Brain and Spine 4 (2024) 102803

Contents lists available at ScienceDirect

Brain and Spine

journal homepage: www.journals.elsevier.com/brain-and-spine

Spinal cord injury: Current trends in acute management

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ARTICLE INFO

Handling Editor: F Kandziora

Keywords:
Spinal cord injury
Trauma
Acute management
Surgery
Hemodynamic management

ABSTRACT

Introduction: Traumatic spinal cord injury (tSCI) is a profoundly debilitating condition necessitating prompt intervention. However, the optimal acute treatment strategy remains a subject of debate.
Research question: The aim of this overview is to elucidate prevailing trends in the acute tSCI management.
Material and Methods: We provided an overview using peer-reviewed studies.
Results: Early surgical treatment (<24h after trauma) appears beneficial compared to delayed surgery. Nonetheless, there is insufficient evidence supporting a positive influence of ultra-early surgery on neurological outcome in tSCI. Furthermore, the optimal surgical approach to decompress the spinal cord remains unclear. These uncertainties extend to a growing aging population suffering from central cord syndrome (CCS). Additionally, there is a paucity of evidence supporting the beneficial effects of strict hemodynamic management.
Discussion and Conclusion: This overview highlights the current literature on surgical timing, surgical techniques and hemodynamic management during the acute phase of tSCI. It also delves into considerations specific to the elderly population experiencing CCS.

1. Introduction

Traumatic spinal cord injury (tSCI) is a relatively infrequent yet profoundly debilitating condition that affects physical, psychological, and societal well-being of tSCI patients. Management of tSCI requires prompt intervention, often involving surgical intervention. However, numerous uncertainties persist regarding the optimal acute treatment strategies, resulting in clinical practice variance (Fransen et al., 2016; ter Wengel et al., 2018).

One of these uncertainties is the most optimal timing of surgery. The existing literature suggests that surgery within 24 h after trauma results in improved neurological outcome (Fehlings et al., 2012). However, there is a growing advocacy for ultra-early surgery (within 8–12 h), despite a paucity of compelling evidence.

This lack of consensus concerning surgical timing in tSCI is further complicated by an evolving epidemiological landscape of tSCI to a more elderly population (Thompson et al., 2015). Elderly tSCI patients frequently sustain low-energy trauma, most commonly through hyperextension injuries, often compounded by pre-existing cervical canal stenosis. This combination of factors can result in the manifestation of central cord syndrome (CCS), defined as disproportional motor weakness in the upper extremities compared to the lower extremities. In this tSCI subgroup, it also pertains to whether (ultra-) early surgical interventions remain the most optimal treatment, given their high burden of comorbidities, often including the use of anticoagulants.

Besides surgical timing, the surgical technique is also a point of debate. The primary aim of surgery is decompression of the spinal cord, yet the optimal technique to achieve this aim remains unsettled. Ongoing investigations are exploring the favorable technique to achieve adequate decompression, and the potential advantages of additional expansion duroplasty to attain "intradural" decompression. Nevertheless, the use of expansion duroplasty in tSCI is still under investigation.

Another critical aspect of acute tSCI treatment involves hemodynamic management, particularly blood pressure management. Current practice guidelines endorse the maintenance of a mean arterial pressure (MAP) above 85 mmHg during the initial seven days (Walters et al., 2013), but these recommendations are based on weak evidence. Consequently, more recent endeavors are increasingly directed toward elucidating the hemodynamic strategies necessary to optimize neurological outcome in tSCI patients, recognizing the potential variability between different SCI subgroups (Lee et al., 2021).

In this review, we will highlight the current trends in acute (surgical)

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https://doi.org/10.1016/j.bas.2024.102803
Received 30 December 2023; Received in revised form 5 March 2024; Accepted 4 April 2024
Available online 7 April 2024

treatment of tSCI patients.

2. Acute phase

In the acute phase, it is of great importance to swiftly identify tSCI patients and refer them to a specialized center. The feasibility of achieving prompt patient transferring, obviously depends on the geographical location within a given country. Timely transportation to a SCI center can result in swift treatment or potential reduction of secondary complications and enhance outcomes by enabling quick surgical decompression and start of spinal cord perfusion pressure management (Ahn et al., 2011; Middleton et al., 2012).

The pharmacological aspect of acute tSCI treatment is rather limited. For many years, the use of steroids in treatment of acute tSCI, such as methylprednisolone, has been a point of debate (Liu et al., 2019; Evaniew et al., 2015; Fehlings et al., 2017). While the current guidelines recommend considering methylprednisolone for acute SCI patients within 8 h of the injury, but for only a 24-h duration (Fehlings et al., 2017), the evidence for supporting the beneficial effects of methylprednisolone is limited (Sultan et al., 2020; Chen et al., 2023). For instance, recently, a large pooled analysis in tSCI patients found no significant improvement in neurological recovery following methylprednisolone administration (Geisler et al., 2023). Because of this little evidence, the continued use of methylprednisolone in acute tSCI treatment remains uncertain.

The role of riluzole in the acute SCI treatment is currently being investigated. Riluzole, a sodium-glutamate antagonist employed in the treatment of amyotrophic lateral sclerosis (ALS), has shown promising results in preclinical animal models (Fehlings et al., 2016; Schwartz and Fehlings, 2002). The suggested explanation is that it attenuates the secondary injury cascade and reduces neurological tissue damage. Riluzole helps maintain neuronal cellular ionic balance and decrease the release of excitotoxic glutamate following tSCI (Jorgensen and Diemer, 1982). A recent randomized controlled trial evaluated the effectiveness and safety of riluzole in cervical tSCI (Fehlings et al., 2023). Riluzole was administered twice a day for 13 days, starting immediately upon arrival at the emergency room. The riluzole patient group exhibited an average upper extremity motor score (UEMS) gain 1.8 times higher than the placebo group, albeit this difference did not reach statistical significance. A positive impact on secondary outcomes, such as functionality and quality of life, due to riluzole was indicated, but this was also not significant. It is worth noting, that the study was prematurely halted due to the global COVID-19 pandemic, resulting in the inclusion of only 55 percent of the intended patient population (n = 193). Adverse events were comparable between both groups. However, due to the limited statistical power, no significant beneficial effects of riluzole were established, necessitating further investigation.

Prophylactic hypothermia therapy administered immediately after trauma is proposed to shield against traumatic neuronal damage, thereby promoting improved neurological recovery in tSCI patients. (Michenfelder and Milde, 1992). Current clinical evidence on the efficacy and safety of both local and systematic hypothermia therapy in tSCI patients is limited. Nonetheless, it is demonstrated that patients undergoing systemic hypothermia therapy demonstrated a higher incidence of AIS conversion compared to those not receiving such treatment (Ransom et al., 2022). However, further research is imperative to ascertain the safety and effectiveness hypothermia treatment as it can also cause adverse events, such as coagulopathy (Mahajan et al., 1981).

3. Hemodynamic management

Secondary damage prevention in the early aftermath of tSCI has been proposed to be crucial in enhancing neurological outcomes in this group of patients. To date, there is no high-level evidence for the current guidelines. Professionals are restricted to prospective case series, retrospective case series and animal models which show conflicting results. Despite a lack of specific evidence, augmentation of mean arterial pressure (MAP) during the first 7 days post injury is thought to be beneficial in the prevention of subsequent damage. Numerous prospective case series, retrospective case series and animal models have been used to investigate the effect of MAP on histological and functional outcomes following SCI. Specifically, two systematic reviews concluded that blood pressure management after tSCI was important in the overall neurological recovery (Sabit et al., 2018; Saadeh et al., 2017). The problem that both reviews described was that there is limited high-quality evidence to guide blood pressure management. On the other hand, limited observational data suggested that frequent episodes of hypotension (<80 mmHg) might be associated with poorer neurological outcome (Hawryluk et al., 2015). More research is needed to understand the role of induced hypertension and the possible detrimental effect of (episodic) hypotension on neurological outcome in patients with tSCI.

4. Surgical phase

4.1. Surgical timing

Determining the optimal surgical timing in tSCI has long been a central focus in the area of acute tSCI management. Since the STASCIS study in 2012, the adoption of early surgery within a 24-h timeframe has gained acceptance on a global scale (Fehlings et al., 2012). This altered point of view is further substantiated by other studies as well as by a recent pooled analysis, which included 1031 tSCI patients drawn from four different, prospective databases (Badhiwala et al., 2021; Ter et al., 2019, 2022; Wilson et al., 2020). This study investigated the impact of early surgical intervention on neurological outcomes in tSCI. The findings underscored the benefits of early decompression, showing a significant improvement of motor recovery in the early surgery group compared to the late surgery group. This positive effect tended to diminish when surgery was delayed beyond the 36-h threshold.

Surgical treatment for tSCI is principally focused on prevention of secondary injury, encompassing factors such as ischemia, inflammation-induced edema and neuronal apoptosis resulting from prolonged compression of the spinal cord (Hachem and Fehlings, 2021; Tator and Fehlings, 1991). In light of this underlying pathophysiology, it is intuitively evident that expedited decompression is associated with reduced spinal cord damage and, consequently, leads to improved neurological outcomes. For this reason, the SCI-POEM study was performed, an European, prospective study which enrolled 294 tSCI patients(Hosman et al., 2023). The efficacy of ultra-early (within 12h after trauma) surgery was examined in comparison to early surgery (after 12h) using the lower extremity score (LEMS) after 12 months as their primary outcome. The study did not reveal any significant difference in LEMS improvements between the ultra-early and early surgery group. Nevertheless, it is crucial to acknowledge certain limitations of the study. Notably, patients in the ultra-early group tended to be significantly younger. These patients also suffered more severe injuries and neurological deficit (as indicated by ISS scores of 19.1 versus 15.6 and AIS A grade of 47.1% vs 29.2%, respectively). Furthermore, the distribution of patients between the ultra-early and later surgery groups was imbalanced, with early surgery accounting for 54 percent of all cases. Moreover, there was considerable missing data which necessitates cautious interpretation. Nonetheless, this study marks an initial step towards exploring the efficacy and safety of ultra-early surgery in tSCI patients.

4.2. Surgical technique

Surgical decompression is of great importance in tSCI treatment, serving to counteract secondary injury. The question remains which surgical approach best achieves adequate spinal cord decompression. Adequate decompression is defined by the presence of perimedullary cerebrospinal fluid as observed in postoperative Magnetic Resonance

Imaging (MRI) (Aarabi et al., 2017). Various decompressive techniques are employed, based on the location of spinal cord compression and the surgeon's preferences. The utilization of intraoperative ultrasound may be contemplated for assessing the adequacy of decompression. Nevertheless, its beneficial effect is predominantly evident in degenerative cases. The association between intraoperative ultrasound and enhanced outcomes remains uncertain (Tat et al., 2022).

Imaging studies have shown a correlation between the expansion of the intramedullary lesion length (IMLL) and American Spinal Injury Association Impairment Scale (AIS) grade conversion (Aarabi et al., 2017). Moreover, studies into the expansion of IMLL over time have revealed that AIS A and B tSCI patients exhibit significantly higher expansion rates compared to AIS C and D patients (Le et al., 2015). Furthermore, Aarabi et al. have suggested that adequate decompression of the spinal cord, confirmed by postoperative MRI, resulted in neurological recovery (Aarabi et al., 2017, 2019). Consequently, it has been suggested that laminectomy may more frequently result in achieving optimal decompression of the spinal cord (Aarabi et al., 2019).

In the pursuit of achieving optimal decompression, the role of an additional expansion duroplasty is currently investigated (Saadoun et al., 2023). This concept draws from the surgical approach employed in the management of traumatic brain injury, where dural expansion is performed alongside decompressive hemicraniectomy, leading to an immediate reduction of intracranial pressure in severe cases. It is hypothesized that relying solely on bony decompression of the spinal cord may, in certain cases, is insufficient, necessitating the opening of the surrounding dura to attain adequate intradural decompression of the spinal cord. Intradural decompression is believed to ultimately enhance cord perfusion, diminish cord ischemia and reduce inflammation, particularly in cases of severe tSCI (AIS A and B). Currently, a randomized controlled trial known as DISCUS (Duroplasty for Injured Cervical Spinal Cord with Uncontrolled Swelling) is actively investigating the efficacy and safety of this additional procedure in cervical tSCI patients (Saadoun et al., 2023).

4.3. Central cord syndrome

Currently, CCS is the most prevalent subcategory of incomplete tSCI, particularly due to global aging (Thompson et al., 2015). CCS is hallmarked by disproportionate weakness of the upper extremities relative to the lower extremities (Pouw et al., 2010), with a particular impact on hand function (Aarabi et al., 2011). Typically, elderly CCS patients are characterized by a classic presentation involving a low-energy trauma (mostly hyperextension injury) and preexisting cervical canal stenosis with new-onset neurological deficit, without any spinal disruption.

Historically, conservative management was the preferred approach to CCS treatment, largely due to concerns about potentially hindering natural recovery through surgery (Schneider et al., 1954). Notably, even though the vast majority of individuals with CCS initially experience spontaneous neurological improvement, a significant portion eventually underwent neurological deterioration in the subsequent months (Aarabi et al., 2013). More recent studies have indicated the need for a reassessment of this conservative approach, possibly owing to advancements in surgical techniques (Badhiwala et al., 2020).

Although surgical treatment in tSCI aims to prevent further secondary injury in general, there is an ongoing debate about the necessity of prompt surgical intervention in CCS patients. Several studies have failed to show a clear benefit of early decompression in CCS (Aarabi et al., 2011, 2021; Kumar et al., 2018). A randomized controlled trial, for example, found comparable neurological outcomes in early (<24h) and late treatment groups and only observed an accelerated recovery within the first six months in the early treated group (OSCIS et al., 2021). Nevertheless, recent research has demonstrated improved outcomes in early surgically treated patients (Zhou et al., 2023; Lenehan et al., 2010). Another study has examined 186 CCS patients and has found improved upper limb recovery with early surgery (<24h) compared to late surgery, without significant difference in lower limb recovery between the two groups (Badhiwala et al., 2022). This, however, appears to be a promising discovery, considering that hand unction is primarily impacted, and enhancing upper limb motor function is top priority for quadriplegic patients (Anderson, 2004). Additionally, early intervention only led to significant improvement in total motor score compared to late intervention in AIS C patients, possibly influenced by the ceiling effect of the AIS grade system.

These beneficial findings of early surgery are supported by a recent meta-analysis including 5619 patients (Sattari et al., 2023). This study compared neurological outcomes, complications and length of stay between early and late surgical treatment. After one year, the early surgery group has displayed significantly higher total motor scores, fewer complications and shorter hospital stay compared to the late surgery group. Mortality rates were similar between the two groups.

There are, however, a few limiting factors for early decompressive surgery in CCS patients. Firstly, the comorbidities of the elderly patients may in some cases need more urgent medical optimization before surgery can be safely performed. The majority of these patients use anticoagulants, which can also further delay surgical treatment. Existing literature suggests poorer neurological and functional outcomes in frail elderly individuals (Elsamadicy et al., 2021; Banaszek et al., 2020). Secondly, CCS is not always promptly recognized, leading to additional delays, possibly attributed to the lower energy trauma mechanism and absence of spinal fractures.

In conclusion, the increasing prevalence of CCS in this elderly population underscores the importance of further research, particularly in addressing the safety of early surgery in this group of patients with multiple comorbidities.

5. Postoperative phase

5.1. Intensive care unit (ICU)

As previously noted, monitoring of MAP on the ICU during the first seven days is of great importance as it may be protective against expansion of secondary spinal cord injury. Moreover, patients suffering tSCI face acute susceptibility to hemodynamic complications, including neurogenic shock, autonomic dysreflexia, respiratory problems and unstable arrhythmias (Sacino and Rosenblatt, 2019). Particularly, patients suffering cervical or high thoracic tSCI are prone to respiratory insufficiency, necessitating close surveillance in the ICU.

5.2. Acute rehabilitation

In line with surgical timing, the question arises regarding the optimal timeframe for commencing mobilization as part of the rehabilitation. Active rehabilitation treatment may encounter delays due to a variety of clinical factors, including critically ill patients, as well as logistical challenges such as staffing shortages. Animal studies have suggested that early mobilization initiated within days after trauma is not only safe, but also effective in promoting neurological recovery (Courtine et al., 2009; Norrie et al., 2005). The underlying rationale is that early mobilization stimulates a relearning process marked by adaptive neuroplasticity, driven by repetitive neuromuscular activation below the level of injury (Brown et al., 2011; Behrman et al., 2017). These animal studies have also demonstrated that early mobilization led to improved motor function and decreased spinal cord damage (Norrie et al., 2005; Brown et al., 2011). This suggests that there potentially is a 'window of opportunity' for fostering this neuroplasticity during the acute phase of tSCI, which implies that early mobilization holds the potential to improve neurological recovery. However, clinical studies assessing the effect of early mobilization remain limited (Burns et al., 2017). There are some preliminary findings from a prospective Canadian study, aimed at investigating the safety and potential benefits of early mobilization within 48 h, which have indicated that early mobilization is safe in tSCI patients

(Dionne et al., 2023).

Commencing early in the ICU, mobilization, involves physical therapy, occupational therapy and in some cases speech and respiratory therapy as well as bladder and bowel care (Sandrow et al., 2015; Rozeboom et al., 2012). Following hospital admission, it is preferable for tSCI patients to be directed to a specialized SCI rehabilitation center, as accumulating evidence suggest that this enhance outcomes for tSCI patients (Cheng et al., 2017). This is particularly crucial for (high) cervical tSCI patients, where specialized rehabilitation centers can maximize the chances of returning home (Dionne et al., 2021).

5.3. Medication

Granulocyte colony-stimulating factor (G-CSF), a hematological cytokine commonly used to treat neutropenia, has shown potential in SCI animal models for enhancing functional recovery. This is achieved by mobilizing bone marrow cells into the injured spinal cord, suppressing neuron apoptosis and inflammatory cytokines and promoting angiogenesis (Koda et al., 2021). A randomized, placebo-controlled trial was conducted in 88 cervical tSCI patients to explore the effect of G-CSF on neurological recovery (Koda et al., 2021). G-CSF was administered for up to five days post-injury. While no significant difference was observed in change in ASIA score between the two groups after three months, noteworthy discrepancies were noted in ASIA motor score after six and twelve months in the G-CSF group. Moreover, there was no notable increase in adverse events in the G-CSF group compared to placebo-group. Nonetheless, further research is warranted.

Currently, the Nogo-A Inhibition in acute Spinal Cord Injury (NISCI) trial is ongoing, comprising a multicenter, multinational, placebo-controlled phase-II study evaluating the safety and efficacy of intrathecal anti-Nogo-A in patients with cervical tSCI. Preclinical studies demonstrated that intrathecal administration of anti-Nogo-A promoted axon growth and improved functional recovery (Merkler et al., 2001). Study participants receive six intrathecal bolus injections with anti-Nogo-A or placebo within four to twenty-eight weeks after injury. It is hypothesized that anti-Nogo-A will improve upper extremity motor scores by facilitating axon growth.

6. Conclusion

While considerable progress has been made in the area of acute tSCI care, a number of important questions remain undetermined. More research is warranted to delve into the potential role of pharmacological interventions in acute tSCI treatment and to elucidate the advantageous impact of refined hemodynamic management strategies.

Declaration of competing interest

All authors declare no conflicts of interest.

Acknowledgements

The authors would like to thank the Rapenburg Race Foundation for supporting our tSCI research team.

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