that decompression within 24 hours resulted in improved outcomes compared with both delayed decompression and conservative treatment.

Neuroprotective measures within the acute phase (48 hours) could also be beneficial. The efficacy of many therapies during the acute phase is still under evaluation like riluzole and minocycline.[95] Both are presently being tested for efficacy and safety in phase III randomized controlled trials. Riluzole is a sodium channel blocking drug that

Table 5 AIS grade conversion (%) in the present series and other series

AIS grade conversion	Spiess et al 2009[45] (%)	Marino et al[46] (%)	Aarabi et al[42] (%)	Current study (%)
A	28.3	29.8	26.9	30.8
B	73.3	75.2	65.5	80
C	79.6	86.2	78.9	81.8

Abbreviations: AIS: American Spinal Injury Association impairment scale; IMLL, intramedullary lesion length.

Fig. 5 A 67-year-old woman sustained a fracture dislocation at C 4–C5 with retrolisthesis of C5 body after a fall from stairs. An initial physical examination showed an American Spinal Injury Association scale (ASIA) impairment scale (AIS) grade A (complete loss of motor and sensory function). She was immediately transported to our hospital (a spinal trauma center). Preoperative magnetic resonance imaging (MRI) of the cervical spine showed C4–C5 dislocation with retrolisthesis of C5 body with cord compression and nonhemorrhagic contusion at the C3–C6 levels with an intramedullary lesion length (IMLL) measuring 46 mm (**A**). First, she was medically stabilized and underwent early (<24 hours) posterior cervical laminectomy and posterior lateral mass screws and rod fixation. Her postoperative MRI after 8 weeks (**B**) showed adequate cervical cord decompression but with myelomalacia at the C5 level. She was discharged after 1 month with AIS B (improvement of grade 1). She was rehabilitated at home and after 6 months her grade improved to AIS grade C. The findings remained the same even after 1 year. This case illustrates that early decompressive surgery in clinically severe cervical injury with MRI showing long segment compression and edema can result in improvement in AIS grade from A to C.

decreases the influx of calcium and prevents the trigger of increased Na^+ influx from continuous activation of voltage-gated Na^+ channels,[96] thus preventing further neuronal damage.[97] Minocycline is an antibiotic that has neuroprotective properties in preclinical studies.[98], It has been shown to reduce apoptosis of oligodendrocytes and microglia and improve neurologic recovery in rodent models of SCI.[99] To date, the most effective clinical treatment to limit tissue damage following primary injury is early surgical decompression (<24 hours postinjury) of the injured spinal cord.[70–72]Overall, the extent of the primary injury determines the severity and outcome of SCI.[83,84]

Limitations

This study has a limitation of being a retrospective, single-center study. Also, the number of patients were low due strict inclusion criteria. Another limitation was not having MRI

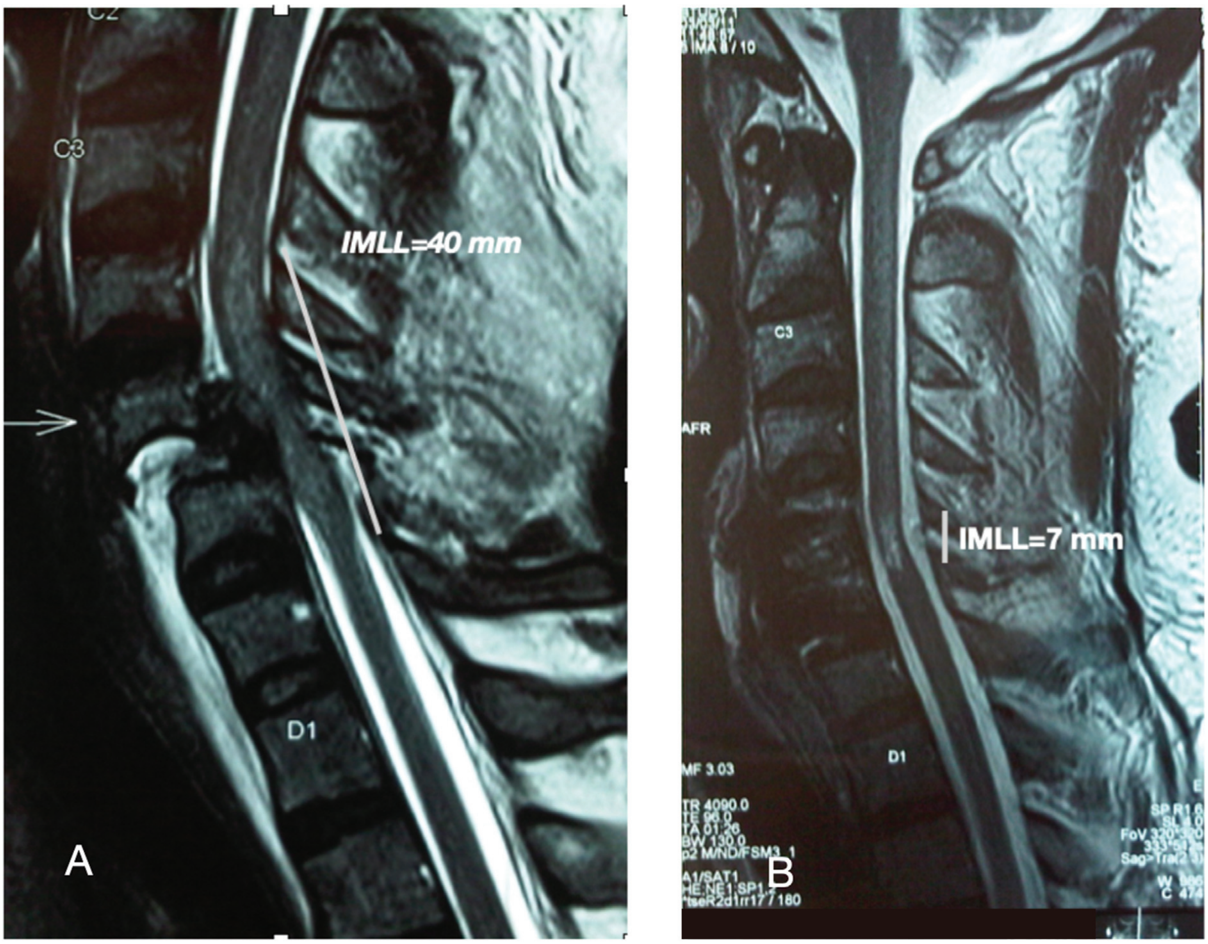

Fig. 6 Pre- and postoperative, midsagittal magnetic resonance imaging (MRI) images of a 44-year-old man who was tetraplegic following cervical injury as a result of a fall from the first floor. His American Spinal Injury Association scale (ASIA) Impairment Scale (AIS) grade was A. Preoperative MRI showed a C5–C6 fracture dislocation, severe spinal cord compression, and an intramedullary lesion of a length of 40 mm (**A**). The patient underwent realignment of the spinal column with C5 corpectomy and anterior cervical plate fixation. His postoperative MRI shows a significant reduction in intramedullary lesion length of 7 mm (**B**). His AIS grade improved after 6 months to AIS grade C.

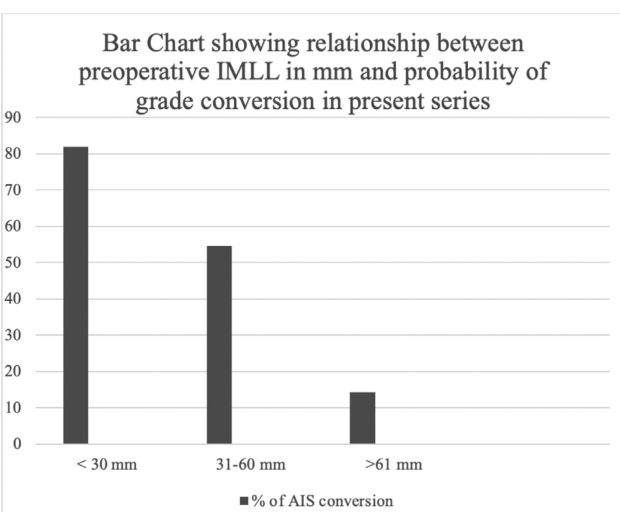

Fig. 7 Bar diagram showing relationship between preoperative IMLL and grade conversion.

prior to trauma to document already preexisting changes in the cervical spine.

Conclusion

Primary injury and early stages of secondary injury of the cervical spinal cord are very well visualized on MRI as an intramedullary lesion . The IMLL on preoperative MRI can reliably predict outcomes after 6 months. Patients who had IMLL of less than 30 mm had a better chance of grade conversion irrespective of the timing of surgery. Patients with an IMLL length of 31 to 60 mm had a higher chance of grade conversion if early surgery is performed. Longer IMLLs (> 61mm) are associated with a higher rate of lacking improvement. Surgical decompression within 24 hours of trauma significantly improves neurologic outcome, reflected by better AIS grade improvement at 6 months of follow-up. Other factors like patient demographics, mechanism of injury, grade on admission, and fracture morphology had no significant effect on long-term prognosis.

Conflict of Interest
None declared.

References

1 Lee BB, Cripps RA, Fitzharris M, Wing PC. The global map for traumatic spinal cord injury epidemiology: update 2011, global incidence rate. Spinal Cord 2014;52(02):110–116
2 Singh A, Tetreault L, Kalsi-Ryan S, Nouri A, Fehlings MG. Global prevalence and incidence of traumatic spinal cord injury. Clin Epidemiol 2014;6:309–331
3 Wyndaele M, Wyndaele JJ. Incidence, prevalence and epidemiology of spinal cord injury: what learns a worldwide literature survey? Spinal Cord 2006;44(09):523–529
4 Zaveri G, Das G. Management of sub-axial cervical spine injuries. Indian J Orthop 2017;51(06):633–652
5 Kirshblum SC, Burns SP, Biering-Sorensen F, et al. International standards for neurological classification of spinal cord injury (revised 2011). J Spinal Cord Med 2011;34(06):535–546
6 Oyinbo CA. Secondary injury mechanisms in traumatic spinal cord injury: a nugget of this multiply cascade. Acta Neurobiol Exp (Warsz) 2011;71(02):281–299
7 Dumont RJ, Okonkwo DO, Verma S, et al. Acute spinal cord injury, part I: pathophysiologic mechanisms. Clin Neuropharmacol 2001;24(05):254–264
8 Sekhon LH, Fehlings MG. Epidemiology, demographics, and pathophysiology of acute spinal cord injury. Spine 2001;26(24, Suppl):S2–S12
9 Tator CH, Fehlings MG. Review of the secondary injury theory of acute spinal cord trauma with emphasis on vascular mechanisms. J Neurosurg 1991;75(01):15–26
10 Choo AM, Liu J, Liu Z, Dvorak M, Tetzlaff W, Oxland TR. Modeling spinal cord contusion, dislocation, and distraction: characterization of vertebral clamps, injury severities, and node of Ranvier deformations. J Neurosci Methods 2009;181(01):6–17
11 Fehlings MG, Smith JS, Kopjar B, et al. Perioperative and delayed complications associated with the surgical treatment of cervical spondylotic myelopathy based on 302 patients from the AOSpine North America Cervical Spondylotic Myelopathy Study. J Neurosurg Spine 2012;16(05):425–432
12 Rowland JW, Hawryluk GW, Kwon B, Fehlings MG. Current status of acute spinal cord injury pathophysiology and emerging therapies: promise on the horizon. Neurosurg Focus 2008;25(05):E2
13 Aarabi B, Olexa J, Chryssikos T, et al. Extent of spinal cord decompression in motor complete (American Spinal Injury Association Impairment Scale Grades A and B) traumatic spinal cord injury patients: post-operative magnetic resonance imaging analysis of standard operative approaches. J Neurotrauma 2019;36(06): 862–876
14 Witiw CD, Fehlings MG. Acute spinal cord injury. J Spinal Disord Tech 2015;28(06):202–210
15 Simard JM, Popovich PG, Tsymbalyuk O, et al. MRI evidence that glibenclamide reduces acute lesion expansion in a rat model of spinal cord injury. Spinal Cord 2013;51(11):823–827
16 Lu K, Liang CL, Chen HJ, et al. Injury severity and cell death mechanisms: effects of concomitant hypovolemic hypotension on spinal cord ischemia-reperfusion in rats. Exp Neurol 2004;185(01): 120–132
17 Alizadeh A, Dyck SM, Karimi-Abdolrezaee S. Traumatic spinal cord injury: an overview of pathophysiology, models and acute injury mechanisms. Front Neurol 2019;10:282
18 Fehlings MG, Tator CH, Linden RD. The relationships among the severity of spinal cord injury, motor and somatosensory evoked potentials and spinal cord blood flow. Electroencephalogr Clin Neurophysiol 1989;74(04):241–259
19 Anthes DL, Theriault E, Tator CH. Ultrastructural evidence for arteriolar vasospasm after spinal cord trauma. Neurosurgery 1996;39(04):804–814
20 Furlan JC, Fehlings MG. Cardiovascular complications after acute spinal cord injury: pathophysiology, diagnosis, and management. Neurosurg Focus 2008;25(05):E13
21 Nelson E, Gertz SD, Rennels ML, Ducker TB, Blaumanis OR. Spinal cord injury. The role of vascular damage in the pathogenesis of central hemorrhagic necrosis. Arch Neurol 1977;34(06):332–333
22 David S, Kroner A. Repertoire of microglial and macrophage responses after spinal cord injury. Nat Rev Neurosci 2011;12 (07):388–399
23 Jia Z, Zhu H, Li J, Wang X, Misra H, Li Y. Oxidative stress in spinal cord injury and antioxidant-based intervention. Spinal Cord 2012;50(04):264–274
24 Renault-Mihara F, Okada S, Shibata S, Nakamura M, Toyama Y, Okano H. Spinal cord injury: emerging beneficial role of reactive astrocytes' migration. Int J Biochem Cell Biol 2008;40(09): 1649–1653
25 Gensel JC, Zhang B. Macrophage activation and its role in repair and pathology after spinal cord injury. Brain Res 2015;1619:1–11
26 Rutges JPHJ, Kwon BK, Heran M, Ailon T, Street JT, Dvorak MF. A prospective serial MRI study following acute traumatic cervical spinal cord injury. Eur Spine J 2017;26(09):2324–2332
27 Aarabi B, Simard JM, Kufera JA, et al. Intramedullary lesion expansion on magnetic resonance imaging in patients with motor complete cervical spinal cord injury. J Neurosurg Spine 2012;17 (03):243–250
28 Chandra J, Sheerin F, Lopez de Heredia L, et al. MRI in acute and subacute post-traumatic spinal cord injury: pictorial review. Spinal Cord 2012;50(01):2–7
29 Losey P, Young C, Krimholtz E, Bordet R, Anthony DC. The role of hemorrhage following spinal-cord injury. Brain Res 2014; 1569:9–18
30 Gupta R, Mittal P, Sandhu P, Saggar K, Gupta K. Correlation of qualitative and quantitative MRI parameters with neurological status: a prospective study on patients with spinal trauma. J Clin Diagn Res 2014;8(11, RC11):RC13–RC17
31 Bilgen M, Abbe R, Liu SJ, Narayana PA. Spatial and temporal evolution of hemorrhage in the hyperacute phase of experimental spinal cord injury: in vivo magnetic resonance imaging. Magn Reson Med 2000;43(04):594–600
32 Ahuja CS, Fehlings M. Concise review: bridging the gap—novel neuroregenerative and neuroprotective strategies in spinal cord injury. Stem Cells Transl Med 2016;5(07):914–924
33 Ahuja CS, Wilson JR, Nori S, et al. Traumatic spinal cord injury. Nat Rev Dis Primers 2017;3:17018
34 Ter Wengel PV, De Witt Hamer PC, Pauptit JC, van der Gaag NA, Oner FC, Vandertop WP. Early surgical decompression improves neurological outcome after complete traumatic cervical spinal cord injury: a meta-analysis. J Neurotrauma 2019;36(06):835–844
35 Collignon F, Martin D, Lénelle J, Stevenaert A. Acute traumatic central cord syndrome: magnetic resonance imaging and clinical observations. J Neurosurg 2002;96(1, Suppl):29–33
36 Mihai G, Nout YS, Tovar CA, et al. Longitudinal comparison of two severities of unilateral cervical spinal cord injury using magnetic resonance imaging in rats. J Neurotrauma 2008;25(01):1–18
37 Fehlings MG, Vaccaro A, Wilson JR, et al. Early versus delayed decompression for traumatic cervical spinal cord injury: results of the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS). PLoS One 2012;7(02):e32037
38 Dimar JR II, Glassman SD, Raque GH, Zhang YP, Shields CB. The influence of spinal canal narrowing and timing of decompression on neurologic recovery after spinal cord contusion in a rat model. Spine 1999;24(16):1623–1633
39 Carlson GD, Gorden CD, Oliff HS, Pillai JJ, LaManna JC. Sustained spinal cord compression: part I—time-dependent effect on long-term pathophysiology. J Bone Joint Surg Am 2003;85(01):86–94
40 Vaccaro AR, Koerner JD, Radcliff KE, et al. AOSpine subaxial cervical spine injury classification system. Eur Spine J 2016;25 (07):2173–2184

41 Parashari UC, Khanduri S, Bhadury S, et al; ParashariUC. Diagnostic and prognostic role of MRI in spinal trauma, its comparison and correlation with clinical profile and neurological outcome, according to ASIA impairment scale. J Craniovertebr Junction Spine 2011;2(01):17–26
42 Aarabi B, Sansur CA, Ibrahimi DM, et al. Intramedullary lesion length on postoperative magnetic resonance imaging is a strong predictor of ASIA Impairment Scale grade conversion following decompressive surgery in cervical spinal cord injury. Neurosurgery 2017;80(04):610–620
43 Gelman A, Park DK. Splitting a predictor at the upper quarter or third and the lower quarter or third. Am Stat 2009;63(01):1–8
44 Bracken MB, Shepard MJ, Collins WF, et al. 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 1990;322(20):1405–1411
45 Spiess MR, Müller RM, Rupp R, Schuld C. EM-SCI Study Group, van Hedel HJ. Conversion in ASIA impairment scale during the first year after traumatic spinal cord injury. J Neurotrauma 2009 Nov;26(11):2027–2036
46 Marino RJ, Burns S, Graves DE, Leiby BE, Kirshblum S, Lammertse DP. Upper- and lower-extremity motor recovery after traumatic cervical spinal cord injury: an update from the national spinal cord injury database. Arch Phys Med Rehabil 2011;92(03):369–375
47 Geisler FH, Coleman WP, Grieco G, Poonian DSygen Study Group. The Sygen multicenter acute spinal cord injury study. Spine 2001; 26(24, Suppl):S87–S98
48 Bracken MB, Shepard MJ, Holford TR, et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the Third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. JAMA 1997; 277(20):1597–1604
49 Bracken MB, Collins WF, Freeman DF, et al. Efficacy of methylprednisolone in acute spinal cord injury. JAMA 1984;251(01):45–52
50 Burns AS, Ditunno JF. Establishing prognosis and maximizing functional outcomes after spinal cord injury: a review of current and future directions in rehabilitation management. Spine 2001; 26(24, Suppl):S137–S145
51 Waters RL, Adkins R, Yakura J, Sie I. Donal Munro Lecture: functional and neurologic recovery following acute SCI. J Spinal Cord Med 1998;21(03):195–199
52 Fehlings MG, Rao SC, Tator CH, et al. The optimal radiologic method for assessing spinal canal compromise and cord compression in patients with cervical spinal cord injury. Part II: results of a multicenter study. Spine 1999;24(06):605–613
53 Scholtes F, Phan-Ba R, Theunissen E, et al. Rapid, postmortem 9.4 T MRI of spinal cord injury: correlation with histology and survival times. J Neurosci Methods 2008;174(02):157–167
54 David G, Mohammadi S, Martin AR, et al. Traumatic and nontraumatic spinal cord injury: pathological insights from neuroimaging. Nat Rev Neurol 2019;15(12):718–731
55 Fujii H, Yone K, Sakou T. Magnetic resonance imaging study of experimental acute spinal cord injury. Spine 1993;18(14): 2030–2034
56 Iizuka H, Yamamoto H, Iwasaki Y, Yamamoto T, Konno H. Evolution of tissue damage in compressive spinal cord injury in rats. J Neurosurg 1987;66(04):595–603
57 Nout YS, Mihai G, Tovar CA, Schmalbrock P, Bresnahan JC, Beattie MS. Hypertonic saline attenuates cord swelling and edema in experimental spinal cord injury: a study utilizing magnetic resonance imaging. Crit Care Med 2009;37(07):2160–2166
58 Aoyama T, Hida K, Akino M, Yano S, Iwasaki Y, Saito H. Ultra-early MRI showing no abnormality in a fall victim presenting with tetraparesis. Spinal Cord 2007;45(10):695–699
59 Hackney DB, Asato R, Joseph PM, et al. Hemorrhage and edema in acute spinal cord compression: demonstration by MR imaging. Radiology 1986;161(02):387–390
60 Mahmood N, Kadavigere R, Avinash K, Rao VR. Magnetic resonance imaging in acute cervical spinal cord injury: a correlative study on spinal cord changes and 1 month motor recovery. Spinal Cord 2009;47(06):504
61 Andreoli C, Colaiacomo MC, Rojas Beccaglia M, Di Biasi C, Casciani E, Gualdi G. MRI in the acute phase of spinal cord traumatic lesions: relationship between MRI findings and neurological outcome. Radiol Med (Torino) 2005;110(5–6):636–645
62 Flanders AE, Spettell CM, Friedman DP, Marino RJ, Herbison GJ. The relationship between the functional abilities of patients with cervical spinal cord injury and the severity of damage revealed by MR imaging. AJNR Am J Neuroradiol 1999;20(05):926–934
63 Shimada K, Tokioka T. Sequential MR studies of cervical cord injury: correlation with neurological damage and clinical outcome. Spinal Cord 1999;37(06):410–415
64 Boldin C, Raith J, Fankhauser F, Haunschmid C, Schwantzer G, Schweighofer F. Predicting neurologic recovery in cervical spinal cord injury with postoperative MR imaging. Spine 2006;31(05): 554–559
65 Henninger B, Kaser V, Ostermann S, et al. Cervical disc and ligamentous injury in hyperextension trauma: MRI and intraoperative correlation. J Neuroimaging 2020;30(01):104–109
66 Le E, Aarabi B, Hersh DS, et al. Predictors of intramedullary lesion expansion rate on MR images of patients with subaxial spinal cord injury. J Neurosurg Spine 2015;22(06):611–621
67 Katzberg RW, Benedetti PF, Drake CM, et al. Acute cervical spine injuries: prospective MR imaging assessment at a level 1 trauma center. Radiology 1999;213(01):203–212
68 Hachem LD, Ahuja CS, Fehlings MG. Assessment and management of acute spinal cord injury: from point of injury to rehabilitation. J Spinal Cord Med 2017;40(06):665–675
69 Swank ML, Sutterlin CE III, Bossons CR, Dials BE. Rigid internal fixation with lateral mass plates in multilevel anterior and posterior reconstruction of the cervical spine. Spine 1997;22 (03):274–282
70 Phang I, Papadopoulos MC. Intraspinal pressure monitoring in a patient with spinal cord injury reveals different intradural compartments: Injured Spinal Cord Pressure Evaluation (ISCoPE) Study. Neurocrit Care 2015;23(03):414–418
71 Wilson JR, Singh A, Craven C, et al. Early versus late surgery for traumatic spinal cord injury: the results of a prospective Canadian cohort study. Spinal Cord 2012;50(11):840–843
72 Miyanji F, Furlan JC, Aarabi B, Arnold PM, Fehlings MG. Acute cervical traumatic spinal cord injury: MR imaging findings correlated with neurologic outcome—prospective study with 100 consecutive patients. Radiology 2007;243(03):820–827
73 Fehlings MG, Rabin D, Sears W, Cadotte DW, Aarabi B. Current practice in the timing of surgical intervention in spinal cord injury. Spine 2010;35(21, Suppl):S166–S173
74 Wilson JR, Tetreault LA, Kwon BK, et al. Timing of decompression in patients with acute spinal cord injury: a systematic review. Global Spine J 2017;7(3, Suppl):95S–115S
75 Papadopoulos SM, Selden NR, Quint DJ, Patel N, Gillespie B, Grube S. Immediate spinal cord decompression for cervical spinal cord injury: feasibility and outcome. J Trauma 2002;52(02):323–332
76 Bourassa-Moreau É, Mac-Thiong JM, Li A, et al. Do patients with complete spinal cord injury benefit from early surgical decompression? Analysis of neurological improvement in a prospective cohort study. J Neurotrauma 2016;33(03):301–306
77 Dvorak MFNV, Noonan VK, Fallah N, et al; RHSCIR Network. 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 2015;32 (09):645–654
78 Chen S, Smielewski P, Czosnyka M, Papadopoulos MC, Saadoun S. Continuous monitoring and visualization of optimum spinal cord perfusion pressure in patients with acute cord injury. J Neurotrauma 2017;34(21):2941–2949

79 Gallagher MJ, Hogg FRA, Zoumprouli A, Papadopoulos MC, Saadoun S. Spinal cord blood flow in patients with acute spinal cord injuries. J Neurotrauma 2019;36(06):919–929

80 Phang I, Werndle MC, Saadoun S, et al. Expansion duroplasty improves intraspinal pressure, spinal cord perfusion pressure, and vascular pressure reactivity index in patients with traumatic spinal cord injury: injured spinal cord pressure evaluation study. J Neurotrauma 2015;32(12):865–874

81 Saadoun S, Papadopoulos MC. Spinal cord injury: is monitoring from the injury site the future? Crit Care 2016;20(01):308

82 Michael Fehlings AR, Boakye M, Rossignol S, Ditunno JF Jr, Anthony S. Burns Essentials of Spinal Cord Injury: Basic Research to Clinical Practice. Denver, CO: Thieme Medical Publishers Inc.; 2013

83 Resnick DK. Updated guidelines for the management of acute cervical spine and spinal cord injury. Neurosurgery 2013;72 (Suppl 2):1

84 Fehlings MG, Wilson JR, Tetreault LA, et al. A clinical practice guideline for the management of patients with acute spinal cord injury: recommendations on the use of methylprednisolone sodium succinate. Global Spine J 2017;7(3, Suppl):203S–211S

85 Burke JF, Yue JK, Ngwenya LB, et al. Ultra-early (<12 hours) surgery correlates with higher rate of American Spinal Injury Association Impairment Scale conversion after cervical spinal cord injury. Neurosurgery 2019;85(02):199–203

86 Nasi D, Ruscelli P, Gladi M, Mancini F, Iacoangeli M, Dobran M. Ultra-early surgery in complete cervical spinal cord injury improves neurological recovery: a single-center retrospective study. Surg Neurol Int 2019;10:207

87 Aarabi B, Akhtar-Danesh N, Chryssikos T, et al. Efficacy of ultra-early (< 12 h), early (12-24 h), and late (>24-138.5 h) surgery with magnetic resonance imaging-confirmed decompression in American Spinal Injury Association Impairment Scale grades A, B, and C cervical spinal cord injury. J Neurotrauma 2020;37(03): 448–457

88 Waters RL, Adkins RH, Yakura JS, Sie I. Effect of surgery on motor recovery following traumatic spinal cord injury. Spinal Cord 1996;34(04):188–192

89 Vaccaro AR, Daugherty RJ, Sheehan TP, et al. Neurologic outcome of early versus late surgery for cervical spinal cord injury. Spine 1997;22(22):2609–2613

90 McKinley W, Meade MA, Kirshblum S, Barnard B. Outcomes of early surgical management versus late or no surgical intervention after acute spinal cord injury. Arch Phys Med Rehabil 2004;85 (11):1818–1825

91 Sewell MD, Vachhani K, Alrawi A, Williams R. Results of early and late surgical decompression and stabilization for acute traumatic cervical spinal cord injury in patients with concomitant chest injuries. World Neurosurg 2018;118:e161–e165

92 Sapkas GS, Papadakis SA. Neurological outcome following early versus delayed lower cervical spine surgery. J Orthop Surg (Hong Kong) 2007;15(02):183–186

93 Lenehan B, Fisher CG, Vaccaro A, Fehlings M, Aarabi B, Dvorak MF. The urgency of surgical decompression in acute central cord injuries with spondylosis and without instability. Spine 2010; 35(21, Suppl):S180–S186

94 Kim M, Hong SK, Jeon SR, Roh SW, Lee S. Early (</ = 48 hours) versus late (>48 hours) surgery in spinal cord injury: treatment outcomes and risk factors for spinal cord injury. World Neurosurg 2018;118:e513–e525

95 Takami T, Shimokawa N, Parthiban J, Zileli M, Ali S. Pharmacologic and regenerative cell therapy for spinal cord injury: WFNS spine committee recommendations. Neurospine 2020;17(04):785–796

96 Satkunendrarajah K, Nassiri F, Karadimas SK, Lip A, Yao G, Fehlings MG. Riluzole promotes motor and respiratory recovery associated with enhanced neuronal survival and function following high cervical spinal hemisection. Exp Neurol 2016;276:59–71

97 Miller RG, Mitchell JD, Moore DH. Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND). Cochrane Database Syst Rev 2012;(03):CD001447

98 Lee SM, Yune TY, Kim SJ, et al. Minocycline reduces cell death and improves functional recovery after traumatic spinal cord injury in the rat. J Neurotrauma 2003;20(10):1017–1027

99 Wells JE, Hurlbert RJ, Fehlings MG, Yong VW. Neuroprotection by minocycline facilitates significant recovery from spinal cord injury in mice. Brain 2003;126(Pt 7):1628–1637