

Clinical Practice Guideline

The Diagnosis and Treatment of Acute Spinal Cord Injury

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Summary

Background: In Germany, the incidence of traumatic spinal cord injury is approximately 16 per million inhabitants per year. This article aims to present evidence-based diagnostic and therapeutic measures for the first 14 days after injury to minimize neural damage, prevent complications, and preserve functioning as much as possible.

Methods: After the formulation of key questions, systematic literature searches were carried out on multiple topics. The findings were evaluated for methodological quality, and recommendations were agreed upon by consensus.

Results: Spinal cord injury may be due to traumatic (e.g., a fall) or non-traumatic causes (e.g., ischemia). The evidence presented here on the diagnosis and treatment of spinal cord injury is mainly based on observational studies. 15 evidence-based and 43 consensus-based recommendations were formulated. The patients' neurological course should be monitored by clinical neurological examination according to the International Standards for Neurological Classification of Spinal Cord Injury (strength of recommendation [SOR]: strong). If traumatic spinal cord injury is suspected, the patient should be transported as rapidly as possible to a tertiary-care trauma center (SOR: strong). Spine decompression surgery should be performed within 24 hours (SOR: weak). Corticosteroids

should not be given in the acute phase of traumatic spinal cord injury (SOR: strong) but are indicated if the spinal cord is compressed by a tumor (SOR: strong). The mean arterial pressure should be between 70 and 90 mmHg for the first 2–3 (maximum 7) days (SOR: weak). Pharmacotherapy with heparin should be started early to prevent thromboembolism, with due attention to the risk of hemorrhagic complications (SOR: strong).

Conclusion: This (S3 level) clinical practice guideline aims to standardize clinical care. Early interdisciplinary management is essential to protect at-risk neural tissue and to prevent complications, and constitutes a key prerequisite for long term neurological and functional recovery. No neuroprotective or neuroregenerative treatments are available to date.

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Spinal cord injury refers to damage of the spinal cord or cauda equina (1). Spinal cord injury leads to motor, sensory, or vegetative deficits of varying severity (1). Spinal cord injury can be caused by trauma (e.g., a fall) or by a non-traumatic event (e.g., ischemia). The incidence of traumatic spinal cord injury in Germany is around 16 per 1 000 000 inhabitants (2–4). The incidence of non-traumatic spinal cord injury in Europe is estimated at 10–60 per 1 000 000 (5–7). An increase in fall-related spinal cord injury among older adults can be attributed to demographic change, as can the vast majority of non-traumatic cases. Comorbidity, mortality, and rehabilitation planning are all impacted by this development (4–6, 8–10).

The German Society of Neurology (*Deutsche Gesellschaft für Neurologie e. V.*, DGN) and the German-Speaking Medical Society for Spinal Cord Injury (*Deutschsprachige Medizinische Gesellschaft für Paraplegiologie e. V.*, DMGP) have now for the first time established the foundations for evidence-based diagnosis and treatment of acute spinal

cord injury. With the aim of further improving the standard of care in Germany, Austria, and Switzerland, the expert recommendations (referred to as level S1 guidelines in the German-speaking countries) on acute spinal cord injury that expired in 2016 have been updated and elevated to the level of a clinical practice guideline (level S3).

Early and appropriate medical care in the acute phase affects mortality, morbidity, and the long-term physical impairments that impact on participation and quality of life (11, 12). The evidence in this regard is based predominantly on the findings of observational studies, underlining the importance of further clinical research. In the acute phase, the goals of treatment are to ensure survival, minimize the spinal cord damage, enable spontaneous neurological recovery, avoid

Table

Evidence-based recommendations: underlying evidence and assessment

Intervention Reference	Results per outcome (number of studies included; effect estimator)	Recommendation strength; GRADE	Summary
Early (≤ 24 h) vs. late (> 24 h) decompression surgery (18)	ASIA motor score, MD 4.50; 95% CI [1.70; 7.29]; 4 studies	B; very low certainty	In comparison with late surgery, early surgery can have a positive effect.
Methylprednisolone/ dexamethasone alone (19)	ASIA motor score, MD 1.38; 95% CI [-11.9; 14.7]; 3 RCT	B; low certainty	Methylprednisolone or dexamethasone probably has no effect in comparison with non-steroidal treatments.
Pharmacologic (non-steroid-based) treatments (20)	No quantitative analysis reported	B; low certainty	Pharmacologic (non-steroid-based) treatments may have no effect on motor recovery.
Cell transplantation, hyperbaric oxygen therapy, hypothermia (21)	No quantitative analysis reported	B; very low certainty	The effect of cell transplantation, hyperbaric oxygen therapy, or hypothermia is very uncertain.
Endovascular revascularization in spinal cord ischemia (22)	Efficacy, OR 2.00; 95% CI [0.23; 17.19]; 125 case reports	Statement; very low certainty	The effect of endovascular revascularization is very uncertain.
Cerebrovascular fluid drainage in spinal cord ischemia (22)	Efficacy, OR 3.08; 95% CI [0.38; 25.25]; 125 case reports	Statement; very low certainty	The effect of cerebrovascular fluid drainage is very uncertain.
Systemic steroid administration in spinal cord ischemia (22)	Efficacy, OR 0.625; 95% CI [0.290; 1.345]; 125 case reports	Statement; very low certainty	The effect of systemic steroid administration is very uncertain.
Dexamethasone in metastases (23)	No quantitative analysis reported	B; low certainty	Steroids with high initial bolus doses probably have no effect in comparison with steroids with low initial bolus doses.
Mean arterial pressure 70–90 mm Hg (24)	No quantitative analysis reported	B; very low certainty	The effect of mean arterial pressure support is very uncertain.
Dobutamine in reduced cardiac ejection fraction (24)	No quantitative analysis reported	B; very low certainty	The effect of dobutamine is very uncertain.
Thromboembolic prophylaxis/ heparin (25–27)	No quantitative analysis reported	A; very low certainty	The effect of heparin is very uncertain.
Respiratory management (28)	No quantitative analysis reported	A; very low certainty	The effect of respiratory management is very uncertain.
Tracheotomy (29)	VAP incidence, RR 0.86; 95% CI [0.75; 0.98]; 10 studies Duration of mechanical ventilation, MD -13.91; 95% CI [-21.11; -6.70]; 10 studies	B; very low certainty	The effect of tracheotomy is very uncertain.
Prognostic statements (34, 35)	No quantitative analysis reported	B; very low certainty	The use of fractional anisotropy to predict the AIS score is very uncertain.
Electrostimulation (37)	No quantitative analysis reported	Statement; very low certainty	The effect of electrostimulation is very uncertain.

AIS, ASIA Impairment Scale; ASIA, American Spinal Injury Association; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation confidence in the evidence; MD, mean difference; OR, odds ratio; RCT, randomized controlled trials; Recommendation strength: A = strong, B = weak; RR, relative risk; VAP, ventilator-associated pneumonia

complications, and prepare the ground for the highest possible degree of self-sufficiency (13). The clinical practice guideline contains recommendations concerning conditions associated with spinal cord injury and aims to create favorable conditions in the long run. The guideline is valid for the first 14 days after the onset of the spinal cord injury, regardless of the cause.

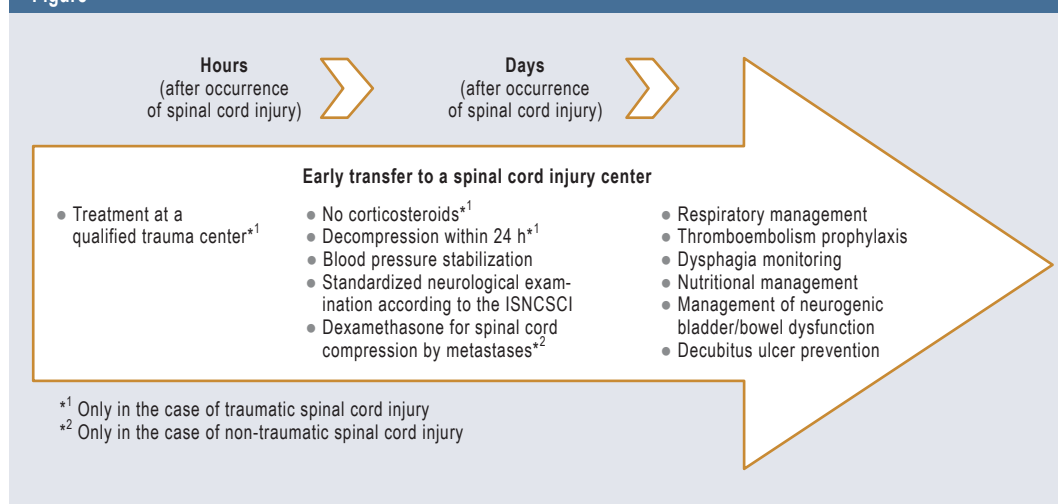
Method

Physicians, other medical and scientific professionals, and patients' representatives contributed to the development of this guideline, which was developed in accordance with the regulations of the Association of the Medical Scientific Societies in Germany (AWMF) for clinical practice guidelines (14). The guideline group was coordinated by

the DGN and the DMGP with the involvement of 17 other professional societies. The guideline was financed by the innovation fund of the German Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA) (01VSF22004). The guideline collaborators are listed in the *eBox*.

The first step was to define key questions. The initial search for systematic reviews covered Medline, Epistemonikos, and the Cochrane Library. If necessary, update searches and additional searches for primary studies were conducted. The search strategies and selection processes are documented in *eSupplement 1*. The reviews selected for inclusion were evaluated according to AMSTAR-II and GRADE (15, 16). All recommendations were formulated in

Figure



Overview of the essential aspects of treatment, in sequential order, after the occurrence of spinal cord injury
ISNCSCI, International Standards for Neurological Classification of Spinal Cord Injury

a structured consensus process. The methodology is described in detail in the guideline report.

Results

This guideline deals with traumatic and non-traumatic spinal cord injury and with commonly occurring associated conditions, including recommendations on the management of respiration, the gastrointestinal system, and the urinary bladder. Other topics covered are prognosis and methods for functional improvement.

A total of 58 recommendations were consented (15 of them evidence-based [EB], the other 43 based on expert consensus [EC]). A selection of these recommendations are presented in this article. The *Table* summarizes the evidence behind the evidence-based recommendations; detailed evidence tables can be found in *eSupplement 2*. The *Figure* provides a sequential overview of the treatment. The long and short versions of the guideline contain all of the recommendations. All documents are available (in German) on the AWMF website. A guideline for patients was also developed.

Introduction to spinal cord injury

Clinical diagnosis and classification

As soon as the patient is awake and cooperative, clinical and neurological examination and classification should be performed in accordance with the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI); this forms the basis for objective and reliable assessment of the course of traumatic spinal cord injury (EC). This examination should comprise at least the Neurological Level of Injury, the ASIA Impairment Scale, and the Zone of Partial Preservation (EC).

Background: The investigation defines the levels of sensory and motor function separately for each side of the body, based on motor scores for ten key muscle groups and sensory scores for sensitivity to touch and discrimination between a pin-prick and a light touch in 28 dermatomes. The neurological level of injury refers to the

most caudal segment of the spinal cord with normal sensory and motor function.

Traumatic spinal cord injury

Emergency rescue and transport/prehospital management

A targeted physical examination including the spine and associated sensorimotor functions should be carried out in persons with severe trauma (EC). Persons in whom spinal cord injury is suspected at the accident site should be transported carefully and swiftly to a qualified level I trauma center or to an emergency medical center with experience in comprehensive interdisciplinary spinal cord injury care (EC). Those confirmed to have spinal cord injury should be transferred as soon as possible to a spinal cord injury center (EC).

Background: With regard to the rescue procedures and transport of persons with suspected spinal trauma, we refer to the clinical practice guideline on the treatment of multiple trauma/serious injury (in German) (AWMF registration number: 187–023) (17).

Surgical management of the spine

Surgical treatment of traumatic spinal cord injury should be carried out by a qualified spine team as early as possible and at the latest 24 hours after the trauma, as soon as the patient's vital parameters have been stabilized, in order to achieve the optimal neurological outcome (EB, very low certainty [18]). The advised procedure in vertebral fractures with neurological deficits at the level of the thoracic and lumbar spine is as follows:

- Open surgical access to the spine
- Adequate bony decompression of the spinal canal
- Stabilization of the spine by means of dorsal external fixation (EC).

Management of accompanying injuries

Regardless of neurological deficit and the level of acute traumatic spinal cord injury, injuries to the extremities should be treated according to AO surgery criteria with the aim of achieving optimal functionality and mobility (EC).

Background: All injuries to the extremities, regardless of the initial neurological deficit and the level of spinal cord injury, are treated according to the AO surgery criteria, a system for localization and description of fractures.

Neuroprotective and neuroregenerative treatment

Methylprednisolone should not be administered in the acute phase of spinal cord injury (EB, low certainty [19]). Non-steroid-based pharmacological agents with the aim of improving neurological/functional recovery should not be used to treat acute traumatic spinal cord injury (EB, low certainty [20]). Cell transplantation, hyperbaric oxygen therapy, and hypothermia should not be used to treat acute traumatic spinal cord injury (EB, very low certainty [21]).

Non-traumatic spinal cord injury

Diagnosis of non-traumatic spinal cord injury

Diagnostic evaluation of non-traumatic spinal cord injury should include a neurological examination including the neurological level and severity of injury (EC).

Spinal ischemia

For patients with acute non-iatrogenic spinal cord ischemia, no recommendation for endovascular revascularization can be given due to the poor evidence (EB, very low certainty [22]). No recommendation can be given for drainage of cerebrospinal fluid in patients with acute non-iatrogenic spinal cord ischemia (EB, very low certainty [22]). No recommendation can be given for systemic steroid treatment in patients with acute non-iatrogenic spinal cord ischemia (EB, very low certainty [22]).

Spinal metastasis

If the spinal cord is being compressed by metastases, dexamethasone should be administered systemically to improve the patient's walking ability (EB, very low certainty [23]).

Associated conditions, pathologies, and prevention of complications

Management of neurogenic shock and hypotension (neurogenic and orthostatic)

In patients with traumatic spinal cord injury and signs of hypotension, the mean arterial pressure (MAP) in the first 1–2 days (at the most, 7 days) should be between 70 mm Hg and 90 mm Hg. Norepinephrine should preferentially be used as vasopressor (EB, very low certainty [24]). In patients with traumatic spinal cord injury and reduced cardiac ejection fraction, dobutamine should be added to achieve the desired mean pressure (EB, very low certainty [24]).

Background: An increase in the MAP is desirable because it presumably elevates the spinal perfusion pressure and promotes neurological recovery.

Prevention of thromboembolism

Thrombosis prophylaxis (with low-molecular heparin or unfractionated heparin) should be administered as early as possible, to reduce the risk of venous thromboembolism in persons with acute spinal cord injury (EB, very low certainty [25–27]). The potential risk of (surgery-associated) bleeding needs to be considered.

Background: With the administration of heparins one has to consider the relevant contraindications, such as high bleeding risk, hemorrhagic stroke, ulcers, malignant neoplasms, and recent brain or spine surgery. For this reason, the timing of thromboembolic prophylaxis needs to be discussed with the surgeon.

Respiratory management

Persons with acute spinal cord injury requiring ventilation should receive comprehensive respiratory care—including adjustment of ventilation volumes, postural drainage, respiration training, and mucus-clearing techniques—to support the recovery of respiratory

function as far as possible (EB, very low certainty [28]). Persons with acute spinal cord injury and respiratory insufficiency in whom an extended weaning phase is anticipated should undergo tracheotomy as early as possible within 4–6 days, to reduce the risk of pneumonia and tracheotomy-associated complications and to minimize both the intensive care stay and the time on the ventilator (EB, very low certainty [29]). The muscles involved in inspiration and expiration that can be trained should be trained, to enhance lung function, strengthen the respiratory musculature, and avoid or reduce pulmonary complications (EC). Persons with acute cervical or high thoracic spinal cord injury should be weaned off the ventilator at a dedicated spinal cord injury center with ventilator support capacity, as weaning of tracheotomized persons is a prolonged, discontinuous process (EC).

Nutritional and gastrointestinal management

Nutritional management of persons with acute spinal cord injury should start on the day of admission, when an individual, stage-appropriate nutrition plan should be drawn up (EC). In the acute phase of spinal cord injury, the patient's peristaltic sounds should be monitored and the rectum checked daily for the presence of feces, so that intestinal activity can be stimulated if required and the optimal time for initiation of oral intake can be identified (EC).

Background: With regard to the development of paralytic ileus in the acute phase, we refer to the description in AWMF guideline 179–004 (in German) (30).

Resumption of oral feeding in persons with acute spinal cord injury should be adapted and reevaluated daily, monitoring for neurogenic bowel dysfunction (peristaltic sounds) and the occurrence of dysphagia (EC). Patients with cervicothoracic spinal cord injury should be examined by a speech therapist in the first few days to identify signs of dysphagia and thus avoid secondary complications (EC).

Urinary bladder management

During the acute phase after the occurrence of spinal cord injury and the period of intensive care, the urinary bladder should be drained via a permanent catheter, ideally a small- to medium-caliber (12–14 Ch) silicon catheter, to ensure reliable bladder emptying (EC).

Management of priapism

If a man with acute spinal cord injury has priapism, a urologist should be consulted so that the urological treatment can be carried out as usual (EC).

Management of the skin

To reduce the incidence of skin lesions (decubitus, lesions due to shear forces), persons with acute spinal cord injury should be treated at a center or hospital where a policy for prevention and treatment of decubitus is in place (EC).

Background: Despite the existence of integrated preventive treatment strategies, pressure injury remain one of the most frequently occurring complications in persons with acute spinal cord injury. The incidence of pressure injury in the acute phase is estimated at 30–50% (31–33).

Every time a person with acute spinal cord injury is repositioned using suitable support surfaces (e.g., every

2–4 hours with pillows, wedges, and alternating pressure mattresses), the skin should be thoroughly examined, especially at predilection sites (e.g., sacrum/coccyx, heel, trochanter, and ischium), and the findings documented (EC). As soon as pressure injuries are observed, pressure on the **affected area** should be relieved. Early mobilization should be continued with appropriate aids, taking account of the individual circumstances and the skin checks (EC). Discovery of a pressure injury in a person with acute spinal cord injury should prompt immediate conservative treatment with pressure relief and local wound care according to the wound treatment policy. This should take place within the framework of an interprofessional and multidisciplinary care plan (EC).

Prognosis and communication

In the acute phase, neither clinical examination according to the ISNCSCI nor supplementary procedures (magnetic resonance imaging, AI-assisted prediction [AI, artificial intelligence]) permit reliable forecasting of the outcome with regard to neurological recovery. Therefore, in the early phase prognosis should not inform treatment decisions and should not be mentioned in discussions with patients or their relatives (EB, very low certainty [34, 35]).

Background: The chance of spontaneous recovery from traumatic spinal cord injury can be estimated most reliably based on the ISNCSCI and the ASIA Impairment Scale (36). This is less reliable in the first few days after occurrence of the injury, however, because cooperation on the part of the patient may be limited owing to the necessity of intensive care. Assessment of the prognosis in the early phase is therefore not purposeful.

Promoting functional recovery: mobility, independence, and participation

Activating measures (physical therapy, occupational therapy) should be carried out as soon as possible and should be adjusted to the patient's circumstances (traumatologic/orthopedic and neurological/general medical limitations, stress) (EC). The use of electrostimulation cannot be recommended in the acute phase of spinal cord injury (EB, very low certainty [37]).

The paralyzed extremities of persons with spinal cord injury should be mobilized daily through the full range of motion, taking the individual patient's pain and other limitations (EC) into account. With increasing muscle tone and impaired joint mobility, the treatment should be reconsidered and adapted (EC). The treatment of tetraplegic hands should be carefully considered in the acute phase so that the treatment can be individualized (EC). Aids to support communication of the patient's needs (e.g., suitable bells/call buttons) should be individually adapted to injury level and cognitive skills so that they can be used reliably (EC).

Discussion and research requirements

Prior to the development of this guideline, it was acknowledged that not all aspects of comprehensive spinal cord injury care could be addressed in a single document. For this reason, the guideline group restricted the time frame to the first 14 days after occurrence of the injury. Thus, studies that focused on later time points were excluded.

The evidence available for the acute phase of spinal cord injury is still sparse.

Only 26% of the recommendations are evidence-based, drafted after a systematic survey and critical appraisal of the evidence. The evidence found was predominantly very weak. A clear definition of the acute phase and explicit information regarding the time since injury in the respective studies would improve the interpretability of spinal cord injury-specific research data. High-quality observational and interventional studies on spinal cord injury are challenging, particularly in the early stage, because of the low incidence, the heterogeneous etiology, and the decentralized nature of primary care.

The search strategy of this clinical practice guideline was oriented predominantly on systematic reviews. Only isolated additional searches for primary studies were conducted. This limitation may have led to relevant primary studies being overlooked.

In summary, more research is needed in the field of acute spinal cord injury. There is still an unmet need for effective neuroprotective and neuroregenerative treatments. Even the recommendation supporting swift surgical decompression in traumatic spinal cord injury is based on non-controlled, mostly retrospective studies.

For many severe comorbidities, such as thromboembolic events, there is only limited evidence on effective primary prophylactic interventions. Nevertheless, this guideline provides valuable new advice on the management of acute spinal cord injury. Recent international guidelines support our recommendations regarding early decompression (38, 39). Simultaneously, the need for active blood pressure management and in general individualized treatment decisions is emphasized. Our recommendation against the administration of corticosteroids due to potential adverse effects is also supported by Picetti et al. (39).

This clinical practice guideline summarizes the current state of knowledge on the diagnosis and treatment of acute spinal cord injury. It serves as a basis for uniform, high-quality clinical care, promoting neurological recovery and minimizing complications.

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Conflict of interest statement

The authors declare that no conflict of interest exists.

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Clinical practice guidelines in the *Deutsches Ärzteblatt*, as in many other journals, are not subject to a peer review process, since clinical practice (S3 level) guidelines are texts which have already been evaluated, discussed, and broadly agreed upon multiple times by experts (peers).

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Supplementary material

Full references including eReferences, eBox, eSupplements:
www.aerzteblatt.de/m2025.0034

CLINICAL SNAPSHOT



Migration of Intravitreal Silicone Oil Into the Lateral Cerebral Ventricles

An 83-year-old male patient with impaired speech underwent native cranial computed tomography (CT) to exclude a stroke. CT showed two indeterminate round structures in both frontal horns of the lateral ventricles that presented as intraventricular blood based on their CT density (arrows in Figure a), but were located at the top rather than at the bottom of the ventricle. Closer scrutiny of the patient's medical history revealed an instance of retinal detachment of the right eye. This had been treated approximately 2 years previously with intravitreal silicone oil tamponade during retinal surgery. To confirm the suspected diagnosis of an extremely rare migration of intravitreal silicone oil (along the optic nerve) into the subarachnoid space and extending as far as the intraventricular space, a CT scan in the prone position and additional magnetic resonance imaging were performed. In the prone position, the structures rose on both sides into the posterior horns of the lateral ventricles (Figure b). Thus, intracranial hemorrhage could be excluded and the suspected diagnosis of intracranial silicone migration confirmed. Most patients exhibit no clinical symptoms. In rare cases, intraventricular silicone may block the flow of cerebrospinal fluid.

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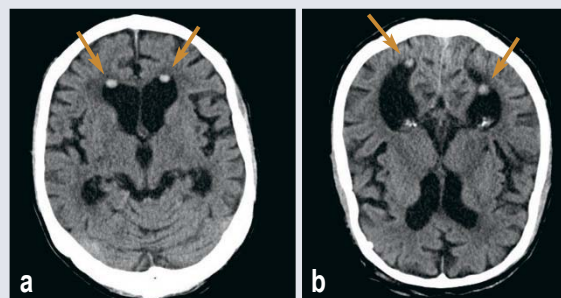


Figure:

- a) In the supine position, CT shows two round hyperdense structures in the ventral aspect of the frontal horns of the lateral ventricles.
- b) In the prone position, these structures rise on both sides into the posterior horns of the lateral ventricles.

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Supplementary material to accompany the article

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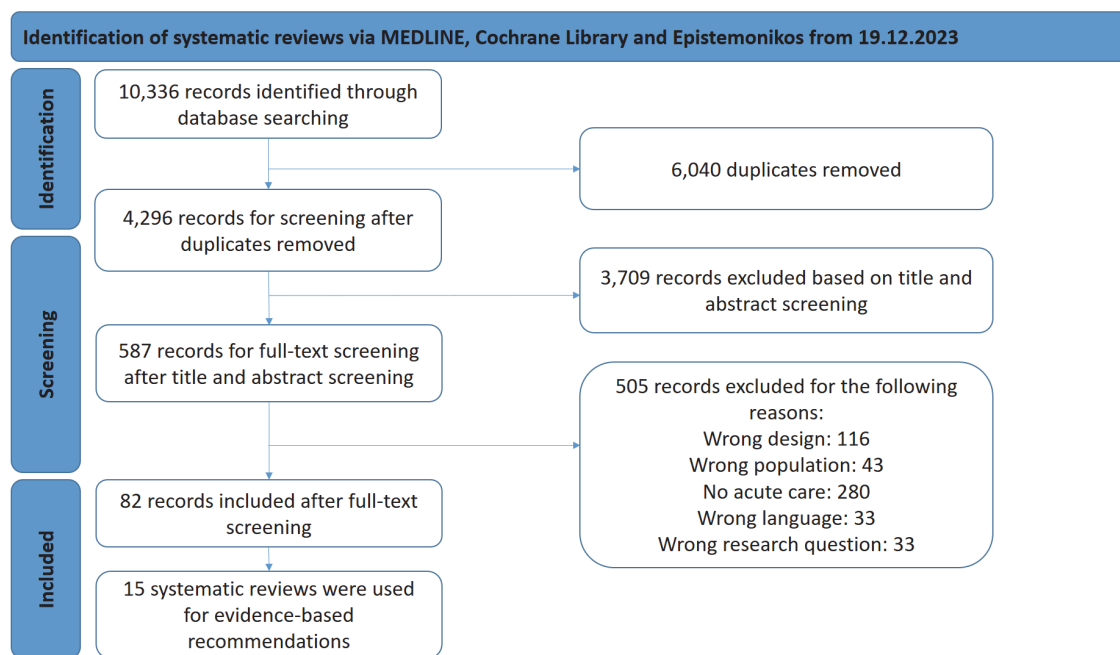
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eSupplement 1

Example of the search strategy and selection process

An example of the search strategy is shown here. All other search strategies and selection processes are documented in the guideline report.

PRISMA Flow chart, search for systematic reviews, search date: 19.12.2023



Suchstrategie MEDLINE

ID	Search
#1	exp Spinal Cord Injuries/
#2	exp Spinal Cord Ischemia/
#3	exp Spinal Cord Diseases/
#4	exp Spinal Cord/su, th
#5	(spinal cord adj3 (contusion or laceration or trauma* or lesion* or injur* or ischemi* or disease* or disorder*)).ti.
#6	((central cord or central spinal) adj2 syndrom*).ti.
#7	acute SCI.tw.
#8	or/1-7
#9	cochrane database of systematic reviews.jn. or search*.tw. or meta analysis.pt. or medline.tw. or systematic review.tw. or systematic review.pt.
#10	8 and 9

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Suchstrategie Epistemonikos

title:(title:((spinal cord AND (contusion OR laceration OR trauma OR lesion* OR injur* OR ischemi* OR disease* OR disorder*)))) OR title:(("central cord" AND syndrom*)) OR title:(("central spinal" AND syndrom*)) OR (title:((acut* SCI)) OR abstract:((acut* SCI)))

Suchstrategie Cochrane Library

ID	Search
#1	MeSH descriptor: [Spinal Cord Injuries] explode all trees
#2	MeSH descriptor: [Spinal Cord Ischemia] explode all trees
#3	MeSH descriptor: [Spinal Cord Diseases] explode all trees
#4	MeSH descriptor: [Spinal Cord] explode all trees and with qualifier(s): [surgery - SU]
#5	(spinal cord NEAR/3 (contusion or laceration or trauma or lesion* or injur* or ischemi* or disease* or disorder*)):TI
#6	((central cord or central spinal) NEAR/2 syndrom*):TI
#7	acut* SCI:TI
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 in Cochrane Reviews

eSupplement 2

Characteristics of the systematic reviews included

Study ID	Population	Intervention	Comparison	Main results	Quality assessment (AMSTAR-II & GRADE)
Study design Included studies					
Fehlings 2024 Systematic review 21 studies (including RCTs and nRCTs)	n= N.R. Adults with traumatic spinal cord injury, adults with complete or incomplete traumatic SCI at any level	Early surgery (≤24 hours)	Late surgery (>24 hours)	ASIA Motor Score: 4 studies, IG n= 618; CG n= 1160 MD (95% CI) 4.50 (1.70 to 7.29) Improvement in AIS by ≥ 2 grades (6 months follow-up) 5 studies, IG n= 306; CG n= 254 RR (95% CI) 2.76 (1.60 to 4.98) Improvement in AIS by ≥ 2 grades (12 months follow-up) 4 studies, IG n= 569; CG n= 508 RR (95% CI) 1.95 (1.26 to 3.18)	Low quality review ⊕○○○ Certainty of evidence: very low
		Ultra early surgery (within 12 hours)	Latest time for thresholds for ultra-early (e.g., ≥8 hours but <24 hours)	AIS Improvement by ≥ 2 Grades: ≤6 month follow-up; threshold: 8 hours 1 study, n= 44 RR (95% CI) 4.55 (1.13 to 18.29) ≤6 month follow-up; threshold: 4 hours 1 study, n= 56 RR (95% CI) 0.50 (0.16 to 1.50)	

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				12 month follow-up; threshold: 12 hours 1 study, n= 49 RR (95% CI) 1.09 (0.39 to 3.04) ≤6 month follow-up; threshold: 5 hours 1 study, n= 57 RR (95% CI) 0.24 (0.07 to 0.85)	
Sultan 2020 Systematic review 12 studies (5 RCTs, 7 Observational studies)	n= 4892 Patients (13 years and above) with ASCI being treated with steroids within eight hours of injury	Methylprednisolone or dexamethasone alone	Placebo or any other, nonsteroid therapeutic agent	Neurological improvement (ASIA motor score improvement) 3 RCTs: n= N.R. MD: 1.38; 95% CI: -11.9, 14.7 2 OBS: n= N.R. MD: 9.62; 95% CI: -5.92, 25.1	Critically low quality review ⊕⊕○○ Certainty of evidence: low
Joaquim 2020 Systematic review 16 studies (16 RCTs)	n= 4231 Acute spinal cord injuries in humans	Minocycline intravenous, for 7 days	Placebo	ASIA Motor Score: 1 RCT: minocycline: n= 27; placebo: n= 25 <i>"Patients treated with minocycline who had thoracic injury did not have any benefits of treatment, but in the setting of cervical SCI, minocycline was associated with 14-point (95% CI: 0–28; P= 0.05) difference in motor score compared with placebo. Patients with cervical motor incomplete injury may have experienced a larger difference, but the results were not statistically significant. Although no statistical significance was observed, there was a trend of improvements in functional outcomes in patients receiving the study drug."</i>	Critically low quality review ⊕⊕○○ Certainty of evidence: low

Khalid 2020 Systematic review 13 studies (randomized and non-randomized clinical trials, animal studies)	n= N.R.	Mesenchymal stem cells	N.A.	Neurological improvement <i>"A number of different clinical studies have examined the use of MSCs in SCI patients. A 2006 study demonstrated neurological improvement in 6/20 patients while a separate study in 2007 demonstrated 30.4% of subacute (<2 weeks), acute (2–8 weeks), and chronic (<8 weeks) SCI patients showed at least one AIS grade improvement with no adverse effects. Two additional 2008 studies demonstrated neurological improvement following intraspinal injection of MSCs with no adverse effects noted."</i>	Critically low quality review ⊕○○○ Certainty of evidence: low
		Schwann Cells/Oligodendrocyte progenitor cells		Adverse events <i>"The clinical use of SCs in SCI treatment has only recently begun with several studies demonstrating no adverse effects following SC transplantation within the spinal cord. Additional clinical trials are currently underway with Anderson et al. which include two ongoing phase I open-label non-placebo controlled studies. The first recently reported no significant safety issues of implanted sural nerve SCs at one year in SCI patients with complete paraplegia."</i>	
		Hypothermia		Efficacy & Adverse events <i>"Smaller phase I studies have implied its potential efficacy/safety in SCI. A study of 14 complete cervical SCI patients were treated for 48 h with modest (33 C) intravascular hypothermia. Final follow-up demonstrated that six (42.8%) patients converted to incomplete SCI and complications were similar to those treated with normothermic therapies."</i>	

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Naik 2022 Systematic review 125 records (Case reports/series)	n = 147 patients	CSF drainage	N.A.	Efficacy n= 147 (total); n= 11 (with CSF drainage) Total: OR (95% CI)= 3.088 (0.378 to 25.253) At discharge: OR (95% CI)= 8.167 (0.988 to 66.815) Follow-up: OR (95% CI)= 1.482 (0.169 to 13.012)	Critically low quality review ⊕○○○
		Steroids	N.A.	Efficacy n= 147 (total); n= 52 (with steroids) Total: OR (95% CI)= 0.625 (0.290 to 1.345) At discharge: OR (95% CI)= 1.022 (0.472 to 2.213) Follow-up: OR (95% CI)= 0.338 (0.127 to 0.896)	Certainty of evidence: low
		Endovascular interventions	N.A.	Efficacy n= 147 (total); n= 7 (with endovascular interventions) Total: OR (95% CI)= 2.000 (0.233 to 17.192) At discharge: OR (95% CI)= 2.069 (0.384 to 11.144) Follow-up: OR (95% CI)= 2.317 (0.120 to 44.720)	
Kumar 2017 Systematic review 6 studies (2 RCTs, 4 case series)	n= 598 Patients with metastatic spinal cord compression	Steroids	Alternative Drug or Control	1-year survival with ambulatory capacity 1 RCT: n= 57 <i>"A Kaplan-Meier curve of the percentage of patients surviving till the 1-year mark with ambulatory capacity showed a statistically significant difference favoring steroid therapy (P= 0.046)."</i>	Critically low quality review ⊕○○○
		Steroids, high initial bolus dose protocols	Steroids, low initial bolus dose protocols	6-months survival with ambulatory capacity 1 RCT: n= 57 <i>"At the 6-month mark, 59% of patients receiving dexamethasone were ambulatory compared with just 33% in the control group (P= 0.05)."</i>	Certainty of evidence: low

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Evaniew 2020 Systematic review 21 studies (20 observational studies, 1 RCT)	n = 1200 Patients with an acute SCI (AIS A-E)	MAP support to optimize spinal cord perfusion	N.A.	Neurological recovery <i>"The effect of MAP support on neurological recovery is uncertain. The majority of evidence favoring MAP support comes from uncontrolled studies. The highest quality study and the largest study failed to identify consistent benefit."</i>	Critically low quality review ⊕○○○ Certainty of evidence: low
Arnold 2017 Systematic review 9 studies (8 RCTs, 1 prospective/non-randomized comparative study)	n = 1517 Adults with traumatic acute SCI (complete or incomplete, at any level)	Unfractionated heparin (UFH)	Placebo/No Prophylaxis	Effectiveness 1RCT, UFH n= 3/166; Placebo n= 4/131 RR (95% CI)= 0.59 (0.13 to 2.6); RD (95% CI)= 1.2 (-2.3 to 4.8); p=0.70 1RCT, UFH n= 8/16; Placebo n= 8/17 RR (95% CI)= 1.06 (0.53 to 2.15); RD (95% CI)= 2.9 (-31.2 to 4.7); p=0.60	Critically low quality review ⊕○○○ Certainty of evidence: low
Liu 2017 Systematic review 16 studies (13 observational studies, 3 RCT)	n = 1605 patients with acute SCI receiving heparin to prevent DVT	Heparin	Placebo or no treatment	Effectiveness 3 RCT, 1 case control study; Heparin n = 7/237, Placebo or no intervention n = 19/202 RR (95% CI) = 0.36 (0.15 to 0.87); p = 0.02	Critically low quality review ⊕○○○ Certainty of evidence: low
			Enoxaparin	Effectiveness 2 retrospective studies, 1 RCT, 1 prospective nRCT, Heparin n = 65/449; Enoxaparin n = 72/426 RR (95% CI) = 0.92 (0.47 to 1.77); p = 0.80	
Lin 2021	n = 1617 patients with SCI treated	LMWH	UFH	Effectiveness	Critically low quality review

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Systematic review 5 studies (5 cohort studies)	with LMWH or UFH			4 cohort studies, LMWH n = 49/178; UFH n = 56/260 RR (95% CI) = 1.33 (0.42 to 4.16); p = 0.63	⊕○○○ Certainty of evidence: low
Lippi 2023 Systematic review 14 studies (2 RCTs, 7 cohort studies, 4 case series, 1 case report)	n= 525 mechanically ventilated patients with spinal cord injury, age > 18 years	Rehabilitation interventions	Standard/low volume mechanical ventilation, usual care/standard weaning protocol, or positioning	Weaning duration 8 studies Studies included in this systematic review show mixed results: - Fenton 2016: IG: 14.5 days, CG: 14 days; p = 0.7349 - Gundogdu 2017: MV weaning duration: 37.0 ± 11.6 days - Korupolu 2021: IG: 19 (18, 22 IQR); CG: 19 (18, 21 IQR); p = 0.9 - McCaughey 2015: IG: 33 ± 14 days, CG: 44 ± 24 days; p = 0.41 - Peterson 1999: 37.6 days vs 58.7 days; p = 0.02 - Wong 2012: 27.6 ± 12.9 days - Atito-Nahr 2008: 56.1 ± 65.9 days - Duarte 2021: IG: 28 ± 15 days; CG: 50 ± 19 days MV duration 2 studies - Duarte 2021: IG: 33 ± 15 days vs. CG: 60 ± 22 days - Korupolu 2021: “no significant differences”, but no specific data Weaning success rate 4 studies - Kim 2007: “All patients succeeded in decannulation/extubation after the rehabilitation	Moderate quality review ⊕○○○ Certainty of evidence: low

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				<i>program. Fifteen patients totally weaned off from ventilators after NIV."</i> - Korupolu 2021: IG: 28 (82%); CG: 45 (90%); p = 0.31 - Gutierrez 2003: 4/4 (100%) - Zhang 2020: <i>"The patient was successfully weaned from mechanical ventilation."</i>	
Foran 2021 Systematic review 17 studies (16 cohort studies, 1 case series)	n= 2804 Patients with acute SCI receiving tracheostomy	Early tracheostomy	Late tracheostomy	Duration of MV 10 studies, IG: n = 410; CG: n = 445 MD (95% CI) -13.91 (-21.11 to -6.70)	Critically low quality review ⊕○○○ Certainty of evidence: low
Costanzo 2022 Systematic review 17 studies (Inclusion criteria: Case reports, cohort prospective and retrospective studies, and clinical trials)	n = 299 Patients with spinal cord injury	Diffusion tensor imaging (DTI)	N.A.	Correlation between FA values and AIS Scores <i>"In all the studies based on AIS score for neurological assessment, a correlation was found between FA values and AIS: patients with complete SCI presented with a statistically significant lower FA value at the injured site compared with patients with incomplete SCI."</i> Correlation between FA values and injured level <i>"In the 2 case report studies included in this review, based on spinal cord hemisection, quantitative DTI findings were estimated and compared between the involved and spared sites of the spinal cord: the mean FA value showed a statistically significant difference between the 2 levels."</i>	Critically low quality review ⊕○○○ Certainty of evidence: low

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Dietz 2022 Systematic review 13 studies (10 retrospective cohort studies, 3 prospective cohort studies)	n = 1983 Adult patients 18 years with spinal cord injury	Machine learning algorithms	Comparison of accuracies of machine learning models and clinical	Prediction of functional ability 6 studies <i>"Functional outcome predictive models used 4 and 11 variables that explained up to 62.3% of variance of spinal cord independence measure. Severity of the neurological deficit at admission was most predictive variable followed by injury severity score, age, neurological level, and surgical delay."</i> <i>"A similarity network of patients was created to predict neurological recovery after spinal cord injury on the basis of mean arterial pressure (MAP) during surgery. The network analysis showed that time outside of an optimum MAP range (hypotension or hypertension) during surgery was associated with lower likelihood of neurological recovery."</i> <i>"Reliability of machine learning tools to predict neurological outcomes after SCI was assessed. XGBoost had the highest accuracy (81.1%), followed by the logistic regression (80.6%) and the decision tree (78.8%) for neurological improvement."</i> <i>"Comparison of unsupervised MLA and LR with total admission neurological information against prior models showed no clinically relevant differences in functional prediction. The F1-score was shown to be more reliable in algorithm assessment than area under the operating curve."</i> <i>"Developed deep-learning based radiomics to quantify</i>	Critically low quality review ⊕○○○ Certainty of evidence: low
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				<i>radiographic characteristics using a convolutional neural network (CNN) to stratify prognosis of patient neurological outcomes after acute spinal cord injury (SCI)."</i> <i>"This study defined the predictive value of impairment measures as measured by the Graded Redefined Assessment of Strength, Sensibility and Prehension (GRASSP) in traumatic cervical spinal cord injury (SCI). The study found that upper extremity motor impairment measures were highly predictive of task performance."</i>	
Irrgang 2024 Systematic review 12 studies (3 Systematic Reviews, 2 RCTs, 2 observational studies, 5 CPGs)	n = N.A. Patients with an acute SCI, regardless the patient characteristics	Electrical stimulation/ neuroelectric devices	N.A.	Muscle function <i>1 systematic review including 39 studies, n = N.A.</i> <i>"Greater improvements in outcomes of walking function when using robotic orthosis during locomotor training compared to overground walking."</i>	Low quality review ⊕○○○ Certainty of evidence: low
		FES-cycling	Passive cycling	Muscle atrophy <i>1 RCT, IG n = 12, CG n = 12</i> <i>"Both interventions may be able to attenuate muscle atrophy compared with published data without intervention."</i> Neurological function (ISNCSCI) <i>1 RCT, IG n = 12, CG n = 12</i> <i>"No significant benefit of one intervention over another (p value > 0.05)."</i>	

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		Orthotic TES + Conventional training	Conventional training	Hand function <i>1 RCT, IG n = 15, CG n = 14</i> <i>"No significant between-group differences for TPM of the fingers, oedema and upper-extremity motor scores at 1 week, 1 month and 3 months after injury. TMP of the fingers tended to be lower in the control group. But TES can be started in the acute phase."</i>	
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AIS = American Spinal Injury Association Impairment Scale; AMSTAR = A Measurement Tool to Assess Systematic Reviews; ASIA = American Spinal Injury Association; CG = Control group; CI = Confidence Interval; CPG = Clinical Practice Guidelines; CSF = Cerebrospinal fluid; FA = Fractional Anisotropy; FES = Functional Electrical Stimulation; IG = Intervention group; IQR = Interquartile Range; LMWH = Low Molecular Weight Heparin; MAP = Mean Arterial Pressure; MD = Mean Difference; MV = mechanical ventilation; N. R. = Not Reported; n = Sample size; nRCT = non-Randomized Controlled Trial; OBS = Observational Study; RCT = Randomized Controlled Trial; RD = Risk Difference; RR = Relative Risk; SCI = Spinal Cord Injury; TES = Transcutaneous Electrical Stimulation; TMP = Total Motion of the Fingers; TPM = Total Passive Motion; UFH = Unfractionated Heparin.