A Series of Systematic Reviews on the Treatment of Acute Spinal Cord Injury: A Foundation for Best Medical Practice

Michael G. Fehlings, David W. Cadotte, and Lauren N. Fehlings

Abstract

The treatment of acute spinal cord injury (SCI) is a multidisciplinary effort that spans from the time of injury through to an acute care center, and in some cases the remainder of the individual's life. Recovery from SCI depends on the care received at each point along this spectrum in time. In order to facilitate the practice of evidence-based medicine and best clinical practices, a multidisciplinary team of clinicians and researchers systematically reviewed the literature on SCI and set out to answer pertinent clinical questions and establish evidence-based recommendations. This article introduces the series of systematic reviews, summarizes the most notable findings, and gives an overview of the questions asked in each review and the evidence-based recommendations for care. Some of the most important recommendations are as follows: (1) Patients should be immobilized before transport to a hospital using a cervical collar, head immobilization, and a spinal board; (2) MRI is strongly recommended for the prognostication of acute SCI; (3) early surgical intervention (from 8–24 h) should be considered following acute traumatic SCI; (4) SCI patients are at significant risk of cardiovascular and respiratory problems and management should proactively anticipate these potential complications; and (5) outcomes can be improved by management in specialized centers with access to intensive care.

Introduction

THE TREATMENT OF SPINAL CORD INJURY (SCI) spans multiple disciplines ranging from pre-hospital immobilization to surgical care to rehabilitation strategies. In some cases, persons suffering from SCI will be dependent on medical practitioners for the duration of their life. This series of systematic reviews aims to establish a set of best medical practice recommendations, formulated by integrating clinical expertise and evidence available from published literature (Sackett et al., 1996). Our objective is to engage those involved in the treatment of SCI to both evaluate the current state of health care delivery and discover opportunities for improvement.

Advances in the care of SCI patients at any point along the spectrum from pre-hospital stabilization to long-term rehabilitation offer a great opportunity to improve the quality and duration of a person's life. Identifying inconsistencies and integrating advances along this spectrum of care will certainly benefit the long-term outcome of persons suffering from SCI. This series of reviews not only integrates all aspects of this spectrum with regard to the published literature, but also incorporates the clinical expertise of health professionals. The recommendations reflect aspects of care that demonstrate evidence-based benefit to patients. The authors of the sys-

tematic reviews also point out opportunities for future research in areas where evidence is lacking. Consensus expert opinion is provided where the evidence is emerging.

Highly-cited works in acute SCI have largely focused on the fundamental science underlying this devastating condition, with a relative paucity of highly-cited works that directly address the application of these therapies to patients (Furlan and Fehlings, 2006). In 2007, experts gathered at the SCI-Translational Research Network in Toronto and developed a list of the most clinically-relevant issues in acute care for SCI that had not been recently reviewed (Furlan et al., 2010d). Members of the Rick Hansen Institute acute care and practice team, which is a multidisciplinary team consisting of researchers and clinicians across Canada, took this list and conducted a series of systematic reviews. The goal of this project was to develop a set of best practices and recommendations to help translate evidence into clinical practice.

The systematic reviews cover the spectrum of acute care, including pre-hospital care, the role of specialized centers of care, assessments of impairment and disability, the role of MRI, the timing of surgery, pediatric SCI, predictors of outcome, deep-vein thrombosis and nutrition management, special cardiopulmonary needs, and the role of therapies for acute SCI. Promising scientific research was also reviewed, as these pre-clinical and experimental treatments may become

TABLE 1. A SUMMARY OF THE TITLES, KEY RESEARCH QUESTIONS, AND MAJOR RECOMMENDATIONS OF EACH SYSTEMATIC REVIEW

<i>Topics</i>	<i>Focused questions</i>	<i>Key recommendations</i>
Pre-hospital care (Ahn et al., 2010)	<ol style="list-style-type: none"> 1. What is the optimal type and duration of pre-hospital spinal immobilization in patients with acute spinal cord injury (SCI)? 2. During airway manipulation in the pre-hospital setting, what is the ideal method of spinal immobilization? 3. What is the impact of pre-hospital transport times to definitive care on the outcomes of patients with acute SCI? 4. What is the role for pre-hospital care providers in cervical spine clearance and immobilization? 	<p>Immobilization in patients with SCI during the pre-hospital setting should include a cervical collar, head immobilization, and a spinal board.</p> <p>Airway management of acute SCI patients requiring intubation in the pre-hospital setting should include the use of manual in-line cervical spine traction.</p> <p>Transport of patients with acute traumatic SCI to the definitive hospital center for care should occur within 24 h of injury.</p> <p>Emergency medical personnel in the pre-hospital setting should be trained to apply criteria in the pre-hospital setting should spinal injuries and immobilize patients suspected of having a cervical spinal injury</p> <p>Early transfer of a patient with traumatic SCI to a specialized center of care should be done promptly to decrease overall length of stay.</p> <p>Early transfer of patients with traumatic SCI to an integrated multi-disciplinary specialized center of care decreases overall mortality, and number and severity of complications.</p> <p>American Spinal Injury Association (ASIA) standards should be used for assessment of motor and sensory function.</p> <p>The Visual Analogue Scale (VAS) should be used for the assessment of pain intensity in patients with acute SCI.</p> <p>Spinal Cord Independence Measure (SCIM) III should be used in the classification and evaluation of patients with acute SCI.</p> <p>MRI should be done in the acute period following a spinal cord injury for prognostication.</p> <p>MRI should be done in all patients with acute SCI, when feasible, to direct management.</p> <p>A sagittal T2 MRI sequence should be included in all MRI protocols to prognosticate neurological outcome in the acute SCI setting.</p> <p>It is recommended that surgical decompression of the injured spinal cord be performed within 24h when medically feasible.</p> <p>There are clinical, neurological, and functional benefits of early decompression of the spinal cord.</p>
Specialized centers of care (Parent et al., 2011)	<ol style="list-style-type: none"> 1. Do centers of excellence in SCI decrease the length of patient stay? 2. Do centers of excellence in SCI reduce mortality and secondary complications? 	
Assessment of impairment (Furlan et al., 2010c)	<ol style="list-style-type: none"> 1. What is the most appropriate outcome measure of motor and sensory impairment of acute SCI patients? 2. What is the most reliable, validated, and responsive outcome measure of pain for patients with acute traumatic SCI? 	
Assessment of disability (Furlan et al., 2010b)	<ol style="list-style-type: none"> 1. What is the most reliable, validated, and responsive functional outcome measure for patients with acute traumatic SCI? 	
Imaging assessment (Bozzo et al., 2010)	<ol style="list-style-type: none"> 1. Does magnetic resonance imaging (MRI) predict the outcome? 2. Can MRI direct the management? 3. What is the recommended protocol for MRI? 	
Timing of spinal cord decompression (Furlan, et al., 2010a)	<ol style="list-style-type: none"> 1. What is the optimal timing for surgical decompression of the spinal cord based on the current evidence? 2. What are the potential effects of early decompression of the spinal cord on the clinical, neurological, and functional outcomes in the acute care setting? 	

(continued)

TABLE 1. (CONTINUED)

<i>Topics</i>	<i>Focused questions</i>	<i>Key recommendations</i>
Pediatric spinal cord injury (Parent et al., In review)	1. What is the epidemiology of pediatric SCI and fractures?	Pediatric spinal cord injuries are relatively uncommon and the mechanism of injury is different depending on the age at time of injury.
	2. Are there unique features of pediatric SCI that distinguish this population from adult SCI?	Pediatric patients with traumatic SCI have different mechanisms of injury and a better neurological recovery potential compared to adults. Patients with SCI before their adolescent growth spurt have a high likelihood of developing scoliosis.
	3. Is there evidence to support the use of neuroprotective approaches, including hypothermia and steroids, in the treatment of pediatric SCI?	There was no evidence in the current literature review to support the use of neuroprotective approaches including steroids and hypothermia.
Predictors of outcome (Al-Habib et al., 2010)	1. What are the clinical and radiological factors that predict neurological and functional recovery following blunt traumatic SCI in adults?	Eight recommendations based on evidence for various predictors of outcome.
Deep vein thrombosis (DVT) and nutrition management (Thibault-Halman, et al., 2010)	1. Is there evidence of metabolic abnormalities that warrant specific nutritional protocols following SCI? 2. What methods for evaluating metabolic demands are best applicable in SCI patients?	Patients have unique requirements mandating the development of specific treatment protocols. The use of indirect calorimetry to calculate measured energy expenditure will most accurately predict the patient's caloric needs.
Intensive care unit (ICU) management (Casha and Christie, 2010)	3. What is the optimal route for administration for nutritional requirements following SCI?	Enteral feeding is the optimal route for administration of nutritional requirements following SCI.
	1. Do spinal cord-injured patients warrant management in specialized centers with specific cardiopulmonary protocols and access to ICU care? 2. What is the time at risk for cardiopulmonary complications requiring ICU management availability?	SCI patients should be managed in a monitored special care unit. The period at risk for intensive management of SCI patients appears to start very early if not immediately following the injury, but may extend beyond a month due to prolonged ventilatory requirements that are frequently encountered.
	3. What parameters for blood pressure and oxygenation/ventilation over what time period are associated with improved outcome?	Mean arterial pressure (MAP) > 85 mm Hg should be maintained following SCI for a period extending to at least 1 week following injury.
	4. Are there any risk factors that are predictive of the need for ICU management?	The cardiovascular complication predictors are largely high cervical and complete SCI. While both of these as well as lack of diaphragm function, advanced age, previous cardiopulmonary disease, tachypnea at admission, copious sputum, pneumonia, and major lobe collapse are predictive of the need for ventilatory support.
	5. What preventive strategies can be undertaken to reduce the risks of cardiopulmonary complications requiring ICU care?	Copious secretions in the chest should be managed with physiotherapy and suctioning in order to avoid further respiratory complications.

(continued)

TABLE 1. (CONTINUED)

<i>Topics</i>	<i>Focused questions</i>	<i>Key recommendations</i>
Directly applied biologic therapies (Kwon et al., 2010b)	1. What are the neuroprotective therapies available that are administered through direct application for acute SCI and have a high potential for clinical translation?	The therapeutic strategies are: the degradation of inhibitory chondroitin sulfate proteoglycans with chondroitinase ABC; the neutralization of myelin-mediated inhibition of neurite outgrowth with anti-Nogo (IN-1) antibodies or other Nogo-related approaches; and the inhibition of Rho activation.
	2. What are the gaps in the research and how can we proceed?	Further investigation is needed into the time window of applicability and the biodistribution of these agents within the injured cord. Further pre-clinical work as well as clinical trials on these therapies is warranted to optimize the treatment paradigms.
Non-invasive pharmacological therapies (Kwon et al., 2010a)	1. What are the neuroprotective therapies available that are administered through systemic distribution for acute SCI and have a high potential for clinical translation?	The therapeutic strategies are: erythropoietin, systemic hypothermia, nonsteroidal anti-inflammatory drugs (NSAIDs), anti-CD11 antibodies, minocycline, progesterone, estrogen, magnesium sulfate, riluzole, polyethylene glycol, atorvastatin, inosine, and pioglitazone.
	2. What are the gaps in the research and how can we proceed?	Further investigation into these therapies is needed to demonstrate robustness and confirm relevant time windows of efficacy. Guidelines analogous to those existing in the stroke field will help provide direction to pre-clinical development of these therapies prior to translation.
Cellular transplantation therapies (Tetzlaff et al., 2010)	1. What are the trends in cellular transplantation therapies for SCI?	There are significant differences between cells that are deemed the same type, making it difficult to compare studies. Many studies use cell transplantations in combination with other strategies. The most extensively-studied cells have been derived from rodent sources, and rodents are the favored model of injury. Nearly all studies reviewed were conducted with transplantations occurring subacutely and acutely.
	2. What are the gaps in the research?	The knowledge gaps are: the lack of independent replication, the lack of clinically-relevant contusion models of injury, the paucity of work in large animal models, and the near absence of chronic injury work.

the next standard of care for SCI. From these reviews, the authors, in conjunction with an expert panel, established a set of recommendations (Table 1). Some of the most notable recommendations are as follows:

- Patients should be immobilized before transport to a hospital using a cervical collar, head immobilization, and a spinal board (Ahn et al., 2010).
- MRI is strongly recommended for the prognostication of acute SCI (Bozzo et al., 2010).
- Early surgical intervention (from 8–24 h) should be considered following acute traumatic SCI (Furlan et al., 2010a).

SCI patients are at significant risk of cardiovascular and respiratory problems. Outcomes can be improved by management in specialized centers with access to intensive care facilities with specific protocols established for the management of SCI (Casha and Christie, 2010).

The overarching goal of this project is to increase the quality of care for people with SCI, and to ensure the uniform implementation of best practices. With these results, doctors and other health care professionals will be better equipped to provide the best care for their patients.

Author Disclosure Statement

No conflicting financial interests exist.

References

- Ahn, H., Singh, J., Nathens, A., Macdonald, R.D., Travers, A., Tallon, J., Fehlings, M., and Yee, A. (2010). Pre-hospital care management of a potential spinal cord injured patient: A systematic review of the literature and evidence-based guidelines. *J Neurotrauma*.
- Al-Habib, A.F., Attabib, N., Ball, J., Bajammal, S., Casha, S., and Hurlbert, R.J. (2010). Clinical predictors of recovery after blunt spinal cord trauma: Systematic review. *J. Neurotrauma* [Epub ahead of print].
- Bozzo, A., Marcoux, J., Radhakrishna, M., Pelletier, J., and Goulet, B. (2010). The role of magnetic resonance imaging in the management of acute spinal cord injury. *J. Neurotrauma* [Epub ahead of print].
- Casha, S., and Christie, S. (2010). A systematic review of intensive cardiopulmonary management after spinal cord injury. *J. Neurotrauma* [Epub ahead of print].
- Furlan, J.C., and Fehlings, M.G. (2006). A Web-based systematic review on traumatic spinal cord injury comparing the "citation classics" with the consumers' perspectives. *J. Neurotrauma* 23, 156–169.
- Furlan, J.C., Noonan, V., Cadotte, D.W., and Fehlings, M.G. (2010a). Timing of decompressive surgery of spinal cord after traumatic spinal cord injury: An evidence-based examination of pre-clinical and clinical studies. *J. Neurotrauma* [Epub ahead of print].
- Furlan, J.C., Noonan, V., Singh, A., and Fehlings, M.G. (2010b). Assessment of disability in patients with acute traumatic spinal cord injury: A systematic review of the literature. *J. Neurotrauma* [Epub ahead of print].
- Furlan, J.C., Noonan, V., Singh, A., and Fehlings, M.G. (2010c). Assessment of impairment in patients with acute traumatic spinal cord injury: A systematic review of the literature. *J. Neurotrauma* [Epub ahead of print].
- Furlan, J.C., Singh, J., Hsieh, J., and Fehlings, M.G. (2010d). Methodology of systematic reviews and recommendations. *J. Neurotrauma* [Epub ahead of print].
- Kwon, B.K., Okon, E.B., Plunet, W., Baptiste, D., Fouad, K., Hillyer, J., Weaver, L.C., Fehlings, M.G., and Tetzlaff, W. (2010b). A systematic review of directly applied biologic therapies for acute spinal cord injury. *J. Neurotrauma* [Epub ahead of print].
- Kwon, B.K., Okon, E., Hillyer, J., Mann, C., Baptiste, D., Weaver, L.C., Fehlings, M.G., and Tetzlaff, W. (2010a). A systematic review of non-invasive pharmacologic neuroprotective treatments for acute spinal cord injury. *J. Neurotrauma* [Epub ahead of print].
- Parent, S., Barchi, S., Lebreton, M.A., Casha, S., and Fehlings, M. (2011). Specialized centers of care for SCI. *J. Neurotrauma* [Epub ahead of print].
- Parent, S., Mac-Thiong, J.-M., Roy-Beaudry, M., Sosa, J.F., and Labelle, H. (In review). Spinal cord Injury in the pediatric population: a systematic review of the literature. *J. Neurotrauma*.
- Sackett, D.L., Rosenberg, W.M., Gray, J.A., Haynes, R.B., and Richardson, W.S. (1996). Evidence based medicine: What it is and what it isn't. *BMJ* 312, 71–72.
- Tetzlaff, W., Okon, E.B., Karimi-Abdolrezaee, S., Hill, C.E., Sparling, J.S., Plemel, J.R., Plunet, W.T., Tsai, E.C., Baptiste, D., Smithson, L.J., Kawaja, M.D., Fehlings, M.G., and Kwon, B.K. (2010). A systematic review of cellular transplantation therapies for spinal cord injury. *J. Neurotrauma* [Epub ahead of print].
- Thibault-Halman, G., Casha, S., Singer, S., and Christie, S. (2010). Acute management of nutritional demands after spinal cord injury. *J. Neurotrauma* [Epub ahead of print].

Address correspondence to:

Michael G. Fehlings, M.D., Ph.D., FRCSC, FACS
 Division of Neurosurgery and Neuroscience Program
 University of Toronto
 399 Bathurst Street
 Toronto, Ontario M5T 2S8, Canada
 E-mail: michael.fehlings@uhn.on.ca