Update on critical care for acute spinal cord injury in the setting of polytrauma

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Traumatic spinal cord injury (SCI) often occurs in patients with concurrent traumatic injuries in other body systems. These patients with polytrauma pose unique challenges to clinicians. The current review evaluates existing guidelines and updates the evidence for prehospital transport, immobilization, initial resuscitation, critical care, hemodynamic stability, diagnostic imaging, surgical techniques, and timing appropriate for the patient with SCI who has multisystem trauma. Initial management should be systematic, with focus on spinal immobilization, timely transport, and optimizing perfusion to the spinal cord. There is general evidence for the maintenance of mean arterial pressure of > 85 mm Hg during immediate and acute care to optimize neurological outcome; however, the selection of vasopressor type and duration should be judicious, with considerations for level of injury and risks of increased cardiogenic complications in the elderly. Level II recommendations exist for early decompression, and additional time points of neurological assessment within the first 24 hours and during acute care are warranted to determine the temporality of benefits attributable to early surgery. Venous thromboembolism prophylaxis using low-molecular-weight heparin is recommended by current guidelines for SCI. For these patients, titration of tidal volumes is important to balance the association of earlier weaning off the ventilator, with its risk of atelectasis, against the risk for lung damage from mechanical overinflation that can occur with prolonged ventilation. Careful evaluation of infection risk is a priority following multisystem trauma for patients with relative immunosuppression or compromise. Although patients with polytrauma may experience longer rehabilitation courses, long-term neurological recovery is generally comparable to that in patients with isolated SCI after controlling for demographics.

Bowel and bladder disorders are common following SCI, significantly reduce quality of life, and constitute a focus of targeted therapies. Emerging biomarkers including glial fibrillary acidic protein, S100β, and microRNAs for traumatic SCIs are presented. Systematic management approaches to minimize sources of secondary injury are discussed, and areas requiring further research, implementation, and validation are identified.

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**KEY WORDS** critical care; functional outcome; hemodynamic stability; polytrauma; prehospital management; risk factors; spinal cord injury; spine surgery

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**ABBRIVIATIONS** AANS = American Association of Neurological Surgeons; AIS = Abbreviated Injury Scale; BASIC = Brain and Spinal Injury Center; CNS = Congress of Neurological Surgeons; DLC = discoligamentous complex; DVT = deep venous thrombosis; GFAP = glial fibrillary acidic protein; LOS = length of stay; MAP = mean arterial pressure; miR = microRNA; PC = principal component; PLC = posterior ligamentous complex; SCI = spinal cord injury; SLIC = Subaxial Cervical Spine Injury Classification and Severity Score; TLICS = Thoracolumbar Injury Classification and Severity Score; UTI = urinary tract infection; Vt = tidal volume.


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ary cord injury from hypoperfusion and hypoxemia. Upon stabilization, decisions for surgical decompression and/or spinal column stabilization remain especially challenging for polytrauma patients. Figure 1 displays the range of co-morbid and/or multisystem injuries suffered by a patient with SCI and polytrauma. This review examines current best practices and recommendations for the evaluation and management of polytraumatic SCI, and identifies important areas for future research.

Immobilization During Prehospital Transport

Although there is expert consensus for immobilizing the spine after acute injury, data to determine standards for immobilization during emergency transport remain sparse and inconclusive. Biomechanical studies recommend the combination of a rigid cervical collar with supportive blocks on a hard backboard with straps.\(^\text{15}\) Abdominal straps fastened to the backboard reduce lateral thoracolumbar spinal motion, and excess slack between the patient and backboard should be eliminated to reduce further injury.\(^\text{28}\) However, tissue necrosis may occur from pressure of the rigid backboard during prolonged transport, and/or short periods of rigid immobilization. A padded board may reduce the risk for pressure necrosis by relieving the excess pressure between the board surface and the occupant and/or sacrum. Although cervical stabilization protocols are implemented in many health care systems, there are limited data to suggest true benefit.\(^\text{25}\) Generally, immobilization protocols are ubiquitous across health care institutions, are relatively easy to standardize and implement, and are unlikely to have negative effects—provided they do not interfere with rapid patient transport to a trauma center, and do not produce pressure ulcers.\(^\text{61}\)

Initial Stabilization and Resuscitation

Following SCI, early intubation and ventilation is indicated for patients with high cervical injuries (C1–5) causing impaired diaphragmatic breathing, respiratory depression, and CO\(_2\) retention—these patients are commonly quadriplegic. More than 20% of patients with cervical SCI require tracheostomy for chronic respiratory insufficiency, and tracheostomy rates are higher in complete (vs incomplete) spinal cord lesions.\(^\text{7}\) At a Level I trauma center, intubation and tracheostomy were performed in 68% and 69%, respectively, of patients with low cervical SCI (C6–7).\(^\text{38}\) The authors recommended mandatory early intubation for any patient with complete lower cervical spine injury, and report that even in patients with incomplete cord injuries, 50% may need tracheostomy.

Evidence regarding optimal intubation techniques for suspected cervical SCI remains controversial. A 2011 systematic review found that cervical movement is reduced from manual in-line stabilization in which a Miller blade is used with direct or indirect laryngoscopy, which should be the standard airway intervention technique in patients with polytrauma who have SCI and vertebral injury.\(^\text{2}\) It is important to note that these recommendations were based on assessment of cervical movement rather than patient outcomes—the perceived benefit of reduced cervical motion may not outweigh the increased time of intubation with indirect methods. Another caveat is the sparse data on prehospital intubation, where indirect viewing methods are largely unavailable.

Pulmonary complications are the leading short- and long-term cause of morbidity and mortality after SCI, also impacting the hospitalization length and costs. Patients who are ventilator dependent have approximately half the life expectancy of those who are similarly injured but not ventilator dependent.\(^\text{21}\) The 2005 Consortium for Spinal Cord Medicine’s Clinical Practice Guidelines on Respiratory Management Following Spinal Cord Injury recommends the use of high tidal volume (V\(_T\); 20–25 ml/kg ideal body weight).\(^\text{19}\) High V\(_T\) is reportedly associated with earlier weaning off of mechanical ventilation and more rapid resolution of atelectasis in patients with SCI.\(^\text{10,22,25}\) In patients without SCI who are at risk for acute respiratory distress syndrome, studies have focused on the safety of high V\(_T\) ventilation and the risk for barotrauma.\(^\text{9}\) Recently, the safety and efficacy regarding high V\(_T\) in patients with SCI has been debated, particularly because of the prevalence of acute respiratory distress syndrome in these patients.

Upon securing the airway and establishing adequate oxygenation, circulation should be assessed. As mentioned previously, polytraumatic SCI is often complicated by systemic hypotension due to hemorrhagic and/or neurogenic shock, which worsen secondary neurological injury. Common sources of occult internal hemorrhage include chest wall injury (associated with thoracic SCI), retroperitoneal hemorrhage, pelvic fractures, and open long-bone fracture. Special attention should be paid to the patient with polytrauma who has a pelvic fracture.\(^\text{24}\) Angiographically guided embolization is the first-line treatment for pelvic bleeding, although this may be less effective in treating venous sources.\(^\text{45}\) Of the alternative therapies, open reduction with internal fixation is considered more stable, and can be used in conjunction with closed reduction with external fixation for hemorrhage control.\(^\text{24}\)

Spinal Cord Perfusion and Vasopressor Support

Hypotension and/or neurogenic shock should be treated with aggressive fluid resuscitation.\(^\text{60}\) Suggested therapeutic targets include systolic blood pressure of 90–100 mm Hg, heart rate of 60–100 beats/minute, urine output > 30 ml/hour, and normothermia.\(^\text{22}\) The joint guidelines of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS) for cervical spine injury management recommend mean arterial pressure (MAP) > 85 mm Hg and avoidance of systolic blood pressure < 90 mm Hg for the first 5–7 days after SCI. More recently, results show that patients with complete SCI may derive greater benefit from MAP augmentation.\(^\text{14}\) The timing of intervention, and the duration for which MAP values are below threshold, may additionally influence neurological outcome. Similarly, a systematic review by Sabit et al. of the effect of MAP on functional outcome revealed that achieving normotension is the most effective treatment for the patient with SCI.\(^\text{67}\) This indicates the need for further research toward
establishing MAP goals in the care of the patient with polytrauma.

The Consortium for Spinal Cord Medicine recommends vasopressor choice by SCI level. Given the occurrence of bradycardias due to unopposed vagal tone in high cervical/thoracic injuries, agents with both α- and β-adrenergic activity (e.g., dopamine, norepinephrine) should be used to maintain MAP goals. In contrast, agents with pure α-adrenergic activity such as phenylephrine are adequate for lower thoracic injuries in which hypotension is more likely to result from vasodilation. In patients with acute traumatic central cord syndrome, high rates of cardiogenic complications are independently associated with dopamine and phenylephrine, and more serious complications were associated with dopamine use in elderly patients. Higher complication rates have been reported when vasopressors were used contrary to guidelines: e.g., use of dopamine for injuries below T-6. Interestingly, in a small study of 11 patients, norepinephrine was found to increase cord perfusion pressure by 2 mm Hg compared with dopamine, which may be of clinical advantage in maintaining strict MAP goals during acute care. Evidence from the trauma literature would suggest that narrowing vasopressor choice by injury level (e.g., above or below T-6), age (e.g., elderly patient with autonomic impairment), and presence of comorbidities (e.g., dopamine potentiation of arrhythmias), as well as careful titration of vasopressor dosage to minimize the duration of below-threshold MAPs during the first 5–7 days after injury, are of high importance.

It should be noted that following penetrating SCI, there is a decreased likelihood of neurological improvement, with implications for the role of MAP management using vasopressors. Aggressive cardiopulmonary management following multisystem trauma involving the spinal cord should weigh equipoise between expected risk of complications and relatively lower likelihoods of recovery.

**Imaging Methods**

Diagnostic imaging and workup should be pursued following initial stabilization. Guidelines recommend a
thorough evaluation of the patient with SCI and high-risk presentation (e.g., male sex, age < 45 years, impairment on the Glasgow Coma Scale, and chest injury from falls > 10 feet or due to motor vehicle accidents > 45 miles per hour). Computed tomography is the first-line imaging for the patient with SCI and polytrauma, because it provides rapid imaging with improved visualization of bony fractures. Vertebral column instability secondary to ligamentous injury should be evaluated, and flexor and extensor views should be obtained if the cervical spine is involved. Magnetic resonance imaging—in particular the sagittal T2-weighted sequence—has become the gold standard to evaluate active spinal cord compression or vascular injury (e.g., spinal cord hemorrhage, contusion, ischemia, infarct, and/or edema), as well as evidence of associated acute ligamentous injury, including traumatic injuries to intervertebral discs and the posterior ligamentous complex (PLC). Because MRI is only suitable for those who are hemodynamically stable, this can present a challenge in the patient with polytrauma. The prognostic ability of fat-suppressed T2-weighted MRI to detect acute changes seen in ligamentous injury decreases with time following trauma. As edema expands with time, the ability of serial T2-weighted sagittal MRI to accurately assess lesion severity decreases accordingly.5-49

The traditional classification system for SCI on T2-weighted MRI consists of Patterns 1–4 (1, normal cord signal; 2, hyperintense intramedullary edema with longitudinal extent at a single vertebral level; 3, multilevel edema; and 4, mixed hemorrhage and edema) to correlate with injury severity and outcome.3,34 However, in the setting of nonhemorrhagic traumatic SCI (Pattern 3 edema), there is insufficient correlation between longitudinal edema and functional recovery.6 Accordingly, the Brain and Spinal Injury Center (BASIC) score was developed in 2015, and it is an ordinal scale ranging from 0 to 4, classifying the extent of transverse injury following blunt cervical SCI (0, no appreciable intramedullary cord signal abnormality; 1, intramedullary T2 hyperintensity confined to central gray matter; 2, intramedullary T2 hyperintensity extending to involve spinal white matter, but not involving the entire transverse extent of the spinal cord; 3, intramedullary T2 hyperintensity involving the entire transverse extent of the spinal cord; and 4, Grade 3 injury plus discrete T2 hypointense foci, consistent with macrohemorrhage). This scale showed strong correlations with AIS grade both at admission and at discharge, with high interrater reliability (kappa 0.81–0.83).69 The stratification of SCI by using the extent of transverse T2 pathology shows promise in enhancing injury classification as well as outcome prediction.

Among advanced neuroimaging modalities, fractional anisotropy on diffusion tensor imaging showed the strongest evidence as a possible emerging biomarker of functional disability across degenerative cord etiologies and SCI,53 but it remains below diagnostic sensitivity and specificity thresholds for qualification. More recently, nonlinear principal component (PC) analysis was used to assess the relationship between early MRI biomarkers (< 24 hours) and their predictive validity on neurological impairment following cervical SCI.77 The 2 PCs are PC1, which is represented by all imaging vari-

Surgical Candidacy and Approach

A number of factors influence the timing and choice of surgical management in the patient with polytrauma who has SCI. The 2005 Thoracolumbar Injury Classification and Severity Score (TLICS) and the 2007 Subaxial Cervical Spine Injury Classification and Severity Score (SLIC) have been widely adopted to guide surgical decision making.21,74 Both TLICS and SLIC incorporate the same 3 categories of injury characteristics: injury morphology, integrity of the PLC or discoligamentous complex (DLC), and neurological status (Table 1).44,63 The TLICS and SLIC sum the patient score in each category, and the final score determines the next treatment step. A score < 4 suggests nonoperative management, 4 is borderline, and > 4 is an indication for operative management. Evidence for the safety of TLICS and SLIC has been widely studied in both adult and pediatric populations.

### TABLE 1. Comparison of TLICS and SLIC systems

<table>
<thead>
<tr>
<th>TLICS Characteristic</th>
<th>Score</th>
<th>SLIC Characteristic</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injury morphology</td>
<td></td>
<td>Injury morphology</td>
<td></td>
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<tr>
<td>No abnormality</td>
<td>0</td>
<td>No abnormality</td>
<td>0</td>
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<tr>
<td>Compression</td>
<td>1</td>
<td>Compression</td>
<td>1</td>
</tr>
<tr>
<td>Burst component</td>
<td>2</td>
<td>Burst component</td>
<td>2</td>
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<tr>
<td>Translation/rotation</td>
<td>3</td>
<td>Translation/rotation</td>
<td>3</td>
</tr>
<tr>
<td>Distraction</td>
<td>4</td>
<td>Distraction</td>
<td>4</td>
</tr>
<tr>
<td>PLC integrity</td>
<td></td>
<td>DLC integrity</td>
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<tr>
<td>Intact</td>
<td>0</td>
<td>Intact</td>
<td>0</td>
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<tr>
<td>Indeterminate</td>
<td>2</td>
<td>Indeterminate</td>
<td>1</td>
</tr>
<tr>
<td>Disrupted</td>
<td>3</td>
<td>Disrupted</td>
<td>2</td>
</tr>
<tr>
<td>Neurological status</td>
<td></td>
<td>Neurological status</td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td>0</td>
<td>Intact</td>
<td>0</td>
</tr>
<tr>
<td>Nerve root injury</td>
<td>2</td>
<td>Nerve root injury</td>
<td>1</td>
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<tr>
<td>Complete cord injury</td>
<td>2</td>
<td>Complete cord injury</td>
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<tr>
<td>Incomplete cord injury</td>
<td>3</td>
<td>Incomplete cord injury</td>
<td>3</td>
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<tr>
<td>Cauda equina injury</td>
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The TLICS and SLIC are used by summing the patient score in each category and using the final score to determine the next treatment step. For each scoring system, a score < 4 suggests nonoperative management, 4 is borderline, and > 4 is an indication for operative management.
The surgical objectives are to achieve mechanical stability and to prevent neurological deterioration. In general, patients with incomplete neurological injury should undergo an anterior procedure in the setting of anterior neural compression and an undisrupted PLC. If the PLC or DLC is disrupted with evidence of nerve root injury, but the patient is overall neurologically intact, a posterior procedure may be more appropriate. In patients presenting with incomplete neurological injury and PLC disruption, a combined anterior-posterior approach is indicated. For complete neurological injury, aggressive decompression is generally performed in an effort to maximize neurological recovery. Reconstruction and/or fixation of the vertebral column can be performed to restore CSF flow. Important considerations are the site of compression, morphology of injury, risk for progressive deformity, and surgical team experience with anterior, posterior, and combined techniques.

Surgical Timing

The timing of surgical intervention remains under debate. There is consensus that nonneurological outcome measures such as hospital and ICU length of stay (LOS), duration of mechanical ventilation, and pneumonia and other complications improve in patients undergoing early surgical stabilization—more markedly in patients with polytrauma and thoracic injuries. Whether early surgical intervention improves neurological outcomes is less clear. Whereas historical trials show no benefit to early (<24 hours from time of injury) surgical intervention, more recent studies report improved motor and neurological recovery. Notably, the prospective multicenter Surgical Timing in Acute Spinal Cord Injury Study trial conducted from 2002 to 2009 reports improved AIS grades among patients with acute cervical SCI who underwent early versus late surgery. This is supported by the systematic review by Lenehan and colleagues showing improved odds of 6- and 12-month functional outcome following early surgery. Early decompression has also been found to be more cost-effective than later surgery for patients with motor-complete and -incomplete SCI. Moreover, incomplete resuscitation of patients prior to surgery may confound the influence of surgical timing on morbidity and mortality.

Under the general consensus of “early” being <24 hours, a recent meta-analysis of 5326 patients identified benefit to early compared with late spinal cord decompression, also noting the considerable heterogeneity of patients and medical practice across studies. The best that current evidence can provide is Level II recommendations for early decompression. Additionally, more refined time points within the first 24 hours are warranted to assess the temporality of early surgical benefits. It is possible that the effects of early intervention may wane within the first 24 hours, further delineating the need for large, well-controlled prospective studies within this time range.

Biomarkers for Early Diagnosis

There is increasing interest in identifying biomarkers for the early diagnosis of SCI. Candidate markers for traumatic SCI include glial fibrillary acidic protein (GFAP), neurofilaments, cleaved tau, myelin basic protein, neuron-specific enolase, S100β, and soluble CD95 ligand. To date, S100β—a calcium-binding protein in astroglial and Schwann cells—is the most studied, showing elevations after traumatic SCI or vertebral fractures. Serum S100β and neuron-specific enolase have been shown to increase after polytrauma, hemolysis, and/or inadequate resuscitation. Some experts have proposed using biomarkers to assess injury severity and treatment response rather than for diagnosis, due to low specificity.

Biomarkers may indicate transient or permanent neurological deficit due to systemic injuries. For example, GFAP also correlated with delayed-onset paraplegia. Findings indicate that S100β and GFAP have potential as biomarkers when evaluating stability of the patient with polytrauma for investigation of injury severity, for diagnostic imaging, and/or MAP-directed therapy. A polytrauma-specific biomarker in SCI remains elusive. The only study to date comparing patients with traumatic SCI to healthy controls reports nonspecific elevations in GFAP and neurofilaments. However, a study by Brisby and colleagues followed elevated CSF levels of neurofilaments and S100β following disc herniation, and patients with symptom duration <3 months showed higher neurofilament levels compared with patients with ≥3 months’ duration. Hence, GFAP and neurofilaments may indicate nerve root compression during acute trauma, but this remains to be validated in larger samples.

MicroRNAs (miRs) are emerging candidates for both diagnostic biomarkers and therapeutic targets for SCI. Notably, miR-21 may be important due to its role in hypertrophy-to-hyperplasia changes characteristic of astrogliosis. In the laboratory it has been shown to have antiapoptotic and antiinflammatory properties, although its expression decreases 14 days postsinult. As a novel therapeutic agent, miR-21 antagonir administered by intrathecal injection decreased recovery of hindlimb motor function, and overexpression of miR-21 has been shown to protect against transient ischemia.

Infection Risk

The patient with polytrauma has increased susceptibility to infection due to the disruption of the neuroimmune axis. Whereas pneumonia and bloodborne infections are the most common causes of death (33% of all deaths in the 1st year), urinary tract infections (UTIs) and decubitus ulcers are risk factors for rehospitalization, with incidences of 34% and 10%, respectively. A retrospective analysis of 5540 patients undergoing cervical spine surgery and recorded in the US Nationwide Inpatient Sample between 2000 and 2011 reported neurological status (myelopathy or SCI) and trauma as the most significant predictors of surgical site infection. Surgical approach, number of levels fused, female sex, black race, medium-size hospital, rural hospital, large hospital, western US hospital, and Medicare coverage were additional significant predictors of surgical site infection. Several studies report decreased infection rates with intrawound vancomycin powder.
Venous Thromboembolism

Patients with spinal polytrauma are at risk for venous thromboembolism, most prominently deep venous thrombosis (DVT). Almost 40% of patients with SCI may suffer DVT within the first 12 weeks following acute injury, often due to stasis and hypercoagulability, which are compounded with multisystem injuries.56 Prophylaxis for patients with polytrauma is complicated because of the risk of worsened bleeding. The American College of Chest Physicians ultimately recommends pharmacological anticoagulation, predominantly with low-molecular-weight heparin following acute SCI (Grade 1A evidence), combined with mechanical prophylaxis for patients with exceptional bleeding risk.32 The 2013 guidelines of the AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves reported evidence for pharmacological prophylaxis using low-molecular-weight heparin (Level I), within 72 hours following spinal injury (Level II).32 Current guidelines recommend continuing prophylaxis for at least 12 weeks after patient stabilization, at which point the risk of DVT declines considerably.30

Bowel and Bladder Disorders

Spinal cord injury may lead to temporary or permanent bowel and bladder disorders, which can result in UTIs and direct renal damage. For patients with SCI at 1 year post-injury, 40% attended urology clinic and 33% were hospitalized due to bladder issues; UTIs accounted for > 20% of these hospitalizations.70 Although procedures such as the Valsalva maneuver may be attempted to induce voiding, current recommendations focus on clean intermittent catheterization. Hughes defined the following 3 different neuropathological patterns of bowel dysfunction: Pattern A, injury above T-7, when voluntary control of abdominal muscles was absent but spinal sacral reflexes were preserved; Pattern B, injury below T-7 with voluntary control of abdominal muscles and preserved sacral reflexes; and Pattern C, injury below T-7 with voluntary control of abdominal muscles and absent sacral reflexes.40 First-line therapy involves timed dietary intake and, if needed, rectal stimulation. Pharmacological management with prokinetic laxatives is also an option, and for patients whose condition is refractory, surgical management via colostomy. Patient preference, ability, and resources will play a large role in determining the direction of management.

Functional Outcomes and Role of Rehabilitation Services

It is generally recognized that patients with traumatic SCIs present with worse functional status than those with nontraumatic SCIs, and patients with polytrauma present with a higher percentage of complete lesions than do those with isolated trauma.65,68 Similarly, patients with trauma who have concurrent severe brain injury demonstrate longer LOS and rehabilitation stays, and lower Functional Independence Measure motor scores at discharge compared with those without brain trauma.52 However, when comparing SCI with and without polytrauma, the complication rates, discharge destination, neurological recovery, and up to 1-year functional outcome were comparable after adjusting for demographics, lesion level, and AIS grade.65 The general consensus is that neurological recovery is dependent on completeness of lesion rather than presence of polytrauma. In smaller studies of SCI resulting in paraplegia, patients with polytrauma demonstrated no differences in neurological improvement compared with their counterparts who had isolated SCI; however, they did demonstrate longer LOS, delayed acquisition of activities of daily living functions, and increased health care costs.65 Future prospective studies with appropriate adjustment for SCI morphology and severity, across various levels of polytrauma, are needed.

Physical and occupational therapists serve central roles in patient recovery. In general, rehabilitation following SCI is divided into acute and long-term phases.57 In the acute hospital setting, the goals for physical therapy are to prevent muscle contracture and muscle wasting, and to reduce the risk of pressure ulcers. For patients suffering paraplegia, physical therapy often focuses on building upper-extremity strength to assist with mobility. Improvements following physical therapy, along with outcome measures of social integration and functional independence at 1 year postinjury, can be predicted by AIS and treatment duration.73

Conclusions

Spinal cord injury with polytrauma poses uniquely challenging considerations due to the increased risk of secondary insults to the spinal cord. Prehospital management should include appropriate spinal immobilization followed by timely transport to a trauma center. The initial assessment and management are focused on optimizing perfusion to the spinal cord. Poststabilization, diagnostic evaluation includes CT for bony fractures or overt cord pathology, and MRI in the patient with hemodynamic stability. Surgical stabilization depends on approach, timing, and perioperative management. Careful consideration of infection risk should be a priority for patients with trauma who have relative immunosuppression or compromise. Patients with polytrauma may experience longer rehabilitation courses; however, long-term neurological recovery is generally comparable to that for patients with isolated SCI, after controlling for demographics. Biomarkers for SCI may aid in early diagnosis and outcomes prognosis, but they require studies in larger data sets to achieve enough sensitivity and specificity to be suitable as recommendations.

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Conception and design: Dhall, Yue, Winkler. Acquisition of data: Yue, Winkler. Analysis and interpretation of data: Yue, Winkler, Rick, Deng, Birk, Chan. Drafting the article: Dhall, Yue, Winkler, Rick, Deng, Partow, Upadhyayula, Chan. Critically revising the article: Dhall, Yue, Winkler, Rick, Deng, Birk, Chan. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Dhall. Statistical analysis: Yue, Winkler. Administrative/technical/material support: Yue, Winkler. Study supervision: Dhall.

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