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Review Article

Early Management of Spinal Cord Injury: WFNS Spine Committee Recommendations

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Scientific knowledge today is being generated more rapidly than we can assimilate thus requiring continuous review of gold-standards for diagnosis and treatment of specific pathologies. The aim of this paper is to provide an update on the best early management of spinal cord injury (SCI), in order to produce acceptable worldwide recommendations to standardize clinical practice as much as possible. The WFNS Spine Committee voted recommendations regarding management of SCI based on literature review of the last 10 years. The committee stated 9 recommendations on 3 main topics: (1) clinical assessment and classification of SCI; (2) emergency care and early management; (3) cardiopulmonary management. American Spinal Injury Association impairment scale, Spinal Cord Independence Measure, and International Spinal Cord Injury Basic Pain Data Set are considered the most useful and feasible in emergency evaluation and follow-up in case of SCI. Magnetic resonance imaging is the most indicated examination to evaluate patients with symptomatic SCI. In early phase, correction of hypotension (systolic blood pressure < 90 mmHg), and bradycardia are strongly recommended. Surgical decompression should be performed as soon as possible with the ideal surgical time being within 8 hours for both complete and incomplete lesions.

Keywords: Guidelines, Spinal cord, Assessment, Emergency care, Cardiopulmonary management

BACKGROUND AND OBJECTIVE

Spinal cord injury (SCI) can produce a sudden and sometimes devastating impact on the quality of life due to severe motor, sensory and autonomic dysfunction; however, while a common pathological process underlies most traumatic SCIs, each case is unique.[1] That is why all phases are considered critical and relevant in the management of SCI and it is important to standardize procedures as much as possible. While the clinical evaluation and classification of SCI are actually well established and universally accepted with the: American Spinal Injury Association (ASIA) Impairment Scale, clinical management, indication for medical treatment and/or surgical intervention are less defined and subject to continuous evolution. It is necessary and crucial to establish a common language and guidelines.[2]

Considering scientific knowledge is being generated more rapidly than we can assimilate it, we must continuously review gold-standards for diagnosis, best treatment options according to the severity of illness, as well as have feedback to understand whether these methods actually serve the purpose they were created for. The aim of this paper is to provide an update on the best assessment and treatment options for "early management of spinal cord injury," in order to produce acceptable worldwide recommendations to standardize clinical practice as much as possible.

METHODS

An international committee of spinal surgeons (members of the World Federation of Neurosurgical Society [WFNS] Spine Committee) performed 2 Consensus Conferences on the Management of Traumatic Spinal Cord Injury. Part I was conducted in Moscow in June 2019 with 13 experienced spinal surgeons of the WFNS Spine Committee present. The aim of the meeting was to assess the statements through a preliminary review of the literature and the present levels of evidence to create one to 6 statements for the voting session. Part II was held in Peshawar in November 2019. The statements and the literature review were presented to 10 members of the WFNS Spine Committee.

Delphi method was used to administer the questionnaire to have a high degree of validity. To establish a consensus, the levels of agreement or disagreement on each item were voted independently in a blind way using a Likert-type scale from 1 to 5 (1 = strongly disagree, 2 = disagree, 3 = somewhat agree, 4 = agree, 5 = strongly agree). Results were expressed as a percentage of respondents who scored each item as 1 or 2 (disagreement) or as 3, 4, or 5 (agreement). Consensus was achieved when the sum for disagreement or agreement was ≥66%. Each consensus point was clearly defined with evidence strength, recommendation grade, and consensus level provided.[3-5]

The literature review included papers from the last 10 years and was conducted using the Cochrane Database of Systematic Reviews and MEDLINE/PubMed. From the identified articles, a secondary search of the listed citations was performed to ensure that all relevant publications had been included. All the reviewers then double-checked abstracts for duplicates and nonrelated papers (according to the topic, early evaluation, or human studies) to be excluded. They then proceeded to the full-text reading of papers to meet inclusion criteria: level I through IV evidence, low to moderate bias, and low or high-quality patient-oriented evidence.

RESULTS

The panel was divided into 3 main topics: (1) clinical assessment and classification of SCI; (2) emergency care and early management; (3) cardiopulmonary management. A total of 10 statements were drafted and voted in the first session in Moscow in June 2019. One statement about emergency care was excluded from the final voting session in Peshawar.

1. Clinical Assessment and Classification of SCI

Research: publication date from 2009 up to 2019; English language; main word search in all-fields: "acute spinal cord injury" and "spinal cord injury"; and a combination of the following: all-fields: "clinical assessment," "classification," "guidelines"; with or without the following on title: "score," "index," "neurological status," "ASIA score," "Frankel score." We obtained 1,201 papers after all search rounds. We excluded 1,020 papers (16 duplicates and 1,004 nonrelated) after abstract review by an independent double-check. Following a full-text review of the remaining 181 papers, we selected 32 papers that met the inclusion criteria to draw conclusions (Fig. 1). Classifications of SCI are intended to standardize clinical evaluation but can also lead to oversimplification precluding the ability to find an effect of an experimental therapeutic.[6]

Five papers evaluated the use of biomarkers to assess neurological injury and prognosis. Only 1 nonrandomized clinical trial (nRCT) level III evidence offered no serious bias and level 1 type-A high-quality patient-oriented evidence; the remaining 7 papers were one nRCT, 3 prospective cohorts, and 1 retrospective cohort, with moderate bias and level 2 type B recommendation. The biomarkers have been extensively studied, and many biological compounds have been highlighted as potentially useful compounds to assess neurological injury at admission and help predict prognosis; nevertheless, the profile is white extensive, and no uniform criteria (or dataset) have been defined.[6] Based on these papers, we can conclude that the use of biomarkers on blood and cerebrospinal fluid (CSF) to predict neurological injury and severity remains on translational research since a specific array of biomarkers needs to be designed and tested before widespread clinical use.[7-11]

Since the initial review on assessment tools for acute SCI was presented by Hadley et al.[12] in 2002, the ASIA Impairment Scale (AIS, short form for ASIA International Standards for Neurological Classification of Spinal Cord Injury [ISNCSCI]) has been designated as the recommended evaluation tool to evaluate and classify initial neurological impairment on admission and provide information on improvement at follow-up. The AIS comprises 5 grades of neurological injury: grade A, complete neurological injury (no motor or sensory function at S4, S5 segment); grade B, no motor function but preserved sensory function below the neurological injury with preservation including S3 and S4; grade C, incomplete neurological injury (with the preserved motor function below the neurological lev-

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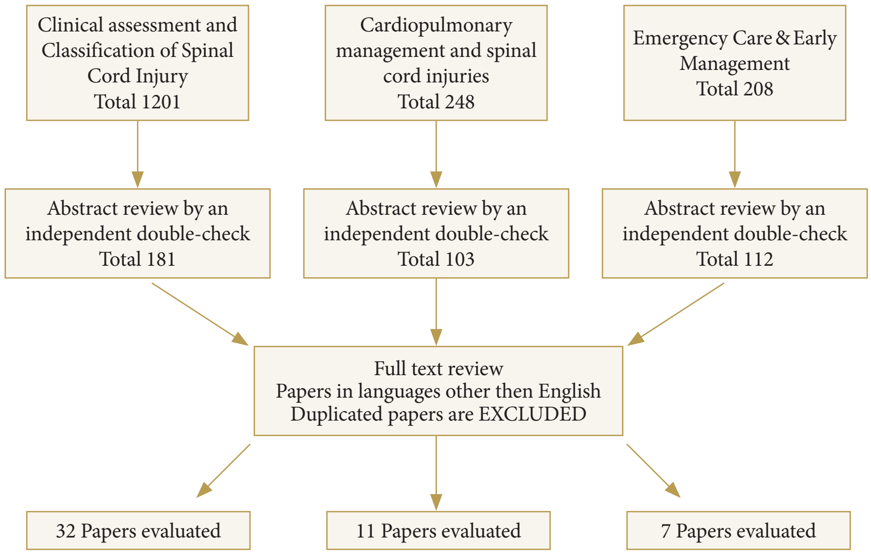

Fig. 1. Literature review flowchart.

el with muscle strength below 3; grade D, Incomplete neurological injury (with the preserved motor function below the neurological level with muscle strength above 3; grade E, normal motor or sensory function; Its primary role is to classify neurological injury based on a practical manner on admission (Fig. 2).[13] Three papers evaluated the use of this scale to assess neurological function at admission. Two of those papers have level I evidence, both systematic reviews following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement offer level 1 high-quality patient-oriented evidence, while the last paper of level III evidence with moderate bias provides level 2 low-quality evidence. We found no papers evaluating other scales. Based on these studies, we found that the AIS, described by the ASIA, is recommended as the preferred clinical evaluation tool to assess and classify neurological impairment at admission in patients with acute SCI. We also found that the Spinal Cord Independence Measure (SCIM III) may be preferred to assess the functional abilities and impairment in the follow-up of patients with chronic SCI. Finally, we found that the International Spinal Cord Injury Basic Pain Data Set (ISCIBPDS) may be the preferred scale to evaluate pain on early assessment to the follow-up on chronically injured patients.[14-16] The ASIA ISNCSCI provides the fundamental for the former classification; it details the neurological pattern of injury in a chart divided in motor and sensory evaluations. The motor score combines the upper extremity motor score and the lower extremity motor score assigning up to 25 points by extremity to a total of 100; The sensory score combines light touch score and pinprick scores to yield a total score out of 2,224 points by grading sensitivity as follows: 0 = absent, 1 = altered, and 2 = normal. Eleven papers evaluated the use of ASIA ISNCSCI to assess the severity of neurological impairment on admission. One paper of level I evidence, unfortunately provides level 2 low-quality patient-oriented evidence, as not adhering to the PRISMA statement. Ten papers of level III evidence with moderate bias provide level 3 low-quality patient-oriented evidence. Based on these results, we found that there is insufficient new evidence to change (not in favor, nor against) the previous consensus statement on the use of ISNCSCI as the assessment tool to classify the severity of neurological impairment on admission for acute

ASIA Impairment Scale	*Description*
A	Complete. No sensory or motor function is preserved in the sacral segments S4–S5.
B	Incomplete. Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4–S5.
C	Incomplete. Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3 (grades 0–2).
D	Incomplete. Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade greater than or equal to 3.
E	Normal. Sensory and motor function are normal.

Fig. 2. American Spinal Injury Association (ASIA) Impairment Scale grading.

SCI.[1,17-26]

The SCIM assess the ability to perform basic daily life activities using a 19-item disability chart, scoring up to 100 points by evaluation: self-care, respiration and sphincter management and mobility, currently it has been demonstrated that its role remains in the long-term assessment of neurological function changes in every day performance (Fig. 3).[27,28] Furthermore, pain is a significant problem for many individuals with SCI, the ISCIBPDS was developed in 2008 by Widerström -Noga et al.,[29,30] as a necessity to understand the nature of pain and to assess the efficacy of treatment with a valid reliable and standardize tool in an individual with SCI. It serves to assess pain, including pain severity, physical functioning, and emotional functioning, among SCI patients as it comprises a pain-intensity rating, a pain classification, and questions related to the temporal pattern of pain for each specific pain problem (Fig. 4).[29] Thirteen papers evaluated the use of magnetic resonance imaging (MRI) to assess SCI at admission. Two level I evidence systematic reviews present level 1 high-quality patient-oriented evidence recommendations. Eight papers of level III evidence (7 prospective, 2 retrospectives) with moderate bias provide level II low-quality patient-oriented evidence. Finally, the last 2 papers are case series with level IV evidence, presenting moderate bias and providing level II low-quality patient-oriented evidence. Based on these results, we concluded that conventional MRI protocol with BASIC (Brain and Spinal Injury Center score) criteria evaluation on T2 axial sequence is the recommended imaging study in the setting of acute SCI to be done whenever possible before surgery to help in decision making. Injury level at C3 (or otherwise above C5), a maximum canal compromise greater or equal to 50%, a lesion length greater or equal to 20 mm, the presence of cord oedema and osteophyte formation at the level of injury significantly predicts the need for early tracheostomy. We also concluded that diffusion tensor imaging has better sensitivity than conventional MRI, especially with fractional anisotropy protocol, but up-to-date, a more straightforward protocol to implement remains to be created in order to facilitate its widespread clinical use.[15,31-43] Literature review is summarized in Tables 1–3.

INTERNATIONAL SPINAL CORD INJURY PAIN BASIC DATA SET

DATA COLLECTION FORM – Version 2.0

Date of data collection: YYYY/MM/DD

Have you had any pain during the last seven days including today?
No Yes

If yes:

Please note that the time period during the last week applies to all pain interference questions.

In general, how much has pain interfered with your day-to-day activities in the last week?
No interference 0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10 Extreme interference

In general, how much has pain interfered with your overall mood in the last week?
No interference 0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10 Extreme interference

In general, how much has pain interfered with your ability to get a good night's sleep?
No interference 0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10 Extreme interference

How many different pain problems do you have?
1; 2; 3; 4; ⩾5

Please describe your three worst pain problems:

Worst pain problem:

Pain locations /sites (can be more than one, check all that apply): right (1), midline (1), or left (L)	R	M	L	**Type of pain** **Intensity** and **duration of pain** **Treatment of pain**
Head				**Type of pain (check one):**
Neck/shoulders throat, neck, shoulder				**Nociceptive** Musculoskeletal, Visceral, Other
Arms/hands upper arm, elbow, forearm, wrist, hand/fingers				**Neuropathic** At-level SCI, Below-level SCI, Other
Frontal torso/genitals chest, abdomen, pelvis/genitalia				**Other** **Unknown**
Back upper back, lower back				**Intensity** and **duration of pain:** **Average pain intensity in the last week:** 0 = no pain; 10 = pain as bad as you can imagine 0; 1; 2; 3; 4; 5; 6; 7; 8; 9; 10
Buttocks/hips buttocks, hip, anus				
Upper leg/thigh				**Date of onset:** YYYY/MM/DD
Lower legs/feet knee, shin, calf, ankle, foot/toes				**Are you using or receiving any treatment for your pain problem?** No Yes

Fig. 3. Spinal Cord Independence Measure III grading.

Based on the presented literature and personal experience the committee voted as follow:

Statement 1: AIS described by the ASIA must be used as the preferred clinical evaluation tool for acute neurological assessment in patients with SCI. This statement reached a strong positive consensus (all voted grade 5 of Linkert scale [LS]).

Statement 2: The SCIM, may be preferred as the best scale to assess the functional abilities and impairment in the follow-up of patients with chronic SCI. This statement reached a strong positive consensus (86% voted grade 5 of LS, 13% voted grade 4 of LS).

Statement 3: The ISCIBPDS may be the preferred scale to evaluate the pain of a chronically injured patient. This statement reached a strong positive consensus (86% voted grade 5 of LS, 13% voted grade 4 of LS).

2. Emergency Care and Early Management

Literature search on PubMed and MEDLINE from 2009 to

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Mobility (room and toilet) DATE Exam 1 2 3 4 5 6

9. Mobility in Bed and Action to Prevent Pressure Sores
0. Needs assistance in all activities: turning upper body in bed, turning lower body in bed, sitting up in bed, doing push-ups in wheelchair, with or without adaptive devices, but not with electric aids
2. Performs one of the activities without assistance
4. Performs two or three of the activities without assistance
6. Performs all the bed mobility and pressure release activities independently

10. Transfers: bed-wheelchair (locking wheelchair, lifting footrests, removing and adjusting arm rests, transferring, lifting feet).
0. Requires total assistance
1. Needs partial assistance and/or supervision, and/or adaptive devices (e.g., sliding board)
2. Independent (or does not require wheelchair)

11. Transfers: wheelchair-toilet-tub (if uses toilet wheelchair: transfers to and from; if uses regular wheelchair: locking wheelchair, lifting footrests, removing and adjusting armrests, transferring, lifting feet)
0. Requires total assistance
1. Needs partial assistance and/or supervision, and/or adaptive devices (e.g., grab-bars)
2. Independent (or does not require wheelchair)

Mobility (indoors and outdoors, on even surface)

12. Mobility indoors
0. Requires total assistance
1. Needs electric wheelchair or partial assistance to operate manual wheelchair
2. Moves independently in manual wheelchair
3. Requires supervision while walking (with or without devices)
4. Walks with a walking frame or crutches (swing)
5. Walks with crutches or two canes (reciprocal walking)
6. Walks with one cane
7. Needs leg orthosis only
8. Walks without walking aids

13. Mobility for Moderate Distances (10–100 meters)
0. Requires total assistance
1. Needs electric wheelchair or partial assistance to operate manual wheelchair
2. Moves independently in manual wheelchair
3. Requires supervision while walking (with or without devices)
4. Walks with a walking frame or crutches (swing)
5. Walks with crutches or two canes (reciprocal walking)
6. Walks with one cane
7. Needs leg orthosis only
8. Walks without walking aids

14. Mobility Outdoors (more than 100 meters)
0. Requires total assistance
1. Needs electric wheelchair or partial assistance to operate manual wheelchair
2. Moves independently in manual wheelchair
3. Requires supervision while walking (with or without devices)
4. Walks with a walking frame or crutches (swing)
5. Walks with crutches or two canes (reciprocal walking)
6. Walks with one cane
7. Needs leg orthosis only
8. Walks without walking aids

15. Stair Management
0. Unable to ascend or descend stairs
1. Ascends and descends at least 3 steps with support or supervision of another person
2. Ascends and descends at least 3 steps with support of handrail and/or crutch or cane
3. Ascends and descends at least 3 steps without any support or supervision

16. Transfers: wheelchair-car (approaching car, locking wheelchair, removing arm and footrests, transferring to and from car, bringing wheelchair into and out of car)
0. Requires total assistance
1. Needs partial assistance and/or supervision and/or adaptive devices
2. Transfers independent; does not require adaptive devices (or does not require wheelchair)

17. Transfers: ground-wheelchair
0. Requires assistance
1. Transfers independent with or without adaptive devices (or does not require wheelchair)

SUBTOTAL (0–40)

TOTAL SCIM SCORE (0–100)

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Fig. 4. International Spinal Cord Injury Basic Pain Data Set grading. Reprinted from Widerström-Noga et al. Spinal Cord 2008;46:818-23, under the terms of Open Access.[29]

Table 1. Studies on biomarkers

Study	Data collection	Level of evidence	Bias	Clinical tool	Rx	Biomarkers	Parameter	Conclusion
Pouw et al.[75] 2009	Retro-spective	Systematic review: 12 human studies, 6 animal studies	Very serious (not PRISMA)	ASIA	CT	S-100b Neuron-specific enolase (NSE) Neurofilament light chain (pNF-H) Glial fibrillary acidic protein (GFAP)	Elevated in acute spinal injury (experimental) at 6 hours	Do not yet provide a sensitive prognostic tool.
Ahadi et al.[10] 2015	Prospec-tive	Prospective cohort	Not serious nonblinded (bioquimical evaluation)	ASIA	None	Serum levels of pNF-H and NSE were signifi cantly higher during 24 and 48 hr after injury in patients. The level of GFAP was appropriate for estimating the severity of SCI in the fi rst 24 hours after injury	Higher serum levels in ASIA A and B	During 48 hours after injury, estimation of serum levels of pNF-H, NSE, and GFAP, combined with neurological testing, could predict the presence of SCI and severity prior to spinal computed tomography and surgical or conservative interventions.
Wu et al.[11] 2016	Prospec-tive	Prospective cohort	Not serious nonblinded (biochemical evaluation)	ASIA ISNCS-CI	None	CSF: citruline N-acetylputrescine Lactic acid glycerol N1, N12-diacetylspermine N-methyl-S-aspartic acid	CSF metabolites were identified as potential biomarkers of baseline injury severity, and good classification performance (AUC > 0.869) was achieved by using combinations of these metabolites in pair-wise comparisons of AIS A, B and C patients	Using the universal metabolome standard strategy, the current data set can be expanded to a larger cohort for biomarker validation, as well as discovering biomarkers for predicting neurologic outcome
Elizei et al.[76] 2017	Review	Review Not specified Nonsystematic review	Very serious (not PRISMA)	ASIA ISNCS-CI Frankel	None	CSF: ubiquitin B-terminal hydrolase-L1 (UCH-L1), spectrin breakdown products (SBDP), myelin basic protein (MBP), and GFAP nitric oxide (NO) interleukin (IL)-6, IL-8 TNF-R1 levels MCP-1, tau, serum neurofilament light chain phosphorylated neurofilament heavy chain (pNF-H), and NSE	UCH-L1, SBDP, GFAP, MBP Elevated in SCI with correlation in severity and improvement NO elevated in FRANKEL A and B (MCP)-1, tau, S100β, and GFAP, peak at 24-36 hr and decresed at 72 hr IL-6 , GFAP, tau and S100β different in severity injury GFAP, phosphorylated neurofilament heavy chain (pNF-H), and NSE	CSF biomarkers could be incorporated into a model that had an 83.3% accuracy at predicting AIS improvement over 6 months GFAP levels were correlated with injury severity.
Ferbert et al.[8] 2016	Prospec-tive	Prospective cohort	Nor serious Nonblinded (biochemical evaluation)	ASIA	None	IGF-1, TGF- β1 and sCD95L	Both groups showed a very similar distribution in TGF-β1 levels as described above. IGF-1	Demonstrated a possible relationship between cytokine concentration in peripheral blood samples and neurological remission

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Table 1. Continued

Study	Data collection	Level of evidence	Bias	Clinical tool	Rx	Biomarkers	Parameter	Conclusion
Ydens et al.[77] 2017	Review	Review Nonsystematic review: 14 animal studies, 36 human studies	Nor serious Nonblinded (biochemical evaluation)	None	None	Oligodendrocyte- and astrocyte-associated proteins such as S100B, GFAP, and MBP have CSF: NSE, tau, and neurofilaments	Even though elevated concentrations of potential biomarkers have been identified in patients with SCI, the current candi- date biomarkers do not yet provide a sensitive diagnostic or prognostic tool.	The panel of biomarkers could even predict motor outcome at 6 months better than the standard clinical AIS classification Independent replication studies are needed to confirm the validity and reproducibility of these markers.
Tong et al.[9] 2018	Retrospective	Retrospective cohort	Serious indirectness imprecise	ASIA	None	Serum albumin concentrations were obtained as part of routine blood chemistry analysis, at trial entry (24-72 hours), 1, 2, and 4 weeks after injury.	Serum albumin concentration was only weakly associated with neurological outcome at baseline (24-72 hours according to our primary analysis) and only significant within individual AIS grades by 4 weeks post injury.	Serum albumin concentrations are a useful biomarker for the prognosis of long-term neurological outcome after an acute SCI.
Tigchelaar et al.[7] 2019	Prospective	Nonrandomized trial	Not serious	ASIA ISNCSCI	None	Serum and CSF: micro RNA	This set of 70 microRNA had cross-validated AUC = 0.75 when classifying AIS A patients vs. all other AIS grades. This set of 30 microRNA had cross-validated AUC = 0.75 when 22 classifying AIS grade A patients who went on to improve at least 1 grade, at 6 months post injury, from those that did not. MiR-423, as one of the strongest prognosticators.	Further testing in an independent cohort of acute SCI patients will be necessary to validate (and potentially improve) the microRNA model.

Rx, radiology; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; ASIA, American Spinal Injury Association Impairment; CT, computed tomography; CSF, cerebrospinal fluid; AUC, area under the curve; AIS, ASIA Impairment Scale; SCI, spinal cord injury; ISNCSCI, International Standards for Neurological Classification of Spinal Cord Injury.

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Table 2. Studies on ASIA Impairment Scale (AIS) to assess neurological function at admission; ASIA International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) to assess the severity of neurological impairment on admission

Study	Data collection	Study type	Neurological outcome measures	No. of patients	Level of injury	Outcomes	Lenght of follow-up
Nandoe Tewarie et al.[78] 2010	Review	Comprehensive review	ASIA, LEMS	N/A	N/A	The assessment of functional loss after SCI has been standardized in the larger part of the world. The AIS is often used to assess the level and the completeness of SCI.	N/A
Hadley et al.[74] 2013	Review	Comprehensive review	ASIA, SCIM	N/A	N/A	Neurological Examination: Level II: • The ASIA international standards for neurological and functional classification of spinal cord injury are recommended as the preferred neurological examination tool for clinicians involved in the assessment and care of acute spinal cord injury patients. Functional Outcome Assessment: Level I: • The Spinal Cord Independence Measure III is recommended as the preferred functional outcome assessment tool for clinicians involved in the assessment, care, and follow- up of patients with spinal cord injuries. Pain Associated With Spinal Cord Injury: Level I: • The International Spinal Cord Injury Basic Pain Data Set is recommended as the preferred means to assess pain, including pain severity, physical functioning, and emotional functioning, among SCI patients	N/A
Boese and Lechler[15] 2013	PRISMA	Systematic review	AIS & MRI Patterns and clinical correlation	52 Papers	N/A	At admission, neurologic deficit assessed by the AIS in 567 patients was A in 19.1%, B in 18.5%, C in 39.7%, and D in 22.8%. At final follow-up, these were 6.5%, 4.8%, 20.1%, and 44.3%, respectively. In 7.1%, no MRI abnormalities (type I) were detected, and 92.9% exhibited abnormal scan results (type II). Of the latter, 11.7% revealed extraneural (type IIa), 36.9% revealed intraneural (type IIb), and 44.3% revealed combined abnormalities (type IIc). Statistical analysis of neurologic impairment at admission and follow-up revealed significant differences in outcome between patients with different imaging findings.	N/A
Carrasco-López et al.[16] 2016	Prospective	Prospective cohort	ASIA, ISNCSCI, UEMS, JTHFT, 9HPT	29	Rostral to T1	Both the JTHFT and 9HPT can be similarly used to quantify functional impairment after cervical SCI. The upper extremity motor score, JTHFT, and 9HPT strongly correlate with the AIS (graded from A to E), but not with the lesion level.	10 Months
Harrop et al.[79] 2018	Non-PRISMA	Systematic review	SCIM, AIS, Sacral sensation, Ankle spasticity Urethral and rectal sphincter, AbH motor function, Abductor Hallucis, Frankel, Sunnyrook scales, FIM	13 Papers	N/A	Numerous neurological assessment scales (Functional Independence Measure, Sunnybrook Cord Injury Scale, and Frankel Scale for Spinal Cord Injury) have demonstrated internal reliability and validity in the management of patients with thoracic and lumbar fractures. Unfortunately, other contemporaneous measurement scales (i.e,. American Spinal Cord Injury Association Impairment Scale) have not been specifically studied in patients with thoracic and lumbar fractures. Entry AIS grade, sacral sensation, ankle spasticity, urethral and rectal sphincter function, and AbH motor function can be used to predict neurological function and outcome in patients with thoracic.	N/A

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Table 2. Continued

Study	Data collection	Study type	Neurological outcome measures	No. of patients	Level of injury	Outcomes	Lenght of follow-up
Furlan et al.[17] 2009	Review	Systematic review	The psychometric properties of ASIA Standards and all previously used outcome measures of pain in the SCI population in the acute care setting	56 Papers	N/A	There was no study that examined pain assessment in the acute care setting. While 18 of 24 articles studied an instrument for assessment of pain intensity, the remaining six studies were focused on classifications of pain in the SCI population. Further investigation of the psychometric properties of the ASIA Standards is recommended due to a lack of studies focused on some key elements of responsiveness, including minimal clinically important difference. The visual analog scale is the most commonly studied instrument of assessment of pain intensity in the SCI population	N/A
Patel et al.[25] 2010	Retrospective	Retrospective cohort	SLIC classification for subaxial cervical spine Injury	65	C2-T1	A widely accepted classification of subaxial cervical trauma does not exist. The SLIC system has been developed to address limitations of prior systems. The SLIC system provides diagnostic information and can guide surgical versus nonsurgical treatment. An algorithm based on the SLIC system can guide surgical approach in the operative treatment of subaxial cervical trauma. References	N/A
Kirshblum et al.[80] 2011	Review	Comprehensive review	AIS ISMCSCI	N/A	N/A	ISMCSCI and AIS definitions	N/A
Berney et al.[19] 2011	Prospective	Prospective cohort	AIS	114	Above C8	For patients suffering an ASIA A injury (n¼72), 48 patients received a tracheostomy (66.7%) and in incomplete injuries 47.6% received a tracheostomy. All patients with injuries above the C4 level received a tracheostomy. Patients with an ASIA A injury are more likely to require a tracheostomy	N/A
Tsou et al.[26] 2011	Retrospective	Retrospective cohort	Data extraction included demographics, mechanism of injury, and neurologic function at the time of admission. A detailed evaluation of the pathomorphology and spinal canal sagittal diameter measurements were performed on the cervical spine CT scans and/or MRI images	333	C3-7	This study demonstrated that the determinants for a comprehensive cervical spine injury severity assessment model should include neural impairment, pre- and postinjury available spinal canal sagittal diameter, and pathomorphology of the injury, each of which may individually predict the probability of surgical intervention. Patho-morphology evaluation is best separated into its two components, actual osseoligamentous failure and displacement. For ease of injury severity recognition, statistical analysis, and outcome comparisons, a model based on separate but similarly scaled numeric scoring for each determinant is a useful tool.	N/A
Radclif et al.[23] 2012	Prospective	Prospective cohort	To proof if the load-sharing score (LSS) predicts ligamentous or neurological injury.	44	T10-L2	The most common neurological injury pat- tern was ASIA grade C (43%), followed by ASIA grade E (30%). Twenty-five of the patients (57%) were treated with operative stabilization. The mean ASIA motor score was 83.0. The LSS does not uniformly correlate with the PLC injury, neurological status, or empirical clinical decision making	N/A

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Table 2. Continued

Study	Data collection	Study type	Neurological outcome measures	No. of patients	Level of injury	Outcomes	Lenght of follow-up
Krishna et al.[6] 2013	Review	Comprehensive review	AIS rational and limitations	N/A	N/A	ASIA impairment grades result in assessments of variable resolution and groupings of heterogeneous populations with different individual recovery potentials. This results in large variations from the mean on outcome measures and a need to enroll a large number of patients in clinical trials	N/A
Vasquez et al.[22] 2013	Retrospective	Retrospective cohort	To confirm a tendency for light touch (LT) to score higher than pin prick (PP) in SCI subjects and discuss possible reasons for such disparity. The clinical neurological evaluation included level of injury and the ISNCSCI scores in total and at each spinal segmental level for LT, PP, upper extremity motor and lower extremity motor function	99	Below C2 to S4/5	The discrepancies between LT and PP could relate to the greater complexity of the PP test or a difference in the extent of injury to the posterior columns (LT) and spinothalamic (PP) tracts. Further interpretation would benefit from additional electrophysiological sensory tests	N/A
Marino et al.[21] 2016	Prospective	Prospective cohort	To determine whether pressure sensation at the S3 dermatome (a new test) could be used in place of deep anal pressure (DAP) to determine completeness of injury as part of the ISNCSCI Design.	141	N/A	S3 pressure sensation is reliable and has substantial agreement with DAP in persons with SCI at least 1-month postinjury. We suggest S3 pressure as an alternative test of sensory sacral sparing for supraconus SCI, at least in cases where DAP cannot be tested. Further research is needed to determine whether S3 pressure could replace DAP for classification of SCI. Archives	6–12 Months
Walden et al.[24] 2016	Retrospective	Retrospective cohort	To describe the development and validation of a computerized application of the ISNCSCI	2,520	Any	The RHI-ISNCSCI Algorithm provides a standardized method to accurately derive the level and severity of SCI from the raw data of the ISNCSCI examination. The web interface assists in maximizing usability while minimizing the impact of human error in classifying SCI.	N/A
Kaul et al.[20] 2017	Prospective	Prospective study	To determine whether the recently introduced AOSpine Classification and Injury Severity System has better interrater and intrarater reliability than the already existing TLICS for thoracolumbar spine injuries and their clinical Correlation with ISNCSCI	550	Any	Recently proposed AOSpine classification has better reliability for identifying fracture morphology than the existing TLICS Near perfect interrater and intrarater agreement was seen concerning neurological status for both the classification systems	N/A

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Table 2. Continued

Study	Data collection	Study type	Neurological outcome measures	No. of patients	Level of injury	Outcomes	Lenght of follow-up
Layer et al.[1] 2017	Prospective	Prospective cohort	To evaluate the clinical effectiveness of the Neuro-Spinal Scaffold, including improvement in AIS grade, sensory scores, motor scores, bladder and bowel function, Spinal Cord Independence Measure III, and Quality of Life Index (QLI-SCI III), as well as possibly decreased pain.	9	T3-T11	Following durotomy, 2 forms of cord damage were observed. In contusion-type injuries, the cord surface is intact. In compound- type injuries, the pia is breached and there is visible but incomplete cord parenchymal separation (Fig. 4). Both injuries were successfully implanted with the Neuro-Spinal Scaffold and AIS improvements were seen in both pathological types.	Up to 12 months
Yugué et al.[18] 2018	Prospective	Prospective cohort	The sensitivity and specificity of the 'knee-up test' were evaluated in patients with acute CSCI classified as AIS C or D	200	Above C8	The sensitivity, specificity, positive predictive and negative predictive values of this test for all patients were 99.1, 76.8, 82.5, and 98.7, respectively. The knee-up test may allow easy and highly accurate estimation, without the need for special skills, of AIS classification for patients with incomplete CSCI.	N/A

ASIA, American Spinal Injury Association Impairment; LEMS, Lower Extremity Motor Score; SCIM, Spinal Cord Independence Measure; N/A, not available; SCI, spinal cord injury; AIS, ASIA Impairment Scale; CT, computed tomography; MRI, magnetic resonance imaging; UEMS, Motor Score combines the Upper Extremity Motor Score; TLICS, Thoracolumbar Injury Classification and Severity Score; JTHFT, Jebsen-Taylor Hand Function Test, 9HPT, 9 Hole Peg Test; SLIC, subaxial cervical injury classification system; CSCI, cervical spinal cord injury; RHI-ISNCSCI, Rick Hansen Institute-International Standards for Neurological Classification of Spinal Cord Injury.

2019 was undertaken using keywords: "spinal cord injury/ies" OR "spinal cord trauma/s" OR "spinal cord transection/s" OR "spinal cord laceration/s" OR "spinal cord contusion" OR "SCI" AND "surgery/ies" OR "operation/s OR "procedure/s" OR "decompression/s" AND "eight hours" OR "timing" OR "early" OR "ultra" OR "urgent". A total of 208 results were obtained. After a first screening for English language and abstract, a total of 112 papers were fully read and 7 papers were considered significant for evaluation. After that we differentiated papers comparing early (< 24 hours) versus late surgery (> 24 hours). Furthermore, we differentiated very early (< 8 hours) versus early (> 8 hours < 24 hours) surgery. Of those articles, we focused on the ones centered on surgical treatment instead of medical therapy (Fig. 1). After the literature review, we obtained the following results. In National Acute Spinal Cord Injury Study Bracken et al identified the optimal therapeutic window for SCI treatment as up to 8 hours in 1990, however, it was a study on pharmacological therapy.[44,45] Lee et al.,[46] based on the fact that minimizing secondary injury is the only therapeutic option to influence neurological outcome, conducted a study comparing early surgical decompression (within 24 hours) and very early surgical decompression (within 8 hours). They found a better neurological outcome if the patient is operated on in the first 8 hours than from 8 to 24 hours from injury. They failed to demonstrate better secondary outcome related to time of surgery. Furthermore, in line with literature, a better improvement has been seen in patients with incomplete SCI. Grassner et al.[47] also examined the early decompression within 8 hours and clinical outcome at 1 year using AIS and SCMI. In detail, they found significant differences in AIS grade after 1 year and between neurological and motor levels that were both caudal in case of early decompression. However, it is necessary to specify that no significant differences were seen between the first assessment after surgery and at 1-year follow-up. Liu et al.,[48] using the same surgical timing, demonstrated shorter hospital stays and fewer perioperative complications associated with early surgery. On the contrary, Pointillart et al.[49] did not identify significant differences in neurological outcome related to time of surgery, but their primary focus was on the pharmacological therapy and not surgery. Ter Wengel et al. studied surgical decompression within 24 hours specifically in complete cervical SCI. In clinical practice, patients with complete SCI are often treated less urgently than those with incomplete SCI, but this does not have a scientific basis. With the purpose of analyzing outcomes in this specific population of patients, they performed a metanalysis providing a class II level of evidence. They concluded that early

Table 3. Papers on MRI imaging in SCI

Study	Data collection	Level of evidence	Sesgos	Clinical	Rx	Parameters	Results	Conclusion
Fehlings et al.[36] 2017	Review	I: Consensus on systematic review No PRISMA mentioned GRADE evaluations	Indirectness No gold standard	Frankel	MRI	Evidence Level. 1 prospective study by Papadopoulos et al (2002) that evaluated the effect of pre-treatment MRI on neurological outcomes	Emergency MRI provided an essential tool for the accurate diagnosis of spinal cord compression and directly influenced our initial clinical management in the majority of protocol patients."	We suggest that MRI be performed in adult patients with acute spinal cord injury prior to surgical intervention, when feasible, to facilitate improved clinical decision making. Quality of Evidence: Very Low Strength of Recommendation: Weak We suggest that MRI should be performed in adult patients in the acute period following SCI, before or after surgical intervention, to improve prediction of neurologic outcome. Quality of Evidence: Low Strength of Recommendation: Weak Introduction
Kleiser et al.[34] 2010	Prospective	Prospective cohort	Multicentric	N/A	MRI	T2-weighted turbo spine echo (TSE) sequence, sagittal orientation, T1-weighted TSE sequence, sagittal orientation, T1-weighted TSE sequence, sagittal orientation, T2-weighted GE sequence	The SCI was clearly visible as a hyperintense area in the T2-weighted images on day 4. On day 7, the spinal cord lesion was visible on 2 up to 4 sagittal sections. The lesions of the spinal cord injury remained constant for the subsequent observation times (Fig. 2) and were clearly evident still on day 84.	• Gadolinium-enhancement starts approximately 4 days after the traumatic spinal cord lesion and is maximal between day 7 and 28. • Gadolinium accumulates in the spinal cord lesion 5 minutes after intravenous injection, reaching a stable enhancement after 10 minutes for up to 30 minutes. • Detection of the disrupted blood-spinal cord barrier requires MR imaging at least 10 minutes after intravenous gadolinium injection
Ghasemi et al.[32] 2015	Prospective	Prospective cohort	Small sample	ASIA A-D	MRI contrst Dutarm (gadoterate meglumine)	MRI finding: Level of spine involvement, type of cord injury (edema-hemorrhagia combined),9,10 and percentage of cord injury (>50%–50% to 75%–<75%)	A classification with 3 patterns of SCIs. Type I, decreased signal intensity consistent with acute intraspinal hemorrhage. Type II: bright signal intensity consistent with acute cord edema. Type III: mixed signal of hypointensity centrally and hyperintensity peripherally consistent with contusion.	We recommend the MRI with contrast only used in cases of suspected severe soft tissue injury, which have been ignored by detection MRI without contrast.
Cheran et al.[33] 2011	Prospective	Prospective cohort	Nonrandomized	ASIA hystoric control	MRI DWI DTI	MR imaging was performed 1 hr–5 days after injury. Imaging was performed within 6 hour of injury	The 2-way interaction between ASIA and $\lambda_{\parallel}$ was able to predict with an overall classification accuracy of 86.4% ($p<0.0026$)	The study demonstrated that regional and injury site MR DTI parameter measurements reflect the severity and are reliable makers of spinal cord injury. Among the DTI parameters, $\lambda_{\parallel}$ and FA values appear to be the most sensitive measurements at the injury site.

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Table 3. Continued

Study	Data collection	Level of evidence	Sesgos	Clinical	Rx	Parameters	Results	Conclusion
Gupta et al.[43] 2014	Prospective	Prospective cohort	Do not describe moment of MRI Not blinded	ASIA	MRI	Based on the MRI findings, patients were divided into six patterns Pattern zero: Normal findings Pattern I: Hemorrhage Pattern II: Oedema Pattern III: Contusion Pattern IV: Compression Pattern V: Transection pattern	The best predictors for baseline ASIA score were MCC, cord oedema and cord hemorrhage. For the final ASIA score, the best predictors were baseline ASIA score and cord hemorrhage	MRI is excellent imaging modality for detecting and assessing severity of spinal trauma. In our study, presence of cord hemorrhage, MCC and cord oedema were best predictors of baseline neurological status at presentation, whereas baseline ASIA score and cord hemorrhage were best predictors of final neurological outcome. Presence of cord oedema, cord hemorrhage and MCC best correlate with neurological deficit at presentation. While poor baseline ASIA score and cord hemorrhage confers a poor long-term outcome. On the other hand, absence of cord hemorrhage usually indicates some potential for neurological recovery.
D'Souza et al.[42] 2017	Prospective	IV: Case and Contros	Done within 7 days of injury	Frankel	MRI DTI	Scoring of extent of clinical severity was done based on the Frankel grading system. MRI was performed on a 3T system within 7 days of sustaining trauma.	Mean FA value at the level of injury (was less than the Mean FA value of cervical spine. Spearman correlation ($r=0.86$) was found between FA values at the level of injury and clinical grading	DTI was superior to conventional. MRI scans in depicting changes in spinal cord integrity after traumatic injury. Qualitative tractography enabled the delineation of changes in the white matter tract of spinal cord, both obvious as well as subtle. Quantitative indices in the form of FA and MD were a more useful parameter for detection of spinal cord injury. FA value was significantly decreased while MD value was significantly increased at the level of injury in cases as compared to controls. FA showed significant correlation with the Frankel score, a clinical measure of the motor and sensory status. Long-term studies would be needed to see if DTI could be used as a reliable prognostic marker of neurological outcome in spinal cord injury
Talekar et al.[81] 2016	Review	Review	Comprehensive review	CT and MRI	MRI DTI	Non systematic	Conventional MR techniques do not appear to differentiate edema from axonal injury.	While MRI and DTI will likely never provide the same high level of granularity as that of a good quality neurologic examination, it does offer three distinct advantages over the INSCSCI assessment: (1) speed, (2) objectivity and (3) direct visualization of the end organ (the spinal cord).

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Table 3. Continued

Study	Data collection	Level of evidence	Sesgos	Clinical	Rx	Parameters	Results	Conclusion
Huang and Ou[41] 2014	Prospective	Prospective Cohort	N/A	ASIA Respiratory failure	MRI	Surgery was indicated if the neurological deficits were compatible with the abnormal findings of the MRI scans	There was a statistically significant intergroup difference in the imaging level of CSCI ($p < 0.001$)	The imaging level of injury at C3 is more frequently associated with respiratory failure than injury to the lower cervical levels. Additionally, the presence of spinal cord edema is a predictor that contributes to respiratory failure. In order to prevent secondary spinal cord injury from prolonged hypoxia and to facilitate pulmonary care, definitive airways with assisted ventilation should be established early in the high-risk patients.
Chandra et al.[82] 2012	Review	Comprehensive review	Nonsytemized	ASIA	MRI	Review	Review	MRI is an essential tool to define the site and nature of cord injury in addition to associated disc, ligamentous and vertebral injuries. The magnetic resonance (MR) appearances of cord hematoma, severity of maximal cord compression and length of cord oedema are all significantly associated with worse long-term functional independence scores and are important considerations in planning acute management. Neurological deterioration in the subacute period constitutes a medical emergency and MRI is pivotal in determing the underlying cause.
Freund et al.[40] 2013	Prospective	Prospective	None	ISNCSCI SCIM	MRI	We assessed patients clinically and by MRI at baseline, 2 months, 6 months, and 12 months, and controls by MRI at the same timepoints	Improvements in SCIM scores at 12 months were associated with a reduced loss in cross-sectional spinal cord) and reduced white matter volume of the corticospinal tracts at the level of the right internal capsule Improvements in ISNCSCI motor scores were associated with less white matter volume change encompassing the corticospinal tract at the level of the right internal capsule	Extensive upstream atrophic and microstructural changes of corticospinal axons and sensorimotor cortical areas occur in the first months after spinal cord injury, with faster degenerative changes relating to poorer recovery. Structural volumetric and microstructural MRI protocols remote from the site of spinal cord injury could serve as neuroimaging biomarkers in acute spinal cord injury.

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Table 3. Continued

Study	Data collection	Level of evidence	Sesgos	Clinical	Rx	Parameters	Results	Conclusion
Mabray et al.[39] 2016	Prospective	Prospetive cohort		AIS TLICS	MRI At 14 hr	BASIC grading Grade 1: normal spinal cord signal; Grade 2: hyperintense intramedullary signal with longitudinal extent confined to a single vertebral level; Grade 3: >1 vertebral level edema; Grade 4: represented mixed hemorrhage and edema.	In a multiple variable model, BASIC was the only statistically significant predictor of AIS at discharge.	This study validates the use of BASIC and other MRI measures of acute SCI specifically in the setting of thoracic SCI. PC analysis identified two distinct patterns of variance: PC1, which was highly related to AIS at discharge, and PC2, which was highly related to surgical decompression. The highest individual correlation with AIS at discharge was seen with the BASIC system, although all metrics of spinal cord signal abnormality had a high degree of individual negative correlation with AIS at discharge. The relationship of MCC and MSCC with AIS at discharge was found to be more complex, likely reflecting the use of these metrics along with TLICS in surgical decision making. A multiple variable regression model identified BASIC as the only statistically significant predictor of AIS at discharge, signifying that BASIC best captured the variance in AIS within our study population
Martin et al.[31] 2015	Review	Systematic review Prisma 104 Articles	Low		MRI	Evidence Low 1 Very Low 1, Insufficient 2 1 Moderate 1 Insufficient 1 Low	Diagnostic MRI utility: Biomarker utility.	Moderate evidence indicates that the quantitative DTI metric FA successfully correlates with impairment in a number of neurological disorders DTI has produced the most substantial results to date, but acquisition methods, data processing, and interpretation require further refinement, followed by standardization and cross-vendor validation, before this technology is ready for widespread clinical adoption.
Jeong et al.[38] 2018	Retrospective	Retrospective cohort	N/A	ASIA	MRI	Authors analyzed the factors believed to increase the risk of requiring a tracheostomy, including the severity of SCI, the level of injury as determined by radiological assessment, three quantitative MR imaging parameters, and eleven qualitative MR imaging parameters	Five factors were detected on multivariate analysis complete SCI, the radiological level of C5 and above, canal compromise, lesion length, and osteophyte formation 40–50 mm	The American Spinal Injury Association grade A, a radiological injury level of C5 and above, an MCC $\geq 50\%$, a lesion length ≥ 20 mm, and osteophyte formation at the level of injury were considered to be predictive values for requiring tracheostomy intervention in patients with cervical SCI.

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Table 3. Continued

Study	Data collection	Level of evidence	Sesgos	Clinical	Rx	Parameters	Results	Conclusion
Seif et al.[37] 2018	Prospective	IV case and control	Low sample Nonrandomized	ISNCSCI	MRI	MRI protocol sensitive to myelin and iron. Patients were examined clinically at baseline, 2, 6, 12, and 24-month post-SCI.	Importantly, early volume and microstructural changes of the cord and cerebellum predicted functional recovery following injury	Neurodegenerative changes rostral to the level of lesion occur early in SCI, with varying temporal and spatial dynamics. Early qMRI markers of spinal cord and cerebellum are predictive of functional recovery. These neuroimaging biomarkers may supplement clinical assessments and provide insights into the potential of therapeutic interventions to enhance neural plasticity.
Talbott et al.[35] 2015	Retrospective	Retrospective cohort	Nonrandomized	ASIA AIS		Five distinct patterns of intramedullary spinal cord T2 signal abnormality were defined in the axial plane at the injury epicenter. These patterns were assigned ordinal values ranging from 0 to 4, referred to as the BASIC scores, which encompassed the spectrum of SCI severity.	The BASIC score strongly correlated with neurological symptoms at the time of both hospital admission and discharge. It also distinguished patients initially presenting with complete injury who improved by at least one AIS grade by the time of discharge from those whose injury did not improve. The authors' proposed score was rapid to apply.	The authors describe a novel 5-point ordinal MRI score for classifying acute SCIs on the basis of axial T2-weighted imaging. The proposed BASIC score stratifies the SCIs according to the extent of transverse T2 signal abnormality during the acute phase of the injury. The new score improves on current MRI-based prognostic descriptions for SCI by reflecting functionally and anatomically significant patterns of intramedullary T2 signal abnormality in the axial plane.

MRI, magnetic resonance imaging; SCI, spinal cord injury; ASIA, American Spinal Injury Association Impairment; DWI, Diffusion-weighted imaging; DTI, diffusion tensor imaging; CSCI, cervical spinal cord injury; MCC, maximum canal compromise; MSCC, maximum spinal cord compression; TLICS, Thoracolumbar Injury Classification and Severity Score; FA, fractional anisotropy; ISNCSCI, International Standards for Neurological Classification of Spinal Cord Injury; BASIC, Brain and Spinal Injury Center; qMRI, quantitative MRI.

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surgical decompression in patients with complete SCI consented a better outcome of 2 ASIA grades, in contrast to patients with incomplete SCI which did not benefit significantly as much from early decompression. This result is in contrast with most common clinical practice and many other studies have demonstrated the opposite conclusion. Further studies with specific subgroups of patients are needed to settle the role of early decompression both for complete and incomplete SCI.[50-52] The same group performed a metanalysis using as surgical timing within 24 hours and they failed to demonstrate a better outcome related to time of surgery. However, they only included patients with thoracic and thoracolumbar injury and this represents a bias of this study due to the lower incidence of trauma at this level with respect to cervical SCI and the fact that at lumbar level the injury affects less quality of life for those patients.[53] Furthermore, the majority of the cited studies analyzed the reason for the delay in surgical decompression and 2 main problems were identified. The first one is the time necessary for transportation in center (preferably a level I neurotrauma center) able to manage and surgically treat the patients. The second one is the necessity to stabilize the patients before surgery in the case of politraumatic patients. Literature review is summarized in Table 4.

Based on the presented literature and personal experience the committee voted as follows:

Statement 4: Early surgery (within 8 hours) should be performed in most cases of SCI. This statement reached a strong positive consensus (6 out of 7 voted grade 5 of LS and only 1 voted grade 4)

Statement 5: If feasible, SCI patients need to be treated in a specialized level 1 neurotrauma center. This statement also reached a strong positive consensus (6 out of 7 voted grade 5 of LS and only 1 voted grade 4).

3. Cardiopulmonary Management and Its Effect on Prognosis

Literature search from 2009 to 2019 was undertaken using keywords "cardiopulmonary management using spinal cord injuries" from Google Scholar resulting in 14,400 hits. 193 were left after refining the search terms and removing non-English articles. The same search was performed in PubMed using the above-mentioned key words resulting in 55 hits and after removing non-English articles the results were reduced to 29 articles. After reviewing, only 7 articles were selected from PubMed and 96 articles were selected from Google Scholar. We focused on 4 specific topics concerning human patients with

Table 4. Studies on early management of SCI

Study	Data collection	Early decompression	Late decompression	Conclusions
Lee et al.[46] 2018	Retrospective	< 8 hr From C1 to L2 Complete and incomplete SCI	> 8 < 24 hr From C1 to L2 Complete and incomplete SCI	Early decompression shows better neurological outcome Better improvement in patients with incomplete SCI
Grassner et al.[47] 2016	Retrospective analysis on prospective collected data	< 8 hr Cervical complete and incomplete SCI	> 8 hr Cervical complete and incomplete SCI	Early surgical intervention after cervical traumatic SCI may lead to a better functional outcome of affected individuals (SCIM and AIS scores)
Liu et al.[48] 2016	Metanalysis	< 24 hr	> 24 hr	Urgent surgery within 24 hours was associated with higher total motor scores, better neurologic improvement, shorter hospital stay and fewer complications compared with those of late surgery
Ter Wengel et al.[53] 2019	Metanalysis	< 24 hr Complete and incomplete thoracic SCI	> 24 hr Complete and incomplete thoracic SCI	Similar neurological recovery was observed after early and late surgery in this meta-analysis of thoracic and thoracolumbar tSCI
Ter Wengel et al.[50] 2019	Metanalysis LoE II	< 72 hr Complete and incomplete cervical SCI	< 72 hr Complete and incomplete cervical SCI	Early decompression in complete SCI shows a better neurological outcome than late decompression Early decompression in incomplete SCI shows a similar neurological outcome than incomplete SCI Decompression within 24 hr in complete SCI shows better results

SCI, spinal cord injury; SCIM, Spinal Cord Independence Measure; AIS, American Spinal Injury Association Impairment Scale; tSCI, traumatic spinal cord injury.

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acute SCI: management in an intensive care unit (ICU), cardiac instability, hypotension, and respiratory/pulmonary dysfunction. Additional citations were extracted from the reference lists of the remaining papers. Finally, members of the author group were asked to contribute articles known to them on the subject matter that was not found by other search means. Articles describing economics, epidemiology, anesthesia, monitoring techniques, penetrating cord injuries, nursing care, infectious or urologic complications, chronic complications, or remote SCIs were excluded. These efforts resulted in 11 articles, which form the foundation for this updated review. All studies provided class III medical evidence (Fig. 1).

The Swiss Paraplegic Center prospectively reported their medical management outcome, of 117 patients with spinal cord injuries, 40 years ago. They monitored those patients in ICU with central venous pressure monitoring, along with volume expansion and they were given steroids for 10 days. They showed an overall improvement in 62% in cervical level and, 70% in of T11–L1 level SCI. Patients admitted early had an early recovery. They reported that early transfer and "immediate treatment of the spinal injury" with attention to the maintenance of acceptable blood pressure (BP) improved the outcome of those patients.[54] Vale et al. published a prospective pilot study of patients with acute SCI, managed aggressively with attention to BP, oxygenation, and hemodynamic performance. They treated 77 patients with acute SCI, in the ICU, with BP augmentation to maintain mean arterial pressure (MAP) more than 85 mmHg for 7 days. 52% of incomplete cervical SCI patients required pressors to maintain MAP above 85 mmHg. There were no harmful effects from this therapy and exhibited improved neurological outcome. Despite these observations, in modern practice patients of acute traumatic SCI are not universally treated with BP augmentation postinjury.[55-58] Levi et al.[59] investigated 50 acute SCI patients with aggressive management protocol with invasive hemodynamic monitoring, volume, and pressor support to maintain a mean BP of more than 90 mmHg. At admission, 8 patients had severe hypotension (systolic BP [SBP] < 90 mmHg). 82% of the patients had volume-resistant hypotension requiring pressors within the first 7 days, which was 5½ times more common with complete motor injuries. Overall, the mean pulmonary vascular resistance was less than normal in 58%. Forty percent of these patients, including the complete injuries, had neurological improvement, 42% remained unchanged, and 9 patients died (18%). Levi et al.[59] suggested that hemodynamic monitoring in the ICU enables the early identification and prompt treatment of cardiac dysfunction and hemodynamic instability, leading to reduce morbidity and mortality. The results of Vale et al. and Levi et al. provide the rationale for the level III recommendation from the American Association of Neurologic Surgeons regarding cardiopulmonary resuscitation in SCI. These guidelines recommend the maintenance of MAP between 85 and 90 mmHg for the first 7 days following acute cervical SCI. Although limited by the paucity of current literature on the topic, this recommendation provides the foundation for the medical management of SCI in many institutions.[47,48]

Regarding the acute cardiopulmonary management of patients with cervical spinal cord injuries, Ryken et al recommended management should be in an ICU or similar monitored setting. In order to detect cardiovascular dysfunction and respiratory insufficiency, they recommend the use of cardiac, hemodynamic, and respiratory monitoring devices. Early correction of hypotension in SCI (SBP < 90 mmHg) when possible is encouraged. The mean arterial BP should be maintained between 85–90 mmHg for the first 7 days following an acute SCI.[60] Hawryluk et al.[61] used q1 minute data to demonstrate that MAP goals > 85 mmHg were associated with improved neurologic outcomes. Elevated mean MAP during the first 2–3 days following injury was associated with improved neurologic outcome. The likely benefit of vasopressor administration for SCI management in this study is backed by the q1 minute MAP monitoring, which provides the strongest evidence. The same group analyzed the association between MAP and neurological improvement in patients stratified by their postresuscitation AIS score. They demonstrated a positive correlation between higher MAP values and neurological improvement in patients who are AIS A, and B/C on the postresuscitation exam, but not those who are AIS D. This suggests the possibility that AIS A patients may have greater benefit from MAP augmentation than AIS D patients and that it is important to avoid pessimism when considering MAP augmentation in patients with initially complete SCIs. Vasopressor administration is associated with greater risk of complications in AIS A patients and duration of therapy should be determined in view of these complications. Despite the absence of benefit from MAP augmentation in AIS D patients, they recommended that we should continue to encourage intensive MAP monitoring in these patients.[62]

Regarding intrathecal pressure (ITP) and its role in SCI, greater emphasis has been placed on augmentation of mean arterial BP in acute SCI, while little data is available on the role of ITP during this period, when spinal cord perfusion pressure (mean arterial blood pressure-ITP) is of vital significance. ITP

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is inversely related to spinal cord perfusion, hence raised ITP postinjury may also lead to secondary injury via reduced perfusion of the spinal cord. Kwon et al.[63] conducted a prospective randomized trial on 22 patients and placed a lumbar intrathecal catheter for 72 hours in these patients. Acute SCI motor scores were documented at baseline and 6 months postinjury. Mean ITP on insertion was 13.8 mmHg, which increased to a mean peak of 21.7 mmHg intraoperatively. The restoration of CSF flow across the injury site after surgical decompression was characterized by changes observed in the ITP waveform. This waveform can be utilized during surgery to determine if the thecal sac has been adequately decompressed. The numbers were too small and at least the drainage of CSF did not show any side effects. 11 patients with AIS A, B, and C injuries were enrolled and studied by Altaf et al to see the differential spinal cord pressure. In comparison with dopamine, norepinephrine maintained a MAP with a lower ITP and correspondingly higher perfusion pressure.[63-65] Different papers discuss the role of vasopressors. Agents with inotropic, chronotropic, and vasoconstrictive properties should be used to maintain BP. Dopamine, norepinephrine, or epinephrine α1- and β1-agonist properties are acceptable options. Phenylephrine acts on α1-receptors as an agonist with minimal risk of reflex bradycardia (β1 effect). Dobutamine can cause vasodilation with the possible risk of reflex bradycardia and has a limited role in SCI.[66,67] Readdy et al.[68] showed that dopamine had a greater complication rate in SCI, although it was non-significant. The complication rate was 68% with dopamine while 45% for phenylephrine. Patients older than 55 years were associated with all kinds of vasopressor complications. 90% of older patients experienced complications in comparison to 52% of the younger patients. The Consortium for Spinal Cord Medicine suggested using vasopressors depending on the level of spinal cord involved. In high cervical and thoracic injuries, agents with both α- and b-adrenergic activity are recommended i.e., Dopamine, norepinephrine because of bradyarrhythmias due to unopposed vagal tone. In lower thoracic injuries, where hypotension can result in vasodilation, pure α -adrenergic agents such as phenylephrine are the drugs of choice.[69] Saadeh et al.,[56] in their systemic review, demonstrated that cardiogenic complications are independently associated with both dopamine and phenylephrine. Dopamine resulted in more serious complications among elderly patients. They explained that vasopressor choice is governed by level of injury (e.g., above or below T-6), age (e.g., an elderly patient with autonomic dysfunction), and presence of comorbid conditions. In updated guidelines for the management of acute cervical spine and SCI patients, Resnick stressed the systemic cardiorespiratory status and the impact it has on outcomes. They narrated that both hypoxia (oxygen saturation < 90%) and hypotension (SBP < 90 mmHg) are relatively common after polytrauma, and even brief periods are associated with worse outcomes. This is recognizable and amenable to treatment.[70,71] Berney et al.[71] did a systemic review of 21 studies including definitive protocols for the respiratory management of acute cervical SCI. Mortality, incidence of respiratory complications, and the requirement for a tracheostomy were significantly reduced when caregivers used a respiratory protocol in the management of acute SCI patients. Specifically, the use of a clinical pathway reduced the duration of mechanical ventilation by 6 days and ICU length of stay by 6.8 days. There is level III evidence that keeping MAP above 85 for 7 days in patients with SCI improves neurological outcome. Early correction of hypotension in SCI (SBP < 90 mmHg) when possible is recommended. Patients with SCI suffer from cardiac issues including hypotension and bradycardia. Phenylephrine is recommended for ionotropic support when compared to dobutamine in patients over 55 years (avoids reflex bradycardia). In cervical or high thoracic lesions with both hypotension and bradycardia, a drug like norepinephrine with chronotropic, inotropic, and vasoconstrictor properties might be required. For low thoracic lesions, where hypotension is usually the result of peripheral vasodilation, a pure vasopressor drug such as phenylephrine may be appropriate. Table 5 summarizes main characteristics of the cited papers.

Based on the presented literature and personal experience the Committee voted as follows:

Statement 6: MAP above 85 for 7 days in patients with SCI improves neurological outcome. Correction of hypotension in SCI (SBP < 90 mmHg) is recommended as soon as possible. This statement reached a strong positive consensus (6 out of 7 voted grade 5 of LS and only 1 voted grade 4).

Statement 7: Patients with SCI suffer from cardiac issues including hypotension and bradycardia and it is worse in complete injuries. Hypotension and bradycardia must be aggressively managed. This statement reached a strong positive consensus (6 out of 7 voted grade 5 of LS and only 1 voted grade 4).

Statement 8: In Cervical or high thoracic lesions with both hypotension and bradycardia, a drug like norepinephrine and chronotropic and inotropic effects as well as vasoconstrictor properties may be used. This statement reached a strong positive consensus (5 out of 7 voted grade 5 of LS and 2 voted grade 4 of LS).

Table 5. Studies on cardiopulmonary management of spinal cord injury

Study	Data collection	Study type	Neurological outcome measures	No. of patients	Level of injury	Outcomes	MAP goal (mmHg)	MAP goal duration	Length of follow-up
Saadeh et al.[56] 2017	Prospective and retrospective data	Systematic Review 11 cohort studies	AIS grade, ASIA motor score Modified Frankel score, Yale Scale score	Variable*	C, T, and L spine	127 Patients, report stable or improved neurological function following management to elevated MAP target during the early phase of care[4]			Variable
Sabit et al.[57] 2018	Prospective and retrospective data	Systematic Review of 9 cohort studies	AIS grade, ASIA motor score Modified Frankel score, Yale Scale score	Variable*	C, T, and L spine	Four of nine studies showed neurological improvement associated with higher MAP targets. Two studies found episodes of hypotension related to poor recovery.[5]			Variable
Squair et al.[83] 2019	Prospective	Case series	ISNCSCI, AIS grade	92	C, T and L Spine	Adherence to SCPP targets was the best indicator of improved neurologic recovery (60–65 mmHg)[6]			6 Months
Dakson et al.[84] 2017	Retrospective	Comparative	AIS grade, ASIA motor score	94*	C, T, and L spine		> 85	5 Days	After neurorehabilitation
Kepler et al.[85] 2015	Retrospective	Case Series	ASIA motor score	92	C, T, and L spine		> 85	≥ 5 Days	Until hospital day 5
Martin et al.[31] 2015	Retrospective	Case Series	AIS motor score	105	C & T spine		NS	NS	Until discharge
Hawryluk et al.[61] 2015	Retrospective	Case Series	AIS grade	74	C, T, and L		> 85	5 Days	Until discharge
Inoue et al.[86] 2014	Retrospective	Case Series	AIS grade	131	C, T, and L spine		> 82	7 Days	Until discharge
Vale et al.[55] 1997	Prospective	Case Series	AIS grade, ASIA motor score	77	C and T spine		> 85	7 Days	12 Months
Levi et al.[59] 1993	Prospective	Case Series	Frankel grade	50	C Spine only		> 90	7 Days	6 Weeks
Wolf et al.[87] 1991	Retrospective	Case Series	Modified Frankel score, Yale Scale score	52	C spine only		> 85	5 Days	12 Months

MAP, mean arterial pressure; ASIA, American Spinal Injury Association; AIS, ASIA Impairment Scale. ISNCSCI, International Standards for Neurological Classification of Spinal Cord Injury; NS, not specified; C, T, and L, cervical, thoracic, and lumbar; SCPP, spinal cord perfusion pressure.

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Statement 9: Level, completeness of the injury, age, previous diseases, and tachypnea at admission are associated with a higher likelihood of respiratory complication. These patients should be aggressively managed. This statement reached a strong positive consensus (all expressed a vote of grade 5 of LS).

DISCUSSION

Early phases of SCI are critical in the management of these patients, and in particular definition of the clinical assessment and classification represent the first essential step to help the therapeutic process decision making. Moreover, these tools can also be used to predict prognosis. The role of worldwide accepted recommendations may help in communication of clinical data, an aspect particularly relevant for those patients who must be referred to a trauma center from a secondary or tertiary hospital.

1. Clinical Assessment and Classification of SCI

A scarcity of papers exists on this topic explained by the widespread use of existing tools; further investigations are required to confirm the performance of those tests in the acute care setting.[11] Most of the research was focused on emerging technologies to better define neurological impairment and predict prognosis. Translational research has proved to provide increasing evidence but unsatisfactory solutions.[14,72,73] From those papers, biomarkers have been extensively studied, and many biological compounds have been highlighted as potentially useful compounds to assess neurological injury at admission and help predict prognosis; nevertheless, the profile is quite extensive, and no uniform criteria (or dataset) have been defined.[6] Since the initial review on assessment tools for acute SCI the AIS has been designated as the recommended evaluation tool to evaluate and classify initial neurological impairment on admission[36] and provide information on improvement at follow-up.[12] Both scores (AIS and ISNCSCI) have been largely studied and validated to assess and predict prognosis and correlate with the severity of SCI on imaging studies, besides it is recognized that additional quantitative assessments may be needed.[5,19,29,74] Currently, the ISCIBPDS is the preferred scale for evaluating pain from early assessment to the follow-up in chronically injured patients as it has the highest reliability and validity of any of the pain classification instruments.[63,65]

Regarding radiological assessment of SCI, MRI defines the profile of neurological damage in the acute setting and helps make a better decision regarding treatment options; nevertheless, further research is needed to increase the precision of diagnosis and decrease the false-negative rates in cases such as SCIWORA, and protocols are to be standardized before widespread clinical use of the advantages can be done.[12,24] We consider that clinical assessment tools and classifications can be changed as there will be the advent of standardized biomarker data sets and more sophisticated MRI protocols. We agree with Krishna et al that in the new MRI era, protocols will be developed and will help define neurological injury better and accurately classify SCI severity in the early future.[63] We hope these advances in neurological assessment can help us change the patient's prognosis for good. In the meantime, we must remain on current tools and resume evidence on critical points to evaluate and care for acute SCI patients.

2. Emergency Care and Early Management

From a pathophysiological point of view, the mechanism of damage in spinal cord injuries can be divided in primary, due to the trauma itself (spinal cord contusion or compression), and secondary, due to blood flow reduction/interruption, inflammation cascade, and edema. The treatment goal is to reverse neurological injury, avoiding secondary injury and stabilize spinal column if necessary. The timing of surgery, age, and initial neurological status affect clinical outcome as independent factors. Nowadays, the concept of early surgery is accepted worldwide but there is a lot of heterogeneity in defining time in term of hours for early surgical decompression. Since 2010, the majority of papers have identified a time limit of 24 hours. But recently a new limit of 8 hours takes importance with an interval considered between 6 and 12 hours. In particular, most studies found that early surgery < 8 hours has advantages on neurological recovery (in terms of AIS score), especially in patients with complete neurological compromise; in terms of postoperative complications and hospitalization the correlation has not been proven. However, we must consider defining the timing of surgery, since it may have importance from a legal issue as well. For this reason, the recommendation must be acceptable worldwide, in accordance with the different facilities of each country. At present, the ideal surgical time is within 8 hours from trauma, if that is not possible it is recommended to not exceed 24 hours. Furthermore, early surgical decompression is indicated not only for incomplete but also in the case of complete SCI.

3. Cardiopulmonary Management and Its Effect on Prognosis

It is well known that patients with SCI may present cardiovascular dysfunction and respiratory insufficiency, and during

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initial management, an ICU or similar monitored setting is advocated in order to detect these complications promptly.[60] Early correction of hypotension (SBP < 90 mmHg) when possible is encouraged and must be performed as soon as possible. The role of vasopressors has been discussed in many papers and globally we accept that agents with inotropic, chronotropic, and vasoconstrictive properties should be used to maintain BP. Dopamine, norepinephrine, or epinephrine α1-and β1-agonist properties are also acceptable options.

CONCLUSION

To guarantee the best neurological outcome in SCI the early management of patients remains crucial from different points of view. Our committee defined the most useful and feasible scales to assess neurological injury and predict severity and they are: the AIS, ISNCSCI, and ISCIBPDS. Cardiopulmonary management plays an essential role in those patients: correction of hypotension (SBP < 90 mmHg), and bradycardia is strongly recommended as soon as possible and drugs like norepinephrine and chronotropic and inotropic effects, as well as vasoconstrictor properties, may be used. Regarding surgical treatment, it is our opinion that it is important to proceed with surgical decompression as soon as possible. At present, the ideal surgical time is within 8 hours from trauma, while if that is not possible it is recommended not to exceed 24 hours. Furthermore, it emerged that early surgical decompression is indicated not only for incomplete but also in the case of complete SCI.

WFNS RECOMMENDATIONS FOR EARLY MANAGEMENT OF SCI

Recommendations for Clinical Assessment and Classification of SCI

- AIS described by the ASIA is recommended as the preferred clinical evaluation tool for acute neurological assessment in patients with SCI.
- The SCIM III, may be preferred to assess the functional abilities and impairment in the follow-up of patients with chronic SCI.
- The ISCIBPDS may be the preferred scale to evaluate the pain in chronically injured patients.

Recommendations for Emergency Care and Early Management of SCI

- Early surgery (within 8 hours) should be performed in most cases of SCI.
- Corticosteroids are not indicated in the majority of acute phase of SCI.
- If feasible, SCI patients need to be treated in a specialized level 1 neurotrauma center.

Recommendations for Cardiopulmonary Management of SCI

- The MAP above 85 for 7 days in patients with SCI improves neurological outcome. Correction of hypotension in SCI (SBP < 90 mmHg) when possible and as soon as possible is recommended.
- Patients with SCI suffer from cardiac issues including hypotension and bradycardia, and it is worse in complete injuries.
- In cervical or high thoracic lesions with both hypotension and bradycardia, a drug like norepinephrine with chronotropic and inotropic effects, as well as vasoconstrictor properties, may be required.
- Level, completeness of the injury, age, previous disease, and tachypnea at admission are associated with a higher likelihood of respiratory complication, hence these patients should be aggressively nursed.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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