Global Spine Journal
2017, Vol. 7(3S) 195S-202S

DOI: 10.1177/2192568217706367
journals.sagepub.com/home/gsj

A Clinical Practice Guideline for the Management of Patients With Acute Spinal Cord Injury and Central Cord Syndrome: Recommendations on the Timing (≤24 Hours Versus >24 Hours) of Decompressive Surgery

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Abstract

Objective: To develop recommendations on the timing of surgical decompression in patients with traumatic spinal cord injury (SCI) and central cord syndrome.

Methods: A systematic review of the literature was conducted to address key relevant questions. A multidisciplinary guideline development group used this information, along with their clinical expertise, to develop recommendations for the timing of

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surgical decompression in patients with SCI and central cord syndrome. Based on GRADE, a strong recommendation is worded as "we recommend," whereas a weak recommendation is presented as "we suggest."

Results: Conclusions from the systematic review included (1) isolated studies reported statistically significant and clinically important improvements following early decompression at 6 months and following discharge from inpatient rehabilitation; (2) in one study on acute central cord syndrome without instability, a marginally significant improvement in total motor scores was reported at 6 and 12 months in patients managed with early versus late surgery; and (3) there were no significant differences in length of acute care/rehabilitation stay or in rates of complications between treatment groups. Our recommendations were: "We suggest that early surgery be considered as a treatment option in adult patients with traumatic central cord syndrome" and "We suggest that early surgery be offered as an option for adult acute SCI patients regardless of level." Quality of evidence for both recommendations was considered low.

Conclusions: These guidelines should be implemented into clinical practice to improve outcomes in patients with acute SCI and central cord syndrome by promoting standardization of care, decreasing the heterogeneity of management strategies, and encouraging clinicians to make evidence-informed decisions.

Keywords
spinal cord injury, center cord syndrome, guideline, surgery, time of surgery

Summary of Recommendations

We suggest that early surgery (≤24 hours after injury) be considered as a treatment option in adult patients with traumatic central cord syndrome.
Quality of Evidence: Low
Strength of Recommendation: Weak
We suggest that early surgery be offered as an option for adult acute SCI patients regardless of level.
Quality of Evidence: Low
Strength of Recommendation: Weak

Introduction

Acute spinal cord injury (SCI) is a traumatic event that results in disturbances to normal sensory, motor, or autonomic function and ultimately affects a patient's physical, psychological, and social well-being. From a biological perspective, preclinical evidence suggests that persistent compression of the spinal cord after the primary injury represents a reversible form of secondary injury, which, if ameliorated in an expeditious fashion, may lead to reduced neural tissue injury and improved outcomes.[1-3] Specifically, a 2013 meta-analysis of 21 animal studies reported that surgical decompression of the spinal cord improves neurobehavioral outcomes by 35% and that early intervention is one of the key predictors of improvement.[4] From a clinical perspective, a number of studies have investigated the impact of early surgery on neurologic, functional, and safety outcomes. Unfortunately, several different time thresholds have been used to define "early" versus "late" surgical decompression, including 24, 48, and 72 hours; the heterogeneity in definitions, along with inconsistency across studies in adjustment for baseline neurological status, has prevented the formation of strong recommendations on when to surgically decompress patients with SCI or central cord syndrome. No studies were identified that compared nonsurgical with surgical decompression.

This guideline provides evidence-based recommendations for timing of surgical decompression in patients with acute SCI and central cord syndrome. The systematic review aimed to clarify (1) whether early surgical intervention (≤24 hours after injury) results in improved neurologic and functional outcomes compared to late decompression (>24 hours after injury) and (2) whether safety profiles differ between intervention groups. The ultimate goal of this guideline is to improve outcomes and reduce morbidity in patients with SCI by promoting standardization of care and encouraging clinicians to make evidence-informed decisions. An introductory article in this focus issue provides further background on SCI and summarizes the rationale, scope, and specific aspects of care covered by this guideline. This article is titled "A Clinical Practice Guideline for the Management of Acute Spinal Cord Injury: Introduction, Rationale, and Scope."

These guidelines are intended to be used by first responders, emergency room physicians, critical care specialists, neurologists, and spine surgeons. The public should also be aware of the importance of early surgery if ever faced with an SCI; this awareness will facilitate shared decision making among physicians, patients, and their caregivers.

Methods

This guideline was developed under the auspices of AOSpine North America, AOSpine International, and the American Association and Congress of Neurological Surgeons. A multidisciplinary guideline development group (GDG) was formed and consisted of clinicians from a broad range of specialties as well as patient representation. The GDG was solely responsible for guideline development and was editorially independent from all funding sources. Members were required to disclose financial and intellectual conflicts of interest (Appendix, Chapter 2, "Guidelines for the Management of Degenerative Cervical Myelopathy and Acute Spinal Cord Injury: Development

Process and Methodology"). A guideline development protocol, based on the Conference on Guideline Standardization (COGS) checklist,[5,6] was created to outline the rationale and scope of the guideline and to direct its development. Systematic reviews were conducted based on accepted methodological standards to summarize the evidence informing the recommendations. Details of specific methods used for each topic are outlined in the individual reviews included in this focus issue. Methods outlined by the Grading of Recommendation, Assessment, Development and Evaluation (GRADE) Working Group were used to assess the overall quality (strength) of evidence for critical outcomes.[7,8] The GRADE Guideline Development Tool was used to document the process, rank the importance of outcomes, weigh the benefits and harms of various options, and determine the strength of recommendations.[9-12] Methodologists from Spectrum Research, Inc worked closely with clinical authors to conduct the systematic reviews and provided methodological expertise on the guideline development process. Guideline development methods are provided in another article included in this focus issue: "Guidelines for the Management of Degenerative Cervical Myelopathy and Acute Spinal Cord Injury: Development Process and Methodology."

Clinical Recommendations

Part 1. Timing of Decompressive Surgery (≤24 Hours After Injury) in Patients With Acute Central Cord Syndrome Without Evidence of Mechanical Instability

Population Description: Patients with central cord syndrome, no radiological evidence of mechanical instability and radiological evidence of spinal cord compression.

Key Question: Should we recommend early decompressive surgery (≤24 hours after injury) for adult patients with an incomplete pattern of neurological injury consistent with central cord syndrome, no radiological evidence of mechanical instability, and radiological evidence of spinal cord compression?

Recommendation 1: We suggest that early surgery (≤24 hours after injury) be considered as a treatment option in adult patients with traumatic central cord syndrome.

Quality of Evidence: Low

Strength of Recommendation: Weak

Evidence Summary

A systematic review of the literature was conducted to address the following key questions: In adult patients with acute complete or incomplete traumatic spinal cord injury, (1) What is the effectiveness of early decompression (≤24 hours) compared with late decompression (>24 hours) or conservative therapy based on clinically important change in neurological status? (2) Does timing of decompression influence other functional or administrative outcomes? (3) What is the safety profile of early decompression (≤24 hours) compared with late decompression (>24 hours) or conservative therapy? (4) What is the evidence that early decompression (≤24 hours) has differential efficacy or safety in subpopulations? (5) What is the cost-effectiveness of these treatment options? This systematic review is published elsewhere in this focus issue.

A single prospective observational study by Lenehan et al evaluated the comparative efficacy and effectiveness of early (≤24 hours) versus late (>24 hours) surgical decompression in patients with acute central cord syndrome without instability.[13] Based on their results, early surgery was marginally associated with an additional 7.47 (95% confidence interval [CI] = −0.04 to 14.91, $P = .0511$) point improvement in total American Spinal Injury Association (ASIA) Motor Score at 6 months and a 6.31 (95% CI = 0.44 to 12.18, $P = .0359$) point improvement at 12 months after propensity score stratification. There were no significant differences in improvement in ASIA Impairment Scale (AIS) between early and late surgical groups at 6 months (odds ratio [OR] = 3.39, 95% CI = 0.75 to 15.34, $P = .1131$) or 12 months (OR = 2.81, 95% CI = 0.48 to 16.6, $P = .2548$). With respect to improvements on the Functional Independence Measure (FIM), patients treated early exhibited an additional 6.92 point improvement (95% CI = −0.11 to 13.96, $P = .0537$) in motor subscore and a 7.79 point (95% CI = 0.09 to 15.49, $P = .0474$) improvement in total score at 12 months. The study by Lenehan et al did not summarize the safety profile of early and late surgery in patients with acute central cord syndrome. The overall strength of evidence for all outcomes was very low.

Rationale for Recommendation

The outcomes ranked as critical for decision making were improvement in ASIA Motor Score, FIM, and Spinal Cord Independence Measure (SCIM). The strength of evidence for findings related to these outcomes was rated as very low; the study by Lenehan et al had serious risk of bias and a serious risk of imprecision. In addition, given that the results were based on a single study, the consistency is unknown. The GDG agreed that the overall certainty of the evidence was very low (very low = 21, low = 1, moderate = 1).

The GDG unanimously agreed that there was probably no important uncertainty or variability about how much stakeholders value the main outcomes. Clinicians, patients, and payers would similarly value improvement in ASIA Motor Score, FIM, and SCIM.

The anticipated desirable effects were clinically meaningful improvements in ASIA score, ASIA Motor Score, FIM, and SCI. Based on the results from Lenehan et al, patients operated on within 24 hours had a better motor score improvement at 6 months than patients treated after 24 hours (group difference = 7.47, 95% CI = −0.04 to 14.91, $P = .0511$).[13] At 12 months, this group difference was 6.31 points and favored the early decompression group (95% CI = 0.44 to 12.18, $P = .0359$). Patients operated on early also had better FIM scores at 12 months than patients treated late (group difference = 7.79, 95% CI = 0.09 to 15.49, $P = .0474$).[13] The GDG agreed that the anticipated desirable effects were probably large (probably no = 1, uncertain = 5, probably yes = 21). Although the

minimum clinically important differences (MCID) for the main outcomes have not been clearly defined, the GDG agreed that even small neurological improvements can be clinically meaningful for certain patients, especially those with motor complete lesions wherein even a few points of motor recovery can have significant impact on function. As an example, for a C5 AIS grade A patient, recovery of several motor points in the C6 myotome (wrist extension) may enable some degree of tenodesis grip and permit functional grasp.

The anticipated undesirable effects were risks and complications associated with surgical intervention. Lenehan et al did not specifically report the rates of complications following early versus late surgical decompression in patients with acute central cord syndrome. In the STASCIS study by Fehlings et al, rates of complications did not differ between patients treated $\leq$24 hours versus >24 hours after cervical SCI.[14] However, historical reports of early surgical decompression in the setting of central cord syndrome have associated this treatment with worsened neurological outcomes and increased morbidity[15]; that said, no report in the modern era has found such an association. In the absence of recent high-quality evidence, clinical expertise was used to determine that the undesirable effects are probably small. The GDG agreed that the desirable effects are probably large relative to the undesirable effects (uncertain = 7, probably yes = 14, yes = 2). Clinical judgement, balancing factors such as age, medical comorbidities, and overall clinical status, is required when making operative decisions in this patient population.

In the absence of literature, the GDG used their clinical expertise to discuss the resources required to operate within 24 hours of injury (versus after 24 hours). The GDG agreed that performing early surgery would probably not require extra resources compared to delayed decompression (are the resources required small?: probably no = 4, uncertain = 6, probably yes = 14, yes = 1). Unfortunately, studies evaluating the cost-effectiveness of early versus late surgical treatment for acute central cord syndrome were not identified. The GDG believed that the costs and resources of surgery do not vary substantially between patients decompressed early versus late; however, early surgery may result in superior clinical outcomes at 12 months and overall cost savings. There was consensus that the incremental cost was likely small relative to the net benefit (probably no = 1, uncertain = 8, probably yes = 16, yes = 1).

The GDG believed that a recommendation for early surgery for acute central cord syndrome would reduce health inequities if policy makers funded initiatives to improve patient flow through the continuum of care, ensure rapid access to surgery, and educate first responders (increased = 1, probably increased = 5, uncertain = 7, probably reduced = 11, reduced = 2). Furthermore, the majority of the GDG agreed that early decompression would probably be an acceptable option to key stakeholders (probably no = 1, uncertain = 10, probably yes = 15, yes = 1). This decision was based on the potential neurological and functional benefits of early surgery, low associated risk, and resource requirement; however, a large proportion of the group answered that the acceptability of this option was uncertain. There is substantial variability in practice and opinion regarding early versus late decompression in patients with acute central cord syndrome; some clinicians are averse to operating on this population as many are elderly, have multiple comorbidities, and may be less tolerant to surgery. In contrast, other clinicians believe that modern anesthesia approaches may help reduce the risks of surgery in the elderly and that surgery can address the underlying degenerative pathology, attenuate posttraumatic secondary injury cascades, and decrease the risk of future catastrophic events. Finally, the GDG unanimously agreed that the option of early surgery for the treatment of acute central cord syndrome is probably feasible to implement, assuming that appropriate policy is executed and sufficient resources are available.

Considering all these factors, the GDG voted that the desirable consequences probably outweigh the undesirable consequences in most settings (n = 16/22); this led to the formation of a weak recommendation for early decompression in patients with acute central cord syndrome (n = 16/19). In making this recommendation, we strongly considered the benefits of early surgical decompression and the potential for increased neurologic and functional improvements. While patients with central cord syndrome are expected to achieve some degree of spontaneous neurologic improvement without surgical decompression, it is recognized that such recovery is often incomplete, leaving patients with significant spasticity, neuropathic pain, balance loss, hand dysfunction, and bowel/bladder dysfunction. In the absence of strong evidence, clinical expertise was used to confirm that the extent of neurologic and functional benefit is likely clinically important to a patient and that the potential benefits likely outweighs the potential harms. Furthermore, in making this recommendation, the GDG assumed that the patient would, at some point, require surgical intervention.

Part 2. Timing of Decompressive Surgery ($\leq$24 Hours After Injury) in Patients With Acute Spinal Cord Injury

Population Description: Patients with acute SCI.
Key Question: Should we recommend early decompressive surgery ($\leq$24 hours after injury) for adult patients with acute SCI regardless of neurological level of injury at hospital admission?
Recommendation 2: We suggest that early surgery be offered as an option for adult acute SCI patients regardless of level.
Quality of Evidence: Low
Strength of Recommendation: Weak

Evidence Summary

As previously described, a systematic review was performed to inform the development of our clinical recommendations. One randomized controlled trial and 4 comparative cohort studies evaluated the effectiveness of early ($\leq$24 hours) versus late

(>24 hours) surgical decompression. Of these, 1 study assessed outcomes in cervical SCI, 1 study in thoracolumbar SCI, 1 study in cervical and thoracolumbar SCI, and 2 studies in all levels of SCI.

Cervical Injury. Based on a single prospective cohort study, patients decompressed early were more likely to exhibit a ≥2 grade improvement at 6 months on the AIS than those decompressed late (OR = 2.83, 95% CI = 1.10 to 7.28, $P = .03$).[14] There was no significant difference in the odds of achieving a ≥1 grade improvement between treatment groups (OR = 1.37, 95% CI = 0.80 to 2.57, $P = .31$; low strength of evidence). This study by Fehlings et al did not compare administrative or functional outcomes between surgical groups.[14] With respect to safety, there was no statistical difference in rates of complications between patients decompressed early versus late; however, for some outcomes, there may not have been sufficient statistical power to detect differences (very low strength of evidence). Unadjusted relative risks (RR) were calculated for the following complications: cardiopulmonary event (RR = 0.68, 95% CI = 0.44 to 1.04), construct failure requiring surgery (RR = 2.16, 95% CI = 0.23 to 20.53), neurologic deterioration (RR = 2.88, 95% CI = 0.33 to 25.46), pulmonary embolism (RR = 0.72, 95% CI = 0.10 to 5.04), systemic infection (RR = 0.54, 95% CI = 0.19 to 1.52), wound dehiscence (RR = 0.72, 95% CI = 0.05 to 11.40), and mortality ≤30 days postinjury (RR = 0.72, 95% CI = 0.05 to 11.40).[14]

Thoracolumbar Injury. Based on a single small randomized controlled trial, there was no difference in the frequency of patients who achieved a ≥1 grade improvement on AIS between the early and late surgical groups (5 vs 7 persons; RR = 0.85, 95% CI = 0.33 to 2.16).[16] More patients in the early decompression group experienced a ≥2 grade improvement on AIS than in the late decompression group; however, this relationship did not reach statistical significance and the wide confidence intervals suggest instability (3 vs 1 patient; RR = 3.56, 95% CI = 0.41 to 30.99). With respect to administrative outcomes, there was no difference in length of stay between the early and late surgical groups (mean difference = 2.7, 95% CI = −8.1 to 2.7, $P = .31$).[16] Finally, there were no differences in rates of deep vein thrombosis (RR = 1.2, 95% CI = 0.08 to 17.5), revision of surgical screws (RR = 0.79, 95% CI = 0.15 to 4.16), or death (RR = 1.2, 95% CI = 0.08 to 17.5) between patients treated early versus late; however, this study is likely underpowered to detect differences between groups.[16] The overall strength of evidence for these findings was very low.

Cervical, Thoracic, and Lumbosacral Injury. In a single prospective study, there was no significant difference in AIS Motor Score improvement between the early and late decompression groups in AIS A patients (Beta = 0.068, 95% CI = −0.625 to 0.76, $P = .848$; timeframe was not reported).[17] In contrast, patients treated early for AIS B, C, or D injuries improved, on average, by 6 additional motor points than those decompressed late (Beta = 6.258, 95% CI = 0.618 to 11.897, $P = .03$). In a second prospective study by Wilson et al, there were no differences in mean AIS Motor Score improvements between the early and late decompression groups at the time of acute care discharge ($P = .18$).[18] At the time of discharge from rehabilitation (mean 89.6 days), however, patients receiving early decompression exhibited an additional 13 point improvement in AIS Motor Score compared to those treated late, after adjusting for completeness of injury and level (mean improvements not reported for either arm; $P = .01$). Similarly, a greater percentage of patients in the early surgery group experienced a ≥2 grade AIS improvement (27.2%) than in the late surgery group (3%) when discharged from inpatient rehabilitation (unadjusted RR = 8.9, 95% CI = 1.12 to 70.64, $P = .0154$). The strength of evidence for all of these outcomes was very low.

With respect to administrative outcomes, there was a significant difference in length of stay (setting undefined) between early versus late surgical groups (favoring early) in patients with AIS A (7.5 vs NR days, respectively; $P = .003$) or B injury severity (12.8 vs NR days, respectively; $P = .004$).[17] In a second study, there was no statistically significant difference between groups with respect to length of stay in either an acute care (early: 24.9 days; late: 24.7 days; $P = .97$, N = 82) or rehabilitation setting (early: 102.9 days; late: 80.2 days; $P = .10$, N = 55).[18] Finally, in terms of safety, risk of complications was not significantly different between the early and late decompression groups, with the exception of pneumonia, which was more common in the late surgery group (RR = 0.62, 95% CI = 0.38 to 1.02; $P = .0496$).[19] The overall strength of evidence for these findings was very low.

No studies were identified that assessed the differential effectiveness or safety of early versus late surgical decompression in subpopulations or the cost-effectiveness of treatment.

Rationale for Recommendation

The outcomes ranked as critical for decision making were improvement in ASIA Motor Score, AIS grade, FIM, SCIM, and risk of complications. Costs and length of hospital stay were also considered important. The strength of evidence related to these outcomes was rated as low or very low; studies were typically downgraded for serious risk of bias and/or imprecision. The GDG unanimously agreed that the overall certainty of the evidence was very low.

The GDG unanimously agreed that there was probably no important uncertainty or variability about how much stakeholders value the main outcomes. Clinicians, patients, and payers would similarly value improvement in ASIA Motor Score, FIM, SCIM, reduced risk of complications, low costs, and decreased length of hospital stay.

The anticipated desirable effects were clinically meaningful improvements in ASIA score, Total Motor Score, FIM, and SCIM. Unfortunately, the MCIDs of these scales have not been established; as a result, patient perspectives must be considered as small neurologic or functional improvements could translate to significantly enhanced quality of life. Results differed based on level and completeness of injury: (1) patients decompressed

early for cervical SCI were more likely to exhibit a ≥2 grade improvement (but not a ≥1 grade improvement) in AIS at 6 months than those decompressed late; (2) in patients with cervical, thoracic, or lumbosacral SCI, a greater percentage of patients in the early surgery group experienced a ≥2 grade AIS improvement (27.2%) at discharge from rehabilitation (but not at the time of discharge from acute care) than in the late surgery group (3%); furthermore, patients treated early for AIS B, C, or D injuries improved, on average, by 6 additional motor points than those decompressed late; and (3) there were no significant differences in neurological outcomes between treatment groups in patients with thoracolumbar injuries likely due to small sample sizes and study limitations. There was disagreement among the GDG whether these improvements were clinically meaningful. The majority of the GDG agreed that the anticipated desirable effects were probably large (n = 13); however, a large portion of the group were uncertain (n = 8) since the MCIDs for the main outcomes have not been established.

The anticipated undesirable effects are surgical risks and complications. Across all levels, there were no statistical differences in rates of complications between early and late surgical groups; however, most events were rare, and in some studies, there was likely insufficient statistical power to detect a difference. The GDG unanimously agreed that the undesirable effects of early versus late surgery are probably small. Based on these findings, the majority of the GDG (n = 17/27) believed that the desirable effects are probably large relative to the undesirable effects; however, a large portion of the group were uncertain (n = 9) given the variability in results across injury levels and the heterogeneity of this population.

In the absence of literature, the GDG used their clinical expertise to discuss the resources required to operate within 24 hours of injury (versus after 24 hours). The GDG unanimously agreed that performing early surgery would probably not require extra resources compared to delayed decompression. A single costing study based in Quebec, Canada, indicated that early surgery may reduce costs[20]; however, the patients undergoing early decompression were younger, and it is unclear whether their findings are generalizable across health care settings or regions of the world. Unfortunately, the cost-effectiveness of early versus late surgical treatment for traumatic SCI is largely unknown. The GDG agreed that the cost and resources required for surgery do not vary substantially between patients operated on early versus late; however, early decompression may result in improved clinical outcomes, reduced length of stay, and overall cost savings. There was consensus that the incremental cost is likely small relative to the net benefit.

The GDG unanimously believed that a recommendation for early surgery for patients with traumatic SCI would reduce health inequities if policy makers funded initiatives to improve patient flow through the continuum of care, ensure rapid access to surgery, and educate first responders. Furthermore, the majority of the GDG agreed that early decompression would probably be an acceptable option to key stakeholders. This decision was based on the potential neurological and functional benefits of early surgery, low associated risk of complications, and resource requirement. Finally, the GDG agreed that the option of early surgery for the treatment of traumatic SCI is probably feasible to implement assuming that appropriate policy is implemented and sufficient resources are available.

Considering all these factors, the GDG voted that the desirable consequences probably outweigh the undesirable consequences in most settings (n = 23/25); this led to the formation of a weak recommendation for early decompression in patients with traumatic SCI regardless of level (n = 21/23).

Evidence Gaps and Future Research Recommendations

The guideline development process has identified important knowledge gaps in the literature and areas for future research. These include (1) insufficient evidence on the differential effectiveness and safety of early versus late surgery in subpopulations (eg, level of injury); (2) limited evidence on the cost-effectiveness of early versus late surgery; (3) uncertainty surrounding the impact of early versus late surgery on functional outcomes in patients with acute SCI and traumatic central cord syndrome; and (4) uncertainty as to what constitutes a clinically meaningful improvement on the outcome measures used to evaluate neurologic and functional status. Furthermore, the level of evidence for most of our findings was low or very low, suggesting that we have limited confidence in the estimate of effect and that the true effect may be substantially different.

Significant limitations exist in the current body of evidence, including (1) substantial clinical heterogeneity across studies prevent data pooling and meta-analyses (eg, differences in populations, injury severity, and injury level); (2) effect estimates were often imprecise with large confidence intervals; (3) results were often based on single studies and so the consistency of findings was unknown; (4) a lack of statistical power to detect differences in complication rates between surgical cohorts; and (5) many studies did not meet one or more criteria of a good-quality randomized controlled trial or observational study (eg, unreported follow-up rates or substantial loss to follow-up, unclear adjustment for baseline factors, and no co-interventions). Future prospective comparative studies are needed that are sufficiently powered, have low loss to follow-up, account for co-interventions, and adjust for baseline neurological status. Prospective multicenter studies that adhere to specific protocols would potentially enhance the evidence base.

Given the heterogeneity of SCI, future work is needed to more accurately identify what subgroups of SCI patients stand to benefit the greatest from early decompressive surgery. This may permit the development of customized treatment plans that encourage, and enable, rapid surgical treatment for those who are likely to benefit the most. In addition, while we examined the timing of decompression relative to a 24-hour cutoff point, future studies investigating the efficacy of surgery relative to earlier time points (eg, 12 hours) would be of interest. However, more aggressive timelines for surgery may be

unrealistic in many centers, given the practical realities of transporting and treating patients with this diagnosis. Along these lines, given that the current evidence suggests early surgery to be of potential benefit to SCI patients, future work is needed to evaluate health systems and transport methods to ensure a streamlined path to early treatment. Finally, research efforts investigating the joint effects of early surgery paired with other putative emerging neuroprotective or neuroregenerative therapies will also be of interest.

Implementation Considerations

It is expected that this guideline will influence clinical practice and facilitate evidence-based decision making. Dissemination of the knowledge from this guideline is of critical importance and will be accomplished at multiple levels:

- Presentation at international spine surgery, critical care, neurology, anesthesiology, and vascular medicine conferences
- Scientific and educational courses in symposium format
- Webinar dissemination of information to a broad audience in an interactive format
- Publication of a focus issue in a peer-reviewed journal
- Submission to the National Guideline Clearinghouse
- AOSpine International Spinal Cord Injury Knowledge Forum

Potential barriers to implementation include the following:

- Given that SCI often occurs in geographically isolated regions, implementation of the timelines suggested in these guidelines may be dependent on location of injury (ie, where the injury occurred) and the local transport and prehospital systems in place.
- There are a number of trials currently underway investigating the effects of acute neuroprotective treatments. It is possible that study and administration of such treatments could affect the process of expediting surgery for patients.
- Given the paucity of studies on the topic of timing of surgery in central cord syndrome, surgeons may opt to base treatment decisions solely on their clinical experience and judgement rather than the suggestions provided in these guidelines.

Internal Appraisal and External Review of This Guideline

Vice-chairs of the GDG conducted an internal appraisal of the final guideline using Appraisal of Guidelines for Research & Evaluation II (AGREE II) standards.[21] A multidisciplinary group of stakeholders, including patients, were invited to externally review the final draft prior to publication. Additional details of these processes and a summary of conflict of interests for external reviewers are found in the accompanying methods paper.

Plans for Updating

The guidelines will be reviewed by the primary sponsor and the Vice-Chairs at 3 years to a maximum of 5 years following publication. The guideline will be updated when new evidence suggests the need to modify our recommendations. An earlier update will be considered if there are changes in (1) the evidence related to harms and benefits, (2) outcomes that would be considered important for decision making, (3) ranking of current critical and important outcomes, and (4) available interventions and resources.[22]

Authors' Note

Guideline Development Committee Members: Co-Chair: Michael G. Fehlings, MD, PhD, Neurosurgery; Co-Chair: James Harrop, MD, Neurosurgery; Vice Chair: Jefferson R. Wilson, MD, PhD, Neurosurgery; Vice Chair: Anthony S. Burns, MD, Physical Medicine/Rehabilitation; General Member of Leadership Group: Brian Kwon, MD, PhD, Orthopedic Surgery; Systematic Review Coordinator: Lindsay Tetreault, PhD, Research.

Acknowledgments

The GDG would like to acknowledge the funding of AOSpine North America, International, and the AANS/CNS. In particular, we would like to thank Chi Lam, Kelly McCormick, Nancy Holmes, and Maria Alvarez for their administrative assistance and for organizing our meetings. We would also like to recognize Dr Carlo Santaguida for his thorough review of this guideline. We were grateful for the opportunity to collaborate with Spectrum Research, Inc, and would like to thank Krystle Pagarigan and Eric Schnell for their administrative support.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This research was supported by AOSpine, the Ontario Neurotrauma Foundation (ONF) and the AANS/CNS Section on Neurotrauma and Critical Care. Dr Fehlings wishes to acknowledge support from the Gerald and Tootsie Halbert Chair in Neural Repair and Regeneration and the DeZwirek Family Foundation. Dr Tetreault acknowledges support from a Krembil Postdoctoral Fellowship Award. Methodological support was provided by Spectrum Research, Inc.

References

1. Guha A, Tator C, Endrenyi L. Decompression of the spinal cord improves recovery after acute experimental spinal cord compression injury. *Paraplegia*. 1987;25:324-339.
2. Dimar J, Glassman S, Raque G, Zhang YP, Shields CB. The influence of spinal canal narrowing and timing of decompression on neurologic recovery after spinal cord contusion in a rat model. *Spine (Phila Pa 1976)*. 1999;24:1623-1633.

3. Fehlings MG, Perrin RG. The timing of surgical intervention in the treatment of spinal cord injury: a systematic review of recent clinical evidence. *Spine (Phila Pa 1976)*. 2006;31(11 suppl): S28-S35. doi:10.1097/01.brs.0000217973.11402.7f.
4. Batchelor PE, Wills TE, Skeers P, et al. Meta-analysis of pre-clinical studies of early decompression in acute spinal cord injury: a battle of time and pressure. *PLoS One*. 2013;8:e72659. doi:10.1371/journal.pone.0072659.
5. Shiffman RN, Michel G. Toward improved guideline quality: using the COGS statement with GEM. *Stud Health Technol Inform*. 2004;107:159-163.
6. Shiffman RN, Shekelle P, Overhage JM, Slutsky J, Grimshaw J, Deshpande AM. Standardized reporting of clinical practice guidelines: a proposal from the Conference on Guideline Standardization. *Ann Intern Med*. 2003;139:493-498.
7. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011; 64:401-406.
8. Agency for Healthcare Research and Quality. *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* (AHRQ Publication No. 10(14)-EHC063-EF). Rockville MD: Agency for Healthcare Research and Quality; 2013.
9. Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. *J Clin Epidemiol*. 2013;66: 719-725. doi:10.1016/j.jclinepi.2012.03.013.
10. Andrews JC, Schunemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. *J Clin Epidemiol*. 2013;66:726-735. doi:10.1016/j.jclinepi.2013.02.003.
11. Schunemann HJ, Oxman AD, Akl EA, et al. Moving from evidence to developing recommendations in guidelines: article 11 in integrating and coordinating efforts in COPD guideline development. An official ATS/ERS workshop report. *Proc Am Thorac Soc*. 2012;9:282-292. doi:10.1513/pats.201208-064ST.
12. Wu JC, Ko CC, Yen YS, et al. Epidemiology of cervical spondylotic myelopathy and its risk of causing spinal cord injury: a national cohort study. *Neurosurg Focus*. 2013;35:E10. doi:10.3171/2013.4.FOCUS13122.
13. Lenehan B, Fisher CG, Vaccaro A, Fehlings M, Aarabi B, Dvorak MF. The urgency of surgical decompression in acute central cord injuries with spondylosis and without instability. *Spine (Phila Pa 1976)*. 2010;35(21 suppl):S180-186. doi:10.1097/BRS.1090b1013e3181f1032a1044.
14. Fehlings MG, Vaccaro A, Wilson JR, et al. Early versus delayed decompression for traumatic cervical spinal cord injury: results of the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS). *PLoS One*. 2012;7:e32037. doi:32010.31371/journal.pone.0032037.
15. Schneider RC, Cherry G, Pantek H. The syndrome of acute central cervical spinal cord injury; with special reference to the mechanisms involved in hyperextension injuries of cervical spine. *J Neurosurg*. 1954;11:546-577. doi:10.3171/jns.1954.11.6.0546.
16. Rahimi-Movaghar V, Niakan A, Haghnegahdar A, Shahlaee A, Saadat S, Barzideh E. Early versus late surgical decompression for traumatic thoracic/thoracolumbar (T1-L1) spinal cord injured patients. Primary results of a randomized controlled trial at one year follow-up. *Neurosciences (Riyadh)*. 2014;19: 183-191.
17. Dvorak MF, Noonan VK, Fallah N, et al. The influence of time from injury to surgery on motor recovery and length of hospital stay in acute traumatic spinal cord injury: an observational Canadian cohort study. *J Neurotrauma*. 2015;32:645-654. doi:10.1089/neu.2014.3632.
18. Wilson JR, Singh A, Craven C, et al. Early versus late surgery for traumatic spinal cord injury: the results of a prospective Canadian cohort study. *Spinal Cord*. 2012;50:840-843. doi:10.1038/sc.2012.59.
19. Bourassa-Moreau E, Mac-Thiong JM, Ehrmann Feldman D, Thompson C, Parent S. Complications in acute phase hospitalization of traumatic spinal cord injury: does surgical timing matter? *J Trauma Acute Care Surg*. 2013;74:849-854. doi:10.1097/TA.1090b1013e31827e31381.
20. Mac-Thiong JM, Feldman DE, Thompson C, Bourassa-Moreau E, Parent S. Does timing of surgery affect hospitalization costs and length of stay for acute care following a traumatic spinal cord injury? *J Neurotrauma*. 2012;29:2816-2822. doi:10.1089/neu.2012.2503.
21. Brouwers MC, Kho ME, Browman GP, et al. Development of the AGREE II, part 2: assessment of validity of items and tools to support application. *CMAJ*. 2010;182:E472-E478. doi:10.1503/cmaj.091716.
22. Shekelle P, Woolf S, Grimshaw JM, Schünemann HJ, Eccles MP. Developing clinical practice guidelines: reviewing, reporting, and publishing guidelines: updating guidelines; and the emerging issues of enhancing guideline implementability and accounting for comorbid conditions in guideline development. *Implement Sci*. 2012;7:62.