ARTICLE





Recovery after traumatic thoracic- and lumbar spinal cord injury: the neurological level of injury matters

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Abstract

Study design Multicenter prospective cohort.

Objective To discern neurological- and functional recovery in patients with a traumatic thoracic spinal cord injury (TSCI), conus medullaris syndrome (CMS), and cauda equina syndrome (CES).

Setting Specialized spinal cord injury centers in Europe.

Method Lower extremity motor score (LEMS) and spinal cord independent measure (SCIM) scores from patients with traumatic TSCI, CMS, and CES were extracted from the EMSCI database. Scores from admittance and during rehabilitation at 1, 3, 6, and 12 months were compared. Linear mixed models were used to statistically analyse differences in outcome, which were corrected for the ASIA Impairment Scale (AIS) in the acute phase.

Results Data from 1573 individuals were analysed. Except for the LEMS in patients with a CES AIS A, LEMS, and SCIM significantly improved over time for patients with a TSCI, CMS, and CES. Irrespectively of the AIS score, recovery in 12 months after trauma as measured by the LEMS showed a statistically significant difference between patients with a TSCI, CMS, and CES. Analysis of SCIM score showed no difference between patients with TSCI, CMS, or CES.

Conclusion Difference in recovery between patients with a traumatic paraplegia is based on neurological (motor) recovery. Regardless the ceiling effect in CES patients, patients with a mixed upper and lower motor neuron syndrome (CMS) showed a better recovery compared with patients with a upper motor neuron syndrome (TSCI). These findings enable stratifications of patients with paraplegia according to the level and severity of SCI.

Members of the EMSCI participants and investigators are listed below Author contributions.

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Introduction

The thoracic spinal cord ranges from vertebrae Th1–Th11 and neurological impairment as a result of a trauma to vertebrae Th1–Th11 is considered as a thoracic spinal cord Injury (TSCI), where any motor weakness of lower limbs

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relates to an axonal damage of the upper motor neuron [1, 2]. The conus medullaris (CM) represents the most caudal part of the spinal cord, which includes axons of both upper- and lower motor neurons [1, 3, 4]. Conus medullaris syndrome (CMS) can occur as a result of injury to vertebrae Th12 to L2, and induces a mixture of central and peripheral axonal damage [2]. The nerve roots of the cauda equina (CE) contain only axons from lower motor neurons [1, 3, 4] and occurs as a result of injury to the lumbar spine involving damages to nerve roots L3 to S5 [2, 5, 6]. The clinical distinction between damages to the thoracic spinal cord, CM and CE is generally performed by a combination of radiological and neurological means. Patients with thoracolumbar spinal cord injury (SCI) may show a mixed upper and lower motor neuron syndrome with unilateral or bilateral lower limb weakness; perineum or "saddle" anesthesia; and bowel and/or bladder dysfunction [3, 4, 7]. In patients with incomplete lesions these symptoms may be subtle [7–9] and lower limb weakness may be present asymmetrically [6, 10]. Beside comprehensive symptoms, distinction between spinal cord syndromes based on neurological symptoms might be challenged in the acute situation by the inability of patients to cooperate with the exams [11] or by spinal shock [3]. Also patients often receive an indwelling catheter per acute care protocols before any disturbances of incontinence/urinary retention are established [7].

Lower motor neurons may have a better regenerative capacity compared with upper motor neurons [12–14], and therefore, patients with a CMS or cauda equina syndrome (CES) may show a higher neurological and functional recovery compared with patients with TSCI. However, this assumption was not clinically supported yet. To proactively manage expectations of patients and their family as well as for improving clinical trial protocols in patients suffering from acute paraplegia, the aim of this work is to quantify differences in neurological and functional recovery as related to TSCI, CMS, or CES.

Materials and methods

Data are retrieved from the European Multicenter Study of Human Spinal Cord Injury (EMSCI). The EMSCI is a collaboration of 19 European specialized spinal cord centers that collect data from patients with an acute traumatic SCI in a predefined time schedule: 2 weeks (between 1 and 15 days) and then 1, 3, 6, and 12 months after trauma. Inclusion in the EMSCI study is based on an "opt in" method. For this paper data between 2001 and 2015 is used. Yearly, eighty to one hundred new SCI patients are treated in each center. Approximately 20 percent of these patients have a traumatic SCI and 80–95 percent of these patients are include in the EMSCI database, the rest do not fulfill the inclusion criteria (e.g., latest time point of first EMSCI assessment). Patients are admitted directly after trauma to one of these centers or they are secondary referred after treatment in a trauma center elsewhere. The EMSCI protocol is approved by the respective local ethics committees and is registered at clinicaltrial.gov (NCT01571531).

Study population

Patients with a cervical SCI, SCI due to other causes (e.g., nontraumatic, disk herniation, tumor, or ischemia), cognitive disorders, preexisting neurological deficit, or traumatic brain injury are excluded. The severity of the SCI in the very acute phase is defined by the ASIA (American Spinal Injury Association) Impairment Score (AIS) of the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) [15].

Neurological assessment

Neurological assessment is performed according to ISNCSCI [16] and classification is performed by the EMSCI-ISNCSCI calculator (http://ais.emsci.org) [17]. All examiners are AIS certified. Allocation of patients to the TSCI, CMS, or CES group is based on the ISNCSCI neurological level of injury (NLI) assessed in first 2 weeks after trauma [15]. This has resulted in the successive allocation: TSCI: NLI between T1 and T10; CMS: NLI between T11 and L1; CES: NLI between L2 and S5. Lower Extremity Motor Scores (LEMS) from all time points (from 1–15 days assessment to 12 months after trauma) are used to evaluate motor recovery. The maximum LEMS is 50 points.

Functional outcomes

Functional recovery is measured by the Spinal Cord Independence Measure (SCIM) [18]. The SCIM is a validated scale that measures independence in all aspects of primary daily activities relevant for patients with SCI [19]. Subcategories self-care, respiration and sphincter management, mobility in room and toilet, mobility indoors and outdoors are analyzed. The maximal total score of the SCIM is 100 points.

Statistical analysis

Continuous data between two groups are analysed using Student *t* tests, and ANOVA in cases with more than two groups. Categorical data are analysed by Chi-squared tests. For statistical evaluation of outcome in time (LEMS and SCIM, respectively), linear mixed models with fixed factor effects for sex, AIS in the very acute phase, neurological

	Thoracic s _l	Thoracic spinal cord injury	ıjury				Conus med	Conus medullaris syndrome	ome				Cauda equi	Cauda equina syndrome	e			
	Total N	Count	Mean	SD	Range	N (%)	Total N	Count	Mean	SD	Range	N (%)	Total N	Count	Mean	SD	Range	$N\left(\% ight)$
Patients (n)	852					54%	415					26%	306					20%
sex Male		698				82%		322				78%		228				75%
Female		154				18%		93				22%		78				25%
Age																		
			42	18	81				41	17	72				41	17	75	
AIS A		550				65%		148				36%		31				10%
AIS B		42				5%		53				13%		42				14%
AIS C		LL				6%		09				15%		38				12%
AIS D		172				20%		151				36%		176				58%
					95% CI						95% CI						95% CI	
LEMS																		
			10	17	8-11				21	19	18-24				35	12	34–38	
SCIM																		
			68	16	69-99				78	15	76-80				88	12	86-90	

level of injury, and timing of examination (1–15 days, 1-, 3-, 6-, and 12-months after trauma) with interactions between AIS and timing of examination, between AIS and NLI, and between NLI and timing of examination and covariate age are used. To deal with the correlation in the recovery as measured by the LEMS and SCIM, a random patient effect is included in the mixed model. The interactions are included to model different time courses of LEMS and SCIM for different AIS grades and locations (NLI) and different effects for AIS depending on the location. Missing data are not imputed.

SPSS (Version 22.0, SPSS Chicago, IL.) and SAS^{*} 9.4 software are used. Data are represent as mean \pm standard deviation or -error. 95% confidence intervals (95% CI) or range are used. A *p* value of <0.05 is considered as significant.

Results

Patient cohorts

The EMSCI database comprised of data from 4824 patients with SCI due to various causes. From this data, 1573 (33%) patients with traumatic TSCI, CMS, or CES were included in this study. Eleven patients did not have a AIS score registered in the 1–15 day assessment and therefore these patients were omit from this study. Six percent of the included patients missed one or more LEMS and SCIM scores in follow-up so available scores were imputed. One thousand, two hundred forty-eight (80%) patients were male. The mean age was 41 years (range 13–94, SD 17). The TSCI group consisted of a higher proportion (65%) of AIS A patients compared to the CMS group (36%) and the CES Group (10%; p < 0.001). Conversely, AIS D patients were more often found in the CES Group (58%; p < 0.001). Patients' characteristics are presented in Table 1.

Time course of recovery

Ninety percent neurological recovery as measured by LEMS and functional improvements assessed with the SCIM was observed within the first 3 months after trauma in all patients with traumatic TSCI, CMS, and CES. A plateau developed between 6 and 12 months. After 6 months, change in recovery was minimal (Figs. 1, 2). Age, the AIS grade in the 1–15 days assessment, NLI, timing of examination (1–15 days, 1-, 3-, 6-, and 12-months after trauma) as well as the interactions had a statistically significant effect on the extent of recovery as measured by the LEMS and SCIM (delta changes) (p < 0.002). Effect of sex was only observed for the SCIM (p < 0.001). Subanalysis for age showed a statistically significant better

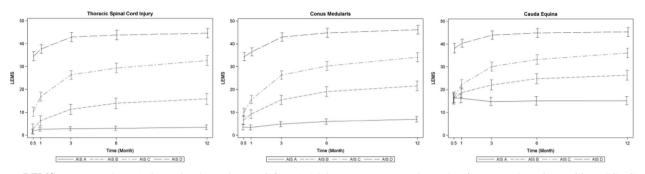


Fig. 1 LEMS recovery. Figure 1 shows the change in LEMS from 1–15 days assessment to 12 months after trauma in patients with a TSCI, CMS or CES per AIS grade.

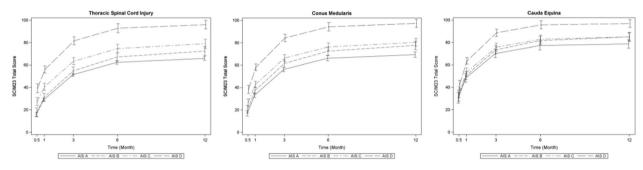


Fig. 2 SCIM recovery. Figure 2 shows the change in the SCIM scores from 1–15 days assessment to 12 months after trauma in patients with a TSCI, CMS and CES per AIS grade.

Table 2 Difference in LEMSfrom baseline to 12 months aftertrauma.

ASIA score	Thoracic spinal cord injury	Conus medullaris syndrome	Cauda equina syndrome
ASIA A	1.8; 0.4 $(p < 0.0001)$	3.5; 0.6 (<i>p</i> < 0.0001)	-1.2; 0.9 (p = 0.19)
ASIA B	13.2; 0.8 $(p < 0.0001)$	15.0; 0.8 $(p < 0.0001)$	10.3; 1.0 $(p < 0.0001)$
ASIA C	22.4; 0.8 $(p < 0.0001)$	24.1; 0.8 $(p < 0.0001)$	19.4; 1.0 $(p < 0.0001)$
ASIA D	10.1; 0.9 $(p < 0.0001)$	11.8; 0.8 $(p < 0.0001)$	7.1; 0.9 $(p < 0.0001)$

Table 2 shows the mean difference as measured by the LEMS, \pm SE and *P* value (95% CI) in patients with traumatic TSCI, CMS, and CES from baseline to 12 months after trauma.

functional improvement as measured by the SCIM for patients aged below 18 years (N = 34) compared with patients aged 18 years or older (p < 0.03). No difference was not found for the LEMS.

Analysis of recovery within the TSCI, CMS, and CES group

Patients with a CES and initially complete injury (AIS A) had a significantly higher LEMS in the 1–15 days assessment (mean 16.4, SE 1.1) compared with patients with a CMS AIS A (mean 3.5, SE 0.6) or a TSCI AIS A (mean 1.7, SE 0.5). However, patients with a CES AIS A showed no LEMS recovery from the 1–15 days assessment to 12 months after trauma (delta -1.2 SE 0.9), while patients with a TSCI AIS A and a CMS AIS A revealed some LEMS recovery (delta 1.8 SE 0.4 and delta 3.5 SE 0.8). All patients with paraplegia (complete and incomplete) from a TSCI,

CMS, and CES, except for CES AIS A patients, showed a significant increase in LEMS over time from the 1–15 days assessment to 12 months after trauma irrespectively of the initial AIS grade (Table 2).

Albeit smaller group differences across the level of injury and injury severity (AIS) of SCIM compared with LEMS, all patients showed a statistically significant functional recovery over time (Table 3).

Analysis of recovery between the TSCI, CMS, and CES group

Statistically significant differences were found in recovery from 1–15 days assessment to 12 months after trauma between patients with a TSCI, CMS, and CES as measured by the LEMS, whereby patients with a CMS showed the best recovery, followed by patients with a TSCI and CES. Irrespective of the AIS score, difference in LEMS recovery **Table 3** Difference in SCIMfrom baseline to 12 months aftertrauma.

•	ASIA	Thoracic spinal cord injury	Conus medullaris	Cauda equina
	ASIA A	50.2; 1.0 (<i>p</i> < 0.0001)	52.4; 1.5 $(p < 0.0001)$	48.0; 2.2 (<i>p</i> < 0.0001)
	ASIA B	54.8; 2.0 (<i>p</i> < 0.0001)	57.0; 2.0 $(p < 0.0001)$	52.6; 2.4 ($p < 0.0001$)
	ASIA C	51.6; 2.1 $(p < 0.0001)$	53.8; 2.0 $(p < 0.0001)$	49.4; 2.4 $(p < 0.0001)$
	ASIA D	56.8; 2.1 $(p < 0.0001)$	59.0; 2.1 $(p < 0.0001)$	54.6; 2.2 $(p < 0.0001)$

Table 3 shows the mean difference as measured by the SCIM, \pm SE and *P* value (95% CI) in patients with traumatic TSCI, CMS and CES from baseline to 12 months after trauma.

 Table 4 Difference in SCIM sub scores from baseline to 12 months after trauma.

	Self-care	Respiratory and sphincter management	Mobility indoor	Mobility outdoor
Thoracic spinal cord injury	11.5; 0.2 (11.1–12.0)	21.7; 0.5 (20.8–22.6)	8.3; 0.2 (8.0-8.7)	9.5; 0.3 (8.9–10.1)
Conus medullaris syndrome	10.1; 0.3 (9.5–10.7)	22.1; 0.6 (20.9–23.3)	8.3; 0.2 (7.8-8.8)	13.8; 0.4 (13.0–14.7)
Cauda equina syndrome	7.8; 0.5 (7.0–8.7)	19.5; 0.9 (17.7–21.3)	5.6; 0.3 (4.9-6.3)	19.1; 0.6 (17.8–20.3)

Table 4 shows the mean recovery measured by SCIM (sub scores) between 1 and 15 days assessment to 12 months after trauma, ±SE, and 95% CI in patients with traumatic TSCI, CMS, and CES.

from 1–15 days assessment to 12 months after trauma between TSCI and CMS patients was 1.74 (range 0.48–3.01, p < 0.01), between TSCI and CES 2.94 (range 1.17–4.71, p < 0.00) and between CMS and CES 4.68 (range 2.88–6.48, p < 0.00).

Whereas the differences between the TSCI, CMS, and CES group from baseline to 12 months after trauma were significant for the LEMS, there were no statistically significant differences in functional recovery between these groups. Irrespective the AIS grade, differences in SCIM scores between TSCI and CMS was 2.17 (range 0.96–5.30, p = 0.17), between TSCI and CMS was 2.20 (range 2.12–6.53 p = 0.32) and difference between CMS and CES was 4.38 (range 0.01–8.76, p = 0.05).

SCIM sub-score analysis showed a statistically significant difference in recovery from 1–15 days assessment to 12 months after trauma between TSCI, CMS, and CES for self-care and mobility outdoor. Statistically significant difference for mobility indoor was found between patients with a TSCI and CES and between patients with a CMS and CES. Recovery of respiratory and sphincter management was not different between the groups. Also these outcomes were irrespective of the AIS score in the 1–15 days assessment. See Table 4.

For outcomes at 12 months after trauma without reckoning the recovery from baseline, see Supplementary Appendix 1.

Discussion

In this study, we present the recovery of lower extremity motor function and improvements in functional independence over 12 months in a representative sample of patients with acute traumatic SCI with distinct levels of paraplegia. Except for patients with a CES AIS A, all patients with a traumatic TSCI, CMS, and CES lesion reveal an increase in LEMS and SCIM scores from the 1–15 days assessment to 12 months after trauma. Irrespective the AIS score, statistically significant differences in recovery from the 1–15 day assessment to 12 months after trauma were found between patients with a TSCI, CMS, and CES as measured by the LEMS, whereas no statistically significant differences were found in functional recovery as measured by the SCIM. These findings will be of value to inform patients and rehabilitation teams to manage expectations of motor and functional recovery, as well as clinical trials for choosing appropriate primary and secondary outcome measures and optimized stratification of patients with acute paraplegia.

The CE confines an assemblage of peripheral sensory and motor nerve fibers (i.e., axons of lower motor neurons) [11]. It is generally assumed that peripheral nerves have a greater capability for recovery than central nerve fibers within the spinal cord (i.e., axons of upper motor neurons) due to more effective re-myelination [12, 20]. This implies that patients with a lesion of the CE might have a greater chance for motor recovery compared with patients with a thoracic SCI [11]. In contrast to the literature, we found that patients with a CMS showed the largest recovery as measured by the LEMS, followed by patients with a TSCI and finally patients with a CES. These findings can be explained by the ceiling effect of the LEMS in CES patients. Patients with a CES showed a higher LEMS and SCIM score at the 1-15 days assessment, compared with patients with a CMS and TSCI, whereby the CES group starts with a score close to the maximum score. Regardless the ceiling effect in CES patients, this study showed that patients with a mixed upper and lower motor neuron syndrome (CMS) showed a better recovery compared with patients with a upper motor neuron syndrome (TSCI).

Kingwell et al. summarized the factors affecting the neurological outcome in CM and CE injuries and concluded that patients with incomplete lesions are more likely to improve than patients with complete lesions [4]. Looking at our data in Table 2 and Fig. 1, indeed patients with an AIS A showed statistically significant lower LEMS recovery from 1–15 days assessment to 12 months after trauma compared with patients with incomplete lesion. Recovery of patients with AIS A as measured by the SCIM however, did not show differences compared with patients with AIS B-C, or D.

A higher percentage of CES patients were initially classified as AIS D (57%) compared with patients with CMS (36%) and TSCI (20%). It is important to emphasize that the overall increased motor recovery in CES and CMS does not relate to the higher percentage of motor incomplete SCI in these groups. The higher rate of AIS D patients in CES could be explained by anatomical dimensions and structures. The spinal canal is wider in the lumbar region and the cross sectional area of the neuronal structures at the level of the CE is relatively small compared to the level at the conus or at the spinal cord itself [1, 21]. Furthermore, the neural tissue at the CE is more flexible. Therefore, an injury of the spine with the same impact is likely to cause less neurological damage at the cauda than at the level of the spinal cord.

Strengths and flaws should be mentioned. The EMSCI group is a large collaboration of European spinal cord centers, specialized in the SCI care in both the acute and rehabilitation phases. Although selection could have occurred since only highly motivated centers participated in this study, we are convinced that our results can also be applied to other SCI centers.

The EMSCI data does not include information from the very acute care setting (e.g., day 1), but instead only data some days after injury (mean 7.9 ± 16 days). In some extent, neurological examination a few days after trauma might be better than the initial neurological situation directly after trauma, however, neurological examination applied in the very acute setting (e.g., within 72 h after injury) must be interpreted with some careful considerations. Accurate neurological examination in the acute setting might be challenging due to suboptimal patient cooperation. Data were obtained by trained experts, in specialized SCI centers, which increased the reliability and validity of the data. This is considered as a strength.

In 1982, the American Spinal Injury Association developed the International Standards for Neurological Classification of SCI(ISNCSCI). In the earlier ISNCSCI revisions, descriptions of less well-defined clinical syndromes, such as the CMS and CES, were included. Due to lack of a clear definition, these syndromes were eliminated in subsequent revisions of the ISNCSCI [22]. Moreover, patients with a CMS and CES have a variation of nonspecific symptoms such as various degrees of lower limb weakness, sensibility loss, and bowel/bladder dysfunction, which makes it difficult to classify these symptoms under the heading of the syndromes [23, 24]. For the allocation of patients in the TSCI, CMS, or CES groups, we used the classification based on ISNCSCI's NLI [2]. We did not determine the level by magnetic resonance imaging as proposed by Kingwell et al. because these data were not available in our database [25], which could be considered a limitation of the study. However, also previous studies used the NLI of L2 as cutoff segment for distinguishing between CMS and CES [2].

Finally, the content of acute phase treatment and rehabilitation was not included in the analysis. This also counts for comorbidity and medical history. The major advantage of our study is the size of our sample minimizing the chance on selection and, therefore, contributing to generalizability of our findings.

Conclusion

In patients with traumatic paraplegia, motor, and functional recovery is related to the NLI. Except for CES AIS A patients, all patients with paraplegia show a significant neurological and functional recovery within 12 months after trauma. Irrespective of the AIS, statistically significant differences between patients with a traumatic TSCI, CMS, and CES are based on neurological recovery as measured by the LEMS. Despite the fact patients with a mixed cord/ cauda syndrome have a better neurological recovery compared to patients with a TSCI, no statistically significant difference was found in the functional recovery as measured by the SCIM. SCIM sub-score analysis for self-care and mobility outdoor are most responsive to distinguish functional recovery. These findings gained in a representative cohort of patients in the subacute stage of SCI allow for a better appreciation of recovery in people with paraplegia and the development of clinical trial protocols.

Data availability

The data that supports the findings of this study are available from EMSCI but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publically available. Data are however available from the authors upon reasonable request and with permission of EMSCI.

Author contributions EB was responsible for designing the study, screening literature, extracting and analyzing data, interpreting results, creating tables, and writing the paper. HvdM was responsible for the

data collection (Radboud University Medical Center), designing the study, and writing the paper. AC is Principal Investigator for the EMSCI study (data collection) and provided feedback on the paper. DM was responsible for the data collection (BG Unfallklinik Murnau) and provided feedback on the paper. RA was responsible for the data collection (Krankenhaus Hohe Warte Bayreuth) and provided feedback on the paper. NW was responsible for the data collection (Spinal Cord Injury Center, Heidelberg University Hospital) and provided feedback on the paper. RR was responsible for the data collection (Spinal Cord Injury Center, Heidelberg University Hospital) and provided feedback on the paper. JK was responsible for the data collection (Motol Hospital, Prague) and provided feedback on the paper. AdH was responsible for the statistical part of this study, designing the figures and writing the statistical part in the methodology section of the paper. JK is expert in analyzing EMSCI data, gave statistical advice, and gave feedback on the paper. AH was responsible for the data collection (Radboud University Medical Center), designing the study, and provided feedback on the paper. RB was responsible for the study design, contributed to writing the paper, analyzing data, and provided feedback on the paper.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

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