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TITLE: The Impact of Surgical Timing in Acute Traumatic Spinal Cord Injury

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14. ABSTRACT The optimal surgical timing following a traumatic spinal cord injury (SCI) remains controversial although some studies suggest improved neurological recovery with early surgery. Consequently, there is wide variability in clinical practice and institutional guidelines regarding optimal surgical timing after a SCI. Our study will help guide clinicians in their practice and health administrators in the distribution of resources, by determining the optimal surgical delay after a traumatic spinal cord injury. The global objective of our study is to determine the impact of surgical delay on costs, length of stay, complications, and outcomes (neurological recovery, functional status and quality of life) in patients with a traumatic SCI. Results obtained in the last reporting period show that early surgery improves neurological recovery in patients with a complete cervical lesion. Moreover, modifiable, extrinsic factors contribute to surgical delay while the patients health status does not affect this delay.					
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1. INTRODUCTION

The optimal surgical timing following a traumatic spinal cord injury (SCI) remains controversial although some studies suggest improved neurological recovery with early surgery. Consequently, there is a wide variability in clinical practice and institutional guidelines regarding optimal surgical timing after a SCI. Our study will help guide clinicians in their practice and health administrators in the distribution of resources, by determining the optimal surgical delay after a traumatic spinal cord injury. The global objective of our prospective research is to determine the impact of surgical delay on costs, length of stay, complications, and outcomes (neurological recovery, functional status and quality of life) in a cohort of patients with a traumatic SCI. By defining the optimal surgical timing after a SCI, this study has the potential to improve the neurological and functional outcome of patients, while decreasing the costs, length of stay and complications for the acute care after a SCI. This study might ultimately modify existing guidelines for pre-hospital, en route care, and early hospital management of SCI patients in order to comply with the optimal surgical timing, and will also determine the optimal surgical timing that will minimize the rate of complications such as pressure ulcers and pneumonia.

2. KEYWORDS

Spinal cord; trauma; complications; costs; length of stay; recovery; quality of life; timing; surgery; rehabilitation; function; fracture; acute hospitalization; ASIA grade

3. ACCOMPLISHMENTS

What were the major goals of the project?

Listed below are the major goals of this project, according to the approved statement of work.

a) Recruitment of patients-completed

Recruitment of patients was completed in September 2014.

b) Follow-up of patients-completed

Follow-up of patients is complete. Sixty-nine patients have completed their long-term follow-up (defined as follow-up completed at least two-years post-trauma) and have thus terminated their participation to this study.

c) Data collection

Socio-demographic, clinical, surgical and radiological data have been collected for all 138 patients enrolled in this study. All patients enrolled had their trauma prior to September 2014; thus, all the follow-up is completed.

d) Data analysis

Data analysis is completed and results obtained so far will be detailed in the next section.

e) Publications and conferences

We have presented 3 abstracts at the 4th ASIA and ISCoS Joint Scientific Meeting held in Montreal (Canada) in May 2015, 5 abstracts at the ASIA 2016 Annual Scientific Meeting in April 2016, 2 abstracts at the ASIA 2017 Annual Scientific Meeting in April 2017 and 3 abstracts at the ASIA 2018 Annual Scientific Meeting in May 2018. Twelve manuscripts pertaining to functional recovery, neurological outcome, resource use, occurrence of complications and respiratory outcomes as well as barriers to early surgery are published or in press.

Paper 1: Richard-Denis A, Feldman DE, Thompson C, Mac-Thiong JM. Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization. J Spinal Cord Med 2017 Feb 15: 1-9 (*epub ahead of print; see Appendix 1*)

Objectives: To determine factors associated with functional status six months following a traumatic cervical and thoracic spinal cord injury (SCI), with a particular interest in factors related to the acute care hospitalization stay.

Design: This is a prospective cohort study. Sixteen potential predictive variables were studied. Univariate regression analyses were first performed to determine the strength of association of each variable independently with the total Spinal Cord Independence Measure (SCIM) score. Significant ones were then included in a General linear model in order to determine the most relevant predictive factors among them. Analyses were carried out separately for tetraplegia and paraplegia.

Setting: A single specialized Level I trauma center.

Participants: 159 patients hospitalized for an acute traumatic SCI between January 2010 and February 2015.

Interventions: Not applicable.

Main outcome measure: The SCIM (version 3) functional score.

Results: Motor-complete SCI (AIS-A, B) was the main predictive factor associated with decreased total SCIM score in tetraplegia and paraplegia. Longer acute care length of stay and the occurrence of acute medical complications (either pneumonia, urinary tract infections or pressure ulcers) were predictors of decreased functional outcome following tetraplegia (Table 1), while increased body mass index and higher trauma severity were predictive of decreased functional outcome following paraplegia (Table 2).

Conclusions: This study supports previous work while adding information regarding the importance of optimizing acute care hospitalization as it may influence chronic functional status following traumatic SCI.

Table 1: Factors associated with the total SCIM score six-months post-injury for patients with acute traumatic tetraplegia (N=43)

<i>Predictive variable</i>	Total SCIM score		
	β coefficient	95%CI	P-value
ASIA grade			
<i>AIS A-B</i>	-27,3	(-42,9;-11,8)	$<10^{-3}$ *
<i>AIS C-D</i>	0 ^d		
Occurrence of complications	-22,7	(-37,6;-7,8)	$<10^{-3}$ *
Acute care LOS	-0,3	(-0,6; -0,1)	0,02*
Presence of early spasticity	-2,5	(-19,3; 14,3)	0,77
$R^2 = 0.671$			

Table 2: Factors associated with the total SCIM score six-months post-injury for patients with acute traumatic paraplegia (N=45)

<i>Predictive variable</i>	Total SCIM score		
	β coefficient	95%CI	P-value
ASIA grade			
<i>AIS A-B</i>	-19,1	(-31,3;-6,9)	$<10^{-3}$ *
<i>AIS C-D</i>	0 ^d		
BMI	-1,3	(-2,3;-0,4)	$<10^{-3}$ *
ISS	-0,8	(-1,4; -0,2)	0,01*
Presence of early spasticity	-6,3	(-13,9;1,4)	0,11
$R^2 = 0.548$			

Paper 2: Richard-Denis A, Feldman DE, Thompson C, Bourassa-Moreau E, Mac-Thiong JM. Costs and length of stay for the acute care of patients with motor-complete spinal cord injury following cervical trauma: the impact of early transfer to specialized acute SCI center. Am J Phys Med Rehabil 2017, 96(7): 449-456. (see Appendix 2)

Acute SCI-centers aim to prevent the occurrence of complications and optimize recovery following a SCI. When receiving individuals with SCI, non-specialized (NS) hospital centers may preconized prompt surgical management in their center before transferring the patient to a SCI-center for post-surgical management. This study evaluates the impact of rapid admission and complete peri-operative management in a SCI-center on costs and acute care hospital length of stay (LOS) following a motor-complete cervical SCI. A retrospective comparative cohort study involving 116 individuals was conducted. Group 1 (N=87) were managed in a SCI-center promptly after the trauma, whereas Group 2 (N=29) were pre-operatively and surgically managed in a NS center before being transferred to the SCI-center (Table 3). A general linear model was used to assess the relationship between costs, LOS and type acute care facility (Group 1 or 2), while accounting for several covariables including the occurrence of complications. While the surgical delay was similar between the two groups, the total LOS was longer for Group 2 (104.7±54.2 days) as compared to Group 1 (57.6±53.1 days; $p<10^{-3}$). The average costs (\$CAN) for Group 2 were higher (19 520\$±10 604\$ vs. 13 647\$±8 286\$; $p=0.004$). The LOS and costs were increased with the occurrence of multiple and respiratory complications, pre-operative and surgical managed in a NS center, urinary track infection and older age (Tables 4, 5). Early referral to a SCI-center for complete management by a specialized multidisciplinary team following a motor-complete cervical SCI could lower the financial burden for the healthcare system and should be preconized.

Table 3: Demographic and clinical characteristics of patients early and lately transferred to an SCI center following a motor-complete cervical SCI

		Early Transfer (SCI Center [Group 1])	Late Transfer (NS Center [Group 2])	<i>P</i>
n	—	87	29	—
Age	Median (interquartile range)	46.0 (28.6–62.0)	48.0 (23.5–64.5)	0.97
Sex	% Male	78.2	82.8	0.60
ISS	% ≥29	39.1	58.6	0.053
ASIA grade	% A	65.5	82.8	0.08
	% B	34.5	17.2	
Neurological level	% C1–C4	51.7	62.1	0.33
Traumatic brain injury	% TBI	51.3	27.6	0.02 ^a
In-hospital death	% Deceased	9.2	6.9	0.70
Surgical delay	% >24 h after injury	54.0	51.7	0.83
Respiratory complications	%	54.0	51.7	0.83
Pneumonia	%	47.1	41.4	0.67
Pressure ulcer	%	36.8	34.5	1.00
UTI	%	20.7	31.0	0.31
At least 1 complication (≥1)	%	71.3	72.1	1.00
Multiple complications (≥2)	%	44.8	37.9	0.67

Table 4 : Factors associated with total hospitalization length of stay at the SCI center in individuals sustaining a severe cervical TSCI: results of the multiple linear regression analysis (N=116)

Factors Associated With Hospital LOS in the SCI Center		
	β Coefficient (95% CI)	<i>P</i>
Timing of SCI center admission (group 2 [NS center] vs. group 1 [SCI])	50.5 (30.8–70.2)	<0.001 ^a
Occurrence of multiple complications	50.2 (33.0–67.4)	<0.001 ^a
Age	0.6 (0.1–1.0)	0.014 ^a
$R^2 = 0.358$ (percentage of the response variable variation that is explained by our linear model).		
CI indicates confidence interval.		

Table 5: Factors associated with costs related to hospitalization at the SCI center in individuals sustaining a severe cervical TSCI (N=116)

Factors Associated With Higher Hospitalization Costs (CA \$)		
	β Coefficient (95% CI)	<i>P</i>
Timing of SCI center admission (group 2 [NS center] vs. group 1 [SCI])	7070.4 (1589.8–12,551.0)	0.013 ^a
Respiratory complications	5796.0 (125.8–11,466.2)	0.045 ^a
$R^2 = 0.186$.		

Paper 3: Richard-Denis A, Feldman DE, Thompson C, Mac-Thiong JM. The impact of acute management on the occurrence of medical complications during the specialized spinal cord injury acute hospitalization following motor-complete cervical spinal cord injury. J Spinal Cord Med 2017, Jul 19: 1-18 (epub ahead of print; see Appendix 3)

CONTEXT/OBJECTIVE:

Determine the impact of early admission and complete perioperative management in a specialized spinal cord injury (SCI) trauma center (SCI-center) on the occurrence of medical complications following tetraplegia.

DESIGN:

A retrospective comparative cohort study of prospectively collected data involving 116 individuals was conducted. Group 1 (N=87) was early managed in a SCI-center promptly after the trauma, whereas Group 2 (N=29) was surgically and preoperatively managed in a non-specialized (NS) center before being transferred to the SCI-center. Bivariate comparisons and multivariate logistic regression analyses were used to assess the relationship between the type of acute care facility and the occurrence of medical complications. Length of stay (LOS) in acute care was also compared.

SETTING:

Single Level-1 trauma center.

PARTICIPANTS:

Individuals with acute traumatic motor-complete cervical SCI.

INTERVENTIONS:

Not applicable Outcome measures: The occurrence of complications during the SCI-center stay.

RESULTS:

There was a similar rate of complications between the two groups. However, the LOS was greater in Group 2 ($p=0.04$; Table 6). High cervical injuries (C1-C4) showed an important tendency to increase the likelihood of developing a complication (Table 7), while high cervical injuries and increased trauma severity increased the odds of developing respiratory complications.

CONCLUSION:

Although complication rates were similar in non-specialized and specialized centers, peri-operative management in a non-specialized center required a longer length of stay. Prompt transfer to a SCI-center may optimize the care trajectory by favoring earlier transfer to rehabilitation.

Table 6

Comparison of medical complications and length of stay according to timing of admission to the specialized SCI-center following a traumatic SCI.

Occurrence of complications		Time of admission to the SCI-center		p-value
		Pre-surgery (Group 1)	Post-surgery (Group 2)	
At least one (one or more)	%	71.3	72.4	1.00
Overall respiratory	%	54.0	51.7	0.83
Pneumonia	%	47.1	41.4	0.67
Pressure ulcer	%	36.8	34.5	1.00
Urinary tract infection	%	20.7	31.0	0.31
LOS in the SCI-center	Mean (SD)	56.6(+/- 51.5)	77.3 (+/- 44.2)	0.04*

LOS, length of stay in the SCI-center (in days)

Table 7

Factors associated with the occurrence of medical complication during the acute care hospitalization using binary logistic regression analyses.

Variable	Odd ratio	95%CI	p-value
Time of admission to the SCI-center	0 ^d		
Group 1 (pre-surgery)	1.1	(0.4 ; 3.0)	0.85
Group 2 (post-surgery)			
Neurologic level of injury			
C1-C4	2.5	(1.0 ; 5.9)	0.04*
C5-C8	0 ^d		
Presence of obesity	11.7	(1.1 ; 129.4)	0.05*
ISS			
<26	0 ^d		
≥26	2.0	(0.84 ; 4.7)	0.12

$R^2 = 0.134$

Paper 4: Kaminski L, Cordemans V, Cernat E, M'Bra KI, Mac-Thiong JM. Functional outcome prediction after traumatic spinal cord injury based on acute clinical factors. J Neurotrauma 2017, 34(12): 2027-2033. (see Appendix 4)

Spinal cord injury (SCI) is a devastating condition that affects patients on both a personal and societal level. The objective of the study is to improve the prediction of long-term functional outcome following SCI based on the acute clinical findings. A total of 76 patients with acute traumatic SCI were prospectively enrolled in a cohort study in a single Level I trauma center. Spinal Cord Independence Measure (SCIM) at 1 year after the trauma was the primary outcome. Potential predictors of functional outcome were recorded during the acute hospitalization: age, sex, level and type of injury, comorbidities, American Spinal Injury Association (ASIA) Impairment Scale (AIS), ASIA Motor Score (AMS), ASIA Light Touch score (LT), ASIA Pin Prick score (PP), Injury Severity Score (ISS), traumatic brain injury, and delay from trauma to surgery. A linear regression model was created with the primary outcome modeled relative to the acute clinical findings. Only four variables were selected in the model, with performance averaging an R-square value of 0.57 (Table 8). In descending order, the best predictors for SCIM at 1 year were: LT, AIS grade, ISS, and AMS. One-year functional outcome (SCIM) can be estimated by a simple equation that takes into account four parameters of the initial physical examination (Table 9). Estimating the patient long-term outcome early after traumatic SCI is important in order to define the management strategies that might diminish the costs and to give the patient and family a better view of the long-term expectations.

Table 8: Parameter estimates for model predicting SCIM score at 1-year follow-up (R²=0.573)

<i>Prognostic variable</i>	<i>Standard. coefficient</i>	<i>Parameter estimate</i>	<i>95% CI</i>	<i>p value</i>
Intercept		69.2	[62.1 – 76.3]	<0.001
ASIA light touch score	0.382	0.283	[0.221 – 0.346]	<0.001
AIS grade	0.281			<0.001
A		-15.0	[-18.9 – -11.1]	
B		-12.4	[-17.3 – -7.57]	
C		-7.01	[-11.6 – -2.42]	
D		0		
ISS	0.272	-0.589	[-0.743 – -0.434]	<0.001
ASIA motor score	0.065	0.134	[0.062 – 0.206]	<0.001

SCIM, Spinal Cord Independence Measure; CI, confidence interval; ASIA, American Spinal Injury Association; AIS, American Spinal Injury Association Impairment Scale; ISS, Injury Severity Score.

Table 9: Predictive model equation

$$\text{SCIM score}_{(1 \text{ year follow-up, \%})} = 69.2 + 0.283(\text{LT}) + (\text{AIS}) - 0.589(\text{ISS}) + 0.134(\text{AMS})$$

With:

LT = American Spinal Injury Association Light Touch score

AIS = American Spinal Injury Association Impairment Scale

ASIA A = -15

ASIA B = -12.4

ASIA C = -7.01

ASIA D = 0

ISS = Injury Severity Score

AMS = ASIA Motor Score

SCIM, Spinal Cord Independence Measure.

Paper 5: Facchinello Y, Beauséjour M, Richard-Denis A, Thompson C, Mac-Thiong JM. The use of regression tree analysis for predicting the functional outcome following traumatic spinal cord injury. In press, J Neurotrauma (see Appendix 5)

Predicting the long-term functional outcome following traumatic spinal cord injury is needed to adapt medical strategies and to plan an optimized rehabilitation. This study investigates the use of regression tree for the development of predictive models based on acute clinical and demographic predictors. This prospective study was performed on 172 patients hospitalized following traumatic spinal cord injury. Functional outcome was quantified using the Spinal Cord Independence Measure collected within the first-year post injury. Age, delay prior to surgery and Injury Severity Score were considered as continuous predictors while energy of injury, trauma mechanisms, neurological level of injury, injury severity, occurrence of early spasticity, urinary tract infection, pressure ulcer and pneumonia were coded as categorical inputs. A simplified model was built using only AIS grade, neurological level, energy and age as predictor and was compared to a more complex model considering all 11 predictors mentioned above. The models built using 4 and 11 predictors were found to explain 51.4% (Figure 1) and 62.3% of the variance of the Spinal Cord Independence Measure total score after validation, respectively. The severity of the neurological deficit at admission was found to be the most important predictor. Other important predictors were the Injury Severity Score, age, neurological level and delay prior to surgery. Regression trees offer promising performances for predicting the functional outcome after a traumatic spinal cord injury. It could help to determine the number and type of predictors leading to a prediction model of the functional outcome that can be used clinically in the future.

Figure 1: Regression tree built considering 4 predictors and their relative importance

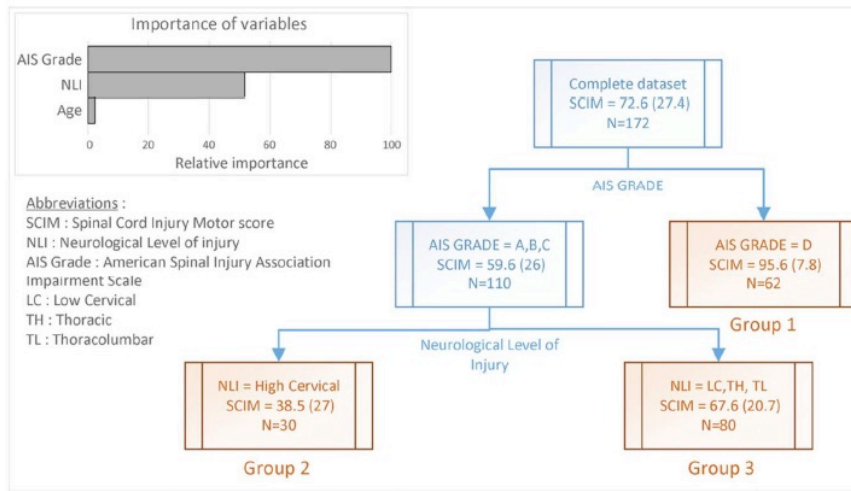


Figure 1 Regression tree built considering 4 predictors and their relative importance
 N: Number of patient, SCIM = mean value (standard deviation)

Figure 2: Regression tree built considering 11 predictors and their relative importance

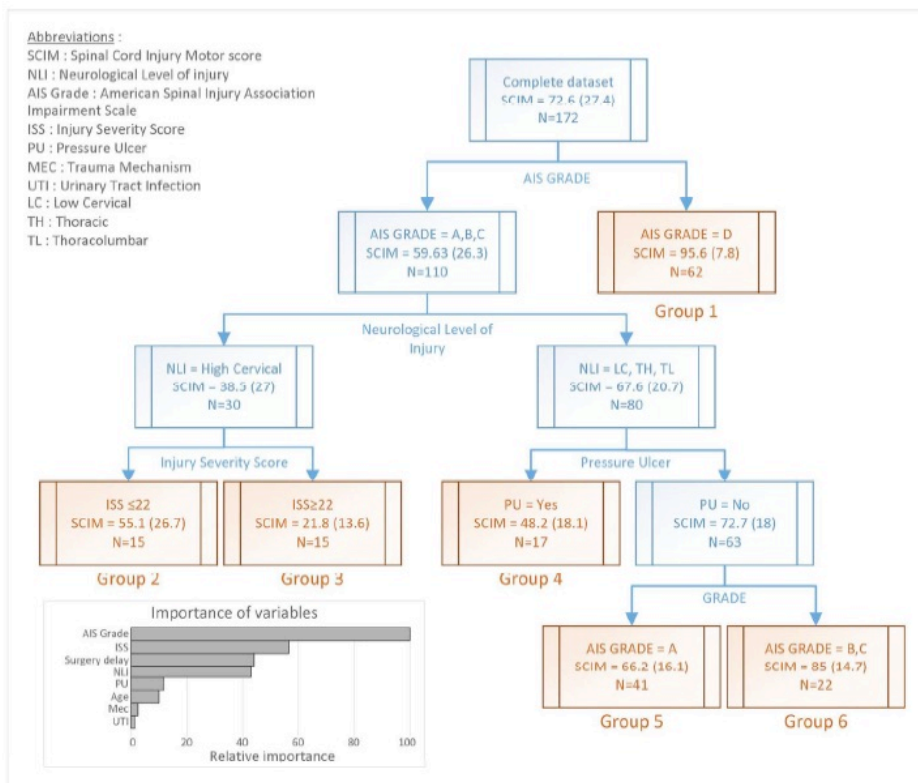


Figure 2 Regression tree built considering 11 predictors and their relative importance
 N: Number of patient, SCIM = mean value (standard deviation)

Paper 6: Richard-Denis A, Feldman DE, Thompson C, Albert M, Mac-Thiong JM. The impact of a specialized spinal cord injury center as compared to non-specialized centers on the acute respiratory management of patients with complete tetraplegia: an observational study. In press, Spinal Cord (see Appendix 6)

Study Design: Retrospective cohort study

Objectives: To compare the proportion of tracheostomy placement and duration of mechanical ventilation (MV) in patients with a complete cervical spinal cord injury (SCI) that were managed early or late in a specialized acute SCI-center. The second objective was to determine the impact of the timing of admission to the SCI-center on the MV support duration.

Setting: A single Level-1 trauma center specialized in SCI care in Quebec (Canada).

Methods: A cohort of 81 individuals with complete tetraplegia over a 6-years period was included. Group 1 (N=57- *early group*-) was admitted prior to surgical management in one specialized acute SCI-center, whereas Group 2 (N=24 -*late group*-) was surgically managed in a non-specialized center and transferred to the SCI-center for post-operative management only. The proportion of tracheostomy placement and MV duration were compared. Multivariate regression analysis was used to assess the impact of the timing of admission to the SCI-center on the MV duration during the SCI-center stay.

Results: Patients in Group 2 had a higher proportion of tracheostomy (70.8% versus 35.1%, $p=0.004$) and a higher mean duration of MV support (68.0 ± 64.2 days versus 21.8 ± 29.7 days, $p=0.006$) despite similar age, trauma severity (ISS), neurological level of injury and proportion of pneumonia (Table 10). Later transfer to the specialized acute SCI-center was the main predictive factor of longer MV duration, with a strong impact factor ($\beta=946.7$, $p<0.001$; Table 11).

Conclusions: Early admission to a specialized acute SCI-center for surgical and peri-operative management after a complete tetraplegia is associated with lower occurrence of tracheostomy and shorter mechanical ventilation duration support.

Table 10: Respiratory outcomes in patients with a complete cervical SCI early and late admitted to the SCI-center (n=81)

Respiratory outcome		Admission to the SCI-center		P
		Prior to surgery (Group 1)	After surgery (Group 2)	
N		57	24	---
Tracheostomy	% with tracheostomy	35.1	70.8	0.004
MV support	% with MV support	86.0	79.2	0.51
	Duration (days) MV support	6.8 (1.1-35.7)	57.2 (6.3-119.8)	0.006
	(Median (IQR) Mean $\pm$ SD)	21.8 (29.7)	68.0 (64.2)	

Table 11: Predictors of duration of mechanical ventilation (in days) for subjects with a complete cervical SCI: results of the multivariate analysis (n=81)

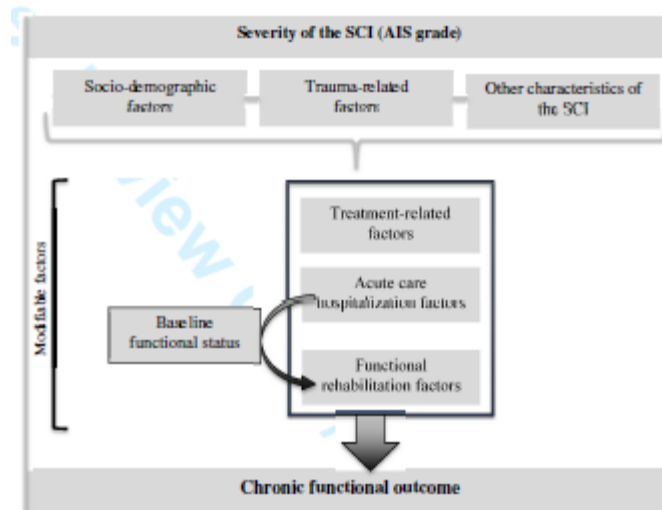
Predictors		Beta coefficient (95% CI)	P
Timing of admission at SCI-center	Prior to surgery (Group 1)	-946.7 (-1413.6, -479.7)	<0.001
	After surgery (Group 2)	Reference category	
NLI	C1-C4	588.7 (142.2,1035.2)	0.010
	C5-C8	Reference category	
ISS		13.5 (0.9, 26.1)	0.036

NLI: Neurological level of injury; CI: confidence interval; ISS: injury severity score

Paper 7: Richard-Denis A, Beauséjour M, Thompson C, Nguyen BH, Mac-Thiong JM. Early predictors of global functioning outcome after traumatic spinal cord injury: a systematic review. Submitted, J Neurotrauma. September 15, 2017. (see Appendix 7)

Accurately predicting functional recovery in an asset for all clinicians and decision makers involved in the care of patients with acute traumatic spinal cord injury (TSCI). Unfortunately, there is a lack of information on the relative importance of significant predictors of global functional outcome. There is also a need for identifying functional predictors that can be timely optimized by the medical and rehabilitation teams throughout the hospitalizations phases. The main objective of this work was to systematically review and rate factors that are consistently and independently associated with global functional outcome in individuals with TSCI. This review also proposes a new conceptual framework that illustrates the impact of specific categories of factors and their interaction with each other. The grade of severity of the SCI is the main predictor of global functional outcome following TSCI. Other factors may modulate this interaction according to their respective strength of impact. Younger age, lower neurologic level of injury and higher initial motor score were the main socio-demographic and trauma-related factors. Surgical management, higher functional status at discharge from acute care, shorter acute care length of stay, and access to specialized multidisciplinary functional rehabilitation were main modifiable factors. Prevention of medical complications, higher intensity and patient participation level in functional rehabilitation therapies were also contributing factors associated with improved global functional outcome.

Figure 3: Conceptual framework illustrating the interaction between factors influencing functional recovery following traumatic spinal cord injury



Paper 8: Facchinello Y, Richard-Denis A, Beauséjour M, Thompson C, Mac-Thiong JM.
The use of classification tree analysis to assess the influence of surgical timing on
neurological recovery following traumatic complete cervical spinal cord injury.
Submitted, Spinal Cord. October 13, 2017. (see Appendix 8)

Study Design: A prospective cohort study

Objectives: Assess the influence of surgical timing on neurological recovery using classification tree analysis in patients sustaining complete cervical traumatic spinal cord injury.

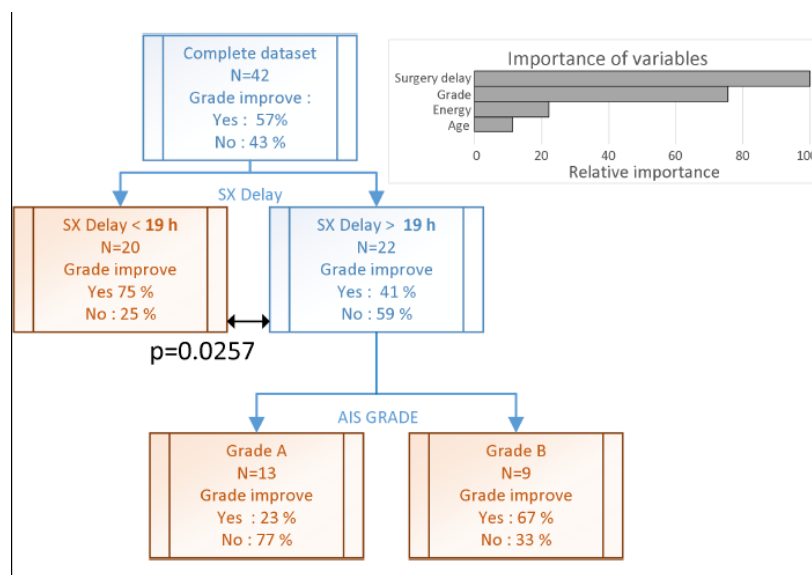
Settings : Hôpital du Sacré-Coeur de Montreal

Methods: 42 patients sustaining a complete cervical SCI treated in a single Level 1 Trauma Center specializing in spinal cord injury were followed for at least 6 months post-injury. Neurological status was assessed from the American Spinal Injury Association impairment scale (AIS) and neurological level of injury at admission to the acute care center and at follow-up 6 months after the injury. Age, surgical timing between trauma and surgery, AIS grade at admission and energy of injury were the four parameters considered as influencing the neurological recovery. Neurological recovery was quantified by the occurrence of improvement by: 1) at least one AIS grade, 2) at least 2 AIS grades and 3) at least 2 neurological level of injury.

Results: Surgical timing had a significant influence on all three endpoints for neurological recovery considered in this study. Early decompression surgery performed within 19 hours post-injury was associated with better neurological outcome (Figure 4).

Conclusions: Neurological recovery of patients sustaining complete cervical traumatic spinal cord injury can be improved by early decompression surgery performed within 19 hours post-trauma. This study is the first to justify an optimized cut-off value defining the concept of early decompression surgery.

Figure 4: Classification tree describing the influence of the four parameters under study on the one AIS grade neurological improvement



Paper 9: Goulet J, Richard-Denis A, Thompson C, Mac-Thiong JM. Relationships between specific functional abilities and health-related quality of life in chronic spinal cord injury. Submitted, Arch Phys Med Rehabil. October 17, 2017. (see Appendix 9)

Objective: To assess which specific functional abilities are most important in the health-related quality of life (HRQoL) of patients in the chronic phase of traumatic spinal cord injury (TSCI).

Design: Cross-sectional study

Participants: A prospective cohort of 195 patients that had sustained a TSCI from C1 to L1, and consecutively admitted to a single Level 1 SCI-specialized trauma center between 2010 and 2016 was studied

Interventions: none

Main outcome measures: The 3rd version of the Spinal Cord Injury Measure (SCIM-III) and Short-Form 36 version 2 (SF-36v2) questionnaires were administered concurrently during routine follow-up visit between 6 to 12 months after the trauma. Correlation coefficients were calculated between SCIM-III scores (total, subgroups and individual items scores), and SF-36v2 summary scores (Physical component score, PCS; Mental component score, MCS). All analyses were repeated separately for subjects with tetraplegia and paraplegia

Results: The total SCIM-III score correlated moderately with the PCS in the entire cohort, correlated strongly with PCS in tetraplegics and did not correlate with PCS in paraplegics. Mobility subgroup and individual items scores showed the strongest correlations with the PCS in the entire cohort as well as in tetraplegic patients, followed by self-care and sphincter management (Table 12). Correlations between SCIM-III scores and MCS for all patients were negligible.

Conclusion: This is the first study to objectively evaluate the relative importance of specific functional abilities in the HRQoL in TSCI patients. This work is significant because it determines which specific functional abilities are mostly related to HRQoL, and highlights the differences between tetraplegic and paraplegic patients, such findings that could help clinicians to guide the patient's treatment and rehabilitation plan.

Table 12: Spearman correlation coefficients between categories of the SCIM and the SF-36 PCS and MCS scores for patients with a traumatic spinal cord injury

		PCS	MCS
SCIM Category		rho coefficient	rho coefficient
Total cohort	Self-care	0.421**	-0.114
	Respiration and sphincter management	0.370**	-0.118
	Mobility	0.516**	-0.147*
	Total	0.482**	-0.124
Tetraplegia	Self-care	0.519**	-0.132
	Respiration and sphincter management	0.444**	-0.202*
	Mobility	0.556**	-0.149
	Total	0.541**	-0.154
Paraplegia	Self-care	0.225	-0.052
	Respiration and sphincter management	0.069	0.138
	Mobility	0.397**	-0.161
	Total	0.236	.041

Paper 10: Richard-Denis A, Thompson C, Mac-Thiong JM. Quality of life in the subacute period following a cervical traumatic spinal cord injury based on the initial severity of the injury: a prospective cohort study. Spinal Cord. Nov 2018 (see Appendix 10)

Study desing: Prospective cohort study

Objectives: To evaluate the relationship between quality of life (QOL) after a traumatic spinal cord injury (TSCI) and acute predictors, with a particular emphasis on the initial severity of the neurological injury. Secondary, to compare the QOL after a TSCI with the general population.

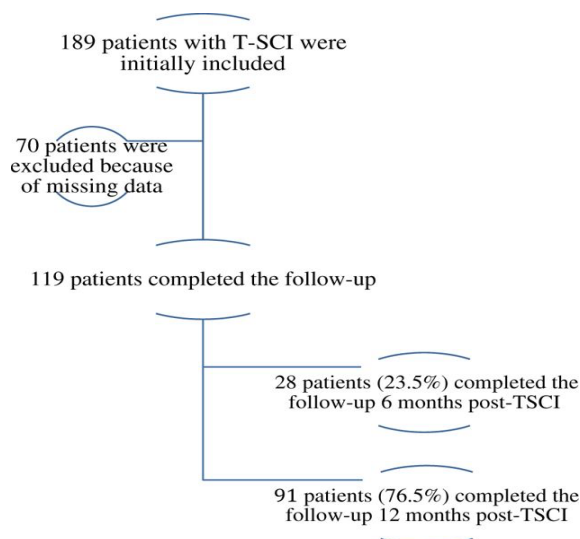
Setting: A single level-1 SCI-trauma center

Methods: A cohort of 119 individuals admitted after a cervical TSCI between April 2010 and September 2016 was studied. QOL was assessed using the SF-36v2 questionnaire 6-12 months following the injury, and compared to the general population. The relationship between the initial severity of the neurological injury and the SF-36 summary scores was assessed using linear multivariable regression analyses.

Results: Individuals sustaining less severe neurological injury (grade D) exhibited higher PCS than individuals with grades A, B or C injury. Individuals with initial grade A injury showed increased MCS than individuals with incomplete grade B, C or D injury, with 42.9% scoring higher than the general population. The initial grade was significantly associated with chronic PCS and MCS.

The initial severity of the neurological injury after a cervical TSCI may be used to estimate QOL in the subacute period following the injury. Individuals with complete tetraplegia may report good mental QOL despite severe physical impairment. Our findings could help clinicians to determine realistic expectations for patients in terms of QOL, and optimize the rehabilitation plan based on the initial evaluation after a TSCI.

Fig.1 Justification of the number of patients:



Paper 11: Richard-Denis A, Benazet D, Thompson C, Mac-Thiong JM. Determining priorities in functional rehabilitation related to quality of life one-year following a traumatic spinal cord injury. J Spinal Cord Med. Sep 6,2018.

Study design: Retrospective review of a prospective cohort.

Setting: A single level-1 trauma center specialized in SCI care

Objectives: To determine the relationship between the different functional aspects (as determined by the Spinal Cord Independence Measure) and quality of life (QOL) following a traumatic spinal cord injury (TSCI), considering clinical confounding factors.

Participants: One hundred and forty-two individuals sustaining an acute traumatic SCI.

Results: Mobility subscore was the only functional aspect significantly associated with all QOL domains (physical, psychological, social and environmental). Females present better chronic social and environmental QOL when compared to males. The level of injury may also influence environmental QOL.

Conclusion: Mobility training (mobility in bed, mobility with or without technical aids, transfers and stair management) should be an important part of the rehabilitation process in order to optimize chronic QOL following a TSCI.

Table 2: Results of the multivariate regression analyses using General Linear Models (GLM) for each of the WHOQOL-Bref domains (physical, psychological, social and environmental) (N=142)

Dependent variables for each final GLM	Significant variable(s) in the final model	Beta (95%CI)	R ² value of the final model	Final model P-value
Model 1 : Physical	SCIM_mobility	0.23 (0.08-0.37)	0.062	0.003
Model 2 Psychological	SCIM_mobility	0.46 (0.26-0.67)	0.123	<10 ⁻³
Model 3 : Social	SCIM_mobility Male	0.52 (0.27-0.76) -8.19 (-15.83- -0.55)	0.128	<10 ⁻³
Model 4 : Environmental	SCIM_mobility Male Level of injury C0-C4 C5-C8 13.27 (2.39-24.16) T8-L1 category ISS	0.58 (0.35-0.80) -8.75 (-15.26—2.25) 9.16 (2.37-15.95) 10.41 (3.30-17.52) T1-T7 reference 0.40 (0.06-0.75)	0.240	<10 ⁻³

ISS, Injury severity score; SCIM, Spinal Cord Independence Measure

Paper 12: Richard-Denis A, Nguyen BH, Mac-Thiong, JM: The impact of early spasticity on the intensive functional rehabilitation phase and community reintegration following traumatic spinal cord injury. J Spinal Cord Med. Dec 3, 2018.

Study desing: Retrospective cohort study

Setting: A single level-1 trauma center specialized in SCI care

Objectives: To determine the impact of spasticity presenting during the acute care hospitalization on the rehabilitation outcomes following a traumatic spinal cord injury (TSCI).

Participants: 150 individuals sustaining an acute TSCI.

Results: 63.3% of the cohort presented signs and/or symptoms of spasticity during acute care. Individuals with early spasticity developed medical complications during acute care and during intensive functional rehabilitation in a higher proportion. They were also hospitalized significantly longer and were less likely to return home after rehabilitation than individuals without early spasticity. Early spasticity was an independent factor associated with increased total inpatient rehabilitation length of stay.

Conclusion: The development of signs and symptoms of spasticity during acute care following a TSCI may impede functional rehabilitation outcomes. In view of its association with the occurrence of early spasticity, higher vigilance towards the prevention of medical complications is recommended. Early assessment of spasticity during acute care is recommended following TSCI.

Table3. *Clinical factors associated with the total inpatient rehabilitation length of stay: results of the final general linear model (n-150)*

Predictive factors	β (95%CI)	P value
Early spasticity		
Absence (Group 1)	-39.7 (-69.7;-9.7)	0.01**
Presence (Group 2)	Ø	
Initial AIS grade		
AIS-A	100.0 (65.0;135.1)	<0.001*
AIS-B	75.2 (30.3;120.1)	0.001**
AIS-C	51.7 (15.0;88.4)	0.006**
AIS-D	Ø	
Complications during acute care		
Absence	-34.9 (-64.5;-5.2)	0.02**
Presence	Ø	
R-square = 31.9%		

AIS, American Spinal Injury Association Impairment Scale.

Ø: Reference category.

*P is significant if <0.05.

What was accomplished under these goals?

For the five year of funding, the major goals were to pursue the long-term follow-up of enrolled patients. As well, we planned to pursue analysis of the data pertaining to the acute hospitalization period and outcome measures.

The statement of work approved by USAMRMC was based on the hypothesis that funding would have begun on April 1, 2013. In fact, we received HRPO approval on February 21, 2014, and thus initiated the study at that time. Therefore, all activities reported in the approved statement of work are delayed by approximately 11 months (April 1, 2013 – February 21, 2014). To compensate for this delay, we obtained a first one-year no-cost extension. We have also obtained a second 1-year no-cost extension in July 2017, which will allowed us to: 1) completed long-term follow-up of patients (≥ 2 -years post-SCI); 2) to finalize analyses pertaining to quality of life, neurological recovery and resource use vs timing of surgery; and 3) to determine the optimal timing of surgery using Classification and Regression Tree analyses (CART). The funding end was September 29, 2018.

a) Recruitment of patients

Recruitment is completed since September 2014.

b) Follow-up of patients

With respect to patients' follow-up, as of September 28, 2018, 84 patients had their 6-month follow-up completed, 87 patients came for their 1-year follow-up and 69 have done their long-term follow-up. For these 69 patients, the participation to this study is terminated. The last five patients added to the final report had their long-term follow-up in February 2019, and we decided to add them in the final report.

c) Data collection

With respect to data, we have collected the information pertaining to the socio-demographic, clinical, surgical and radiological characteristics for all patients. Since all enrolled patients had their trauma before September 2014, all information was compiled.

What opportunities for training and professional development has the project provided?

The project has led to the training in research of 3 students (1 post-doctoral student: Yann Facchinello; 1 doctoral student: Pascal Mputu; 1 MSc student: Andréane Richard-Denis, 2 research assistants and 1 research nurses. Among these students, one has recently joined our team as a clinician-scientist (Andréane Richard-Denis) specialized in the acute rehabilitation of spinal cord injured patients. It also helped to develop the career of the three researchers involved in this project (J-M Mac-Thiong, D Feldman and S Parent).

How were the results disseminated to communities of interest?

Results were disseminated to researchers, clinicians and decision-makers mainly through 12 scientific articles published in peer-reviewed journals, 10 presentations in local/national/international conferences such as the Annual Scientific Meeting of the American Spinal Injury Association and International Meeting on Advanced Spine Techniques.

4. IMPACT

What was the impact on the development of the principal discipline(s) of the project?

Results from papers 1, 4, 5 and 7 emphasize the importance of optimizing acute care hospitalization as factors pertaining to early management following a traumatic spinal cord injury can predict chronic functional outcome.

Results from papers 2, 3 and 6 highlight the importance of surgical and peri-operative management in a SCI specialized center, especially in traumatic tetraplegia, reducing resource use and improving respiratory outcomes and complication management. This indirectly supports the importance of early surgical management by a specialized multidisciplinary team for optimizing outcomes in tetraplegia.

Results from paper 8 demonstrate the importance of early surgery for better neurological recovery in patients with complete tetraplegia, and propose an optimal cut-off of 19 hours for defining the concept of early and late surgery in terms of chronic neurological outcome.

Results from paper 9 describe the relationship of specific functional abilities with quality of life in patients with a traumatic SCI, which will guide clinicians in developing appropriate treatment and rehabilitation plans.

Results from paper 10 demonstrate Individuals sustaining less severe neurological injury (grade D) exhibited higher PCS than individuals with grades A, B or C injury. Individuals with initial grade A injury showed increased MCS than individuals with incomplete grade B, C or D injury, with 42.9% scoring higher than the general population. The initial grade was significantly associated with chronic PCS and MCS.

Results from paper 11 describe mobility subscore was the only functional aspect significantly associated with all QOL domains (physical, psychological, social and environmental). Females present better chronic social and environmental QOL when compared to males. The level of injury may also influence environmental QOL.

Results from paper 12 emphasize of 63.3% of the cohort presented signs and/or symptoms of spasticity during acute care. Individuals with early spasticity developed medical complications during acute care and during intensive functional rehabilitation in a higher proportion. They were also hospitalized significantly longer and were less likely to return home after rehabilitation than individuals without early spasticity. Early spasticity was an independent factor associated with increased total inpatient rehabilitation length of stay.

What was the impact on other disciplines?

Our project involved different statistical techniques and has therefore shown their relative benefits for predicting clinical outcomes such as those used in our studies. In addition, our project has raised the need to search for biomechanical predictors characterizing the traumatic event in order to better predict the outcome. Accordingly, we are now collaborating with engineers to develop computer-based simulations to reconstitute the traumatic event of patients sustaining spinal cord injuries.

What was the impact on technology transfer?

Locally, our results have been transferred to the decision-makers such that there is now a strict protocol for performing surgery within 24 hours of the injury, according to the benefits of early surgery demonstrated by our study. Surgery within 24 hours has also become a standard of care throughout Canada.

What was the impact on society beyond science and technology?

Our studies have shown that early surgery had the potential to decrease the costs associated with the management of spinal cord injuries, in addition to a decrease in complications and length of stay for patients. Our results have shown the importance of acute centers specialized in SCI care for optimizing the outcome of patients. In addition, our project has shown that it was possible to predict the long-term function and quality of life based on acute predictors. It has also helped to identify the priorities in functional rehabilitation related to quality of life of patients.

Summarizing, how you plan to move this research closer to patients?

1 – Timing of surgery

We have shown that early timing of surgery improves the neurological and functional outcome, decreases the rate of complications and shortens the acute length of stay. Locally, these findings have been presented to administrators and clinicians, and have been used to implement our prioritization system for surgical emergencies, such that early surgery within 24 hours of the injury are performed for >90% patients nowadays, compared to <20% before 2012. While the definition of early surgery in the literature was arbitrary, our studies have confirmed that the rule of thumb for early surgery (within 24 hours following the injury) was indeed an adequate target for clinicians performing early surgery after acute traumatic spinal cord injury. We have presented our results in multiple conferences and publications to reach clinicians and decision-makers, and early surgery within 24 hours is now recognized as a gold standard for spinal cord injured patients throughout the world. For example, these results were featured in two workshop sessions organized by Dr Mac-Thiong in international meetings.

- a) Spine and acute trauma symposium: Point/counter point - Early or late surgery for traumatic central cord syndrome. 2018 Annual Scientific Meeting of the American Spinal Injury Association, Rochester, Minnesota, USA, May 4 2018.
- b) Instructional Course Lecture: The Benefits of early intervention and emergent therapies for traumatic spinal cord injury. 2014 American Orthopaedic Association/Canadian Orthopaedic Association Combined Meeting, Montreal, Canada, June 19 2014

With the collaborative network developed by the PI through this project, Dr Mac-Thiong plans to further present our latest results and future studies on surgical timing, and engage discussions with policy-makers/stakeholders at the local (Institut national d'excellence en santé et en services sociaux du Québec), national (Rick Hansen Institute), and international (American Spinal Cord Injury Association, AO Spine) level, in order to improve the rate of patients undergoing early surgery after a traumatic spinal cord injury.

2 – Early preoperative transfer to acute center specialized in spinal cord injury

We have shown the critical importance of early transfer to acute centers specialized in the care of patients with spinal cord injuries. While some centers/clinicians were thinking that performing early surgery in a non-specialized center and then transferring patients to a specialized center could be beneficial for patients, we have shown that it is preferable for patients to be transferred as soon as possible to a specialized center prior to surgery. Integrated care and surgery in a specialized center will decrease costs, length of stay and complications. Based on our findings, the government agency responsible for healthcare in Quebec has amended its guidelines on SCI care, stressing on the importance of early transfer prior to surgery in acute centers specialized in spinal cord injury. Locally at our hospital, we have modified our triage and referral system such that all patients with suspected spinal cord injuries are rapidly transferred to our spine unit.

Our studies have been widely disseminated through publications and presentations at conferences. We believe that our studies will be highly influential to better define the standards for the care pathways of patients following a spinal cord injury, considering that there is a wide variability in the standard of care for this population around the world. In line with these efforts, our next step will be to define the optimal structure/services for specialized centers, in order to lead to optimal outcomes and further define the standard of care for spinal cord injured patients.

3 – Prevention of complications

Our studies have identified acute predictors of chronic functional outcome following traumatic spinal cord injury. Based on our findings, we have modified our postoperative care protocols, particularly for preventing pressure ulcers. Our rate of pressure ulcers has decreased from about 40% to less than 20% with our new protocols. This project has confirmed the importance of decreasing the rate of complications for optimizing the outcome of patients, and our next step will be to identify modifiable factors that we can improve to further decrease the rate of complications and improve the recovery of patients. For example, we are now involved in a study evaluating the benefit of new dressings to prevent pressure ulcers.

4 – Large prospective database of patients with low-term follow-up

Through this project, we have already collected 6-month+ prospective data for more than 300 patients following their spinal cord injury. We believe that our database including acute variables as well as neurological, functional and quality of life follow-up data is the most comprehensive database collected at a single center throughout the world. This database will serve as a reference for studies evaluating new care modalities or outcome predictors. In the following months, we plan to use our database to assess the benefits of new rehabilitation treatments designed to improve the recovery of patients as well as decrease the rate of complications using a matched-cohort study design.

5. CHANGES / PROBLEMS

Changes in approach and reasons for change

The biggest challenge we had was keeping up to date with patient's follow-ups. We have changed our method of reaching our patients. With the new staff set up, it is now easier to reach our patients and follow-up with them. We have set up a new reminder system for patient follow-ups. An EXCEL chart with formulas, which allows us to see when patients are due for upcoming follow-ups. We are also working on setting up an interdisciplinary clinic. This way of proceeding will allow the patient to come only once for his follow-up, as the patient can at that time meet all the specialists (radiologist, research team, physiatrist and orthopedic surgeon).

Actual or anticipated problems or delays and actions or plans to resolve them

The main problem in this study was patient compliance with their follow-up appointments. Long-term follow-up (≥ 2 years after spinal cord injury) is always a problem for our patients. This is why we have put in place the tools listed in the previous point. Follow-ups more than two years after the injury should not introduce a significant bias in our data, as recovery generally reaches a plateau around one year after the injury.

Changes that had a significant impact on expenditures

Nothing to report

Significant changes in use or care of human subjects

The arrival of Dre. Richard-Denis in our team brought a rehabilitation side to our patients. During follow-ups, we carry out a neurological follow-up with ASIA and Dre. Richard-Denis can also manage the pain and rehabilitation side.

Significant changes in use or care of vertebrate animals

Nothing to report

Significant changes in use of biohazards and / or select agents

Nothing to report

6. PRODUCTS

Publications, conference papers, and presentations

Journal publications

Richard-Denis A, Feldman DE, Thompson C, Mac-Thiong JM. Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization. *J Spinal Cord Med* 2017 Feb 15: 1-9 (*epub ahead of print; see Appendix 1*)

Richard-Denis A, Feldman DE, Thompson C, Bourassa-Moreau E, Mac-Thiong JM. Costs and length of stay for the acute care of patients with motor-complete spinal cord injury following cervical trauma: the impact of early transfer to specialized acute SCI center. *Am J Phys Med Rehabil* 2017, 96(7): 449-456. (*see Appendix 2*)

Richard-Denis A, Feldman DE, Thompson C, Mac-Thiong JM. The impact of acute management on the occurrence of medical complications during the specialized spinal cord injury acute hospitalization following motor-complete cervical spinal cord injury. *J Spinal Cord Med* 2017, Jul 19: 1-18 (*epub ahead of print; see Appendix 3*)

Kaminski L, Cordemans V, Cernat E, M'Bra KI, Mac-Thiong JM. Functional outcome prediction after traumatic spinal cord injury based on acute clinical factors. *J Neurotrauma* 2017, 34(12): 2027-2033. (*see Appendix 4*)

Facchinello Y, Beauséjour M, Richard-Denis A, Thompson C, Mac-Thiong JM. The use of regression tree analysis for predicting the functional outcome following traumatic spinal cord injury. *J Neurotrauma* (*see Appendix 5*)

Richard-Denis A, Feldman DE, Thompson C, Albert M, Mac-Thiong JM. The impact of a specialized spinal cord injury center as compared to non-specialized centers on the acute respiratory management of patients with complete tetraplegia: an observational study. *Spinal Cord* (*see Appendix 6*)

Richard-Denis A, Beauséjour M, Thompson C, Nguyen BH, Mac-Thiong JM. Early predictors of global functioning outcome after traumatic spinal cord injury: a systematic review. *J Neurotrauma*. September 15, 2017. (*see Appendix 7*)

Facchinello Y, Richard-Denis A, Beauséjour M, Thompson C, Mac-Thiong JM. The use of classification tree analysis to assess the influence of surgical timing on neurological recovery following traumatic complete cervical spinal cord injury. *Spinal Cord*. October 13, 2017. (*see Appendix 8*)

Goulet J, Richard-Denis A, Thompson C, Mac-Thiong JM. Relationships between specific functional abilities and health-related quality of life in chronic spinal cord injury. *Arch Phys Med Rehabil*. October 17, 2017. (*see Appendix 9*)

Richard-Denis A, Thompson C, Mac-Thiong JM. Quality of life in the subacute period following a cervical traumatic spinal cord injury based on the initial severity of the injury: a prospective cohort study. *Spinal Cord*. Nov 2018 (*see Appendix 10*)

Richard-Denis A, Benazet D, Thompson C, Mac-Thiong JM. Determining priorities in functional rehabilitation related to quality of life one-year following a traumatic spinal cord injury. *J Spinal Cord Med.* Sep 6, 2018. (see Appendix 11)

Richard-Denis A, Nguyen BH, Mac-Thiong, JM: The impact of early spasticity on the intensive functional rehabilitation phase and community reintegration following traumatic spinal cord injury. *J Spinal Cord Med.* Dec 3, 2018. (see Appendix 12)

Conference papers and presentations

Richard-Denis A, Mac-Thiong JM, Thompson C, Parent S, Feldman, D. Early development of spasticity in persons with spinal cord injury and impact on function 6 months post injury. (presented at the 4th ASIA and ISCoS Joint Scientific Meeting in May 2015)

Cynthia Thompson, Stefan Parent, Debbie Ehrmann Feldman, Jean-Marc Mac-Thiong. Factors predicting the delay between trauma and surgery in a prospective cohort admitted with a traumatic spinal cord injury; Oral presentation at the Montreal Interprofessional Trauma Conference (Montreal, Canada, September 2016); Oral presentation at the 2016 ASIA Annual Scientific Meeting (international conference; Philadelphia, April 2016) *

Andréane Richard-Denis, Cynthia Thompson, Debbie Ehrmann Feldman, Étienne Bourassa-Moreau, Jean-Marc Mac-Thiong. Costs and length of stay for the acute care of patients with motor-complete spinal cord injury following cervical trauma: the impact of early peri-operative management in a specialized acute SCI center. Oral presentation at the 2016 ASIA Annual Scientific Meeting (international conference; Philadelphia, April 2016) *

Cynthia Thompson, Andréane Richard-Denis, Debbie E. Feldman, Stefan Parent, Jean-Marc Mac-Thiong. Factors predicting functional outcome one year after a traumatic spinal cord injury: results from a prospective study; Poster presentation at the 2016 ASIA Annual Scientific Meeting (international conference; Philadelphia, April 2016) *

Andréane Richard-Denis, Cynthia Thompson, Debbie Ehrmann Feldman, Jean-Marc Mac-Thiong. The impact of acute management in a specialized spinal cord injury center on the occurrence of medical complications following motor-complete cervical spinal cord injury. Oral presentation at the 2016 ASIA Annual Scientific Meeting (international conference; Philadelphia, April 2016)

Andréane Richard-Denis, Cynthia Thompson, Debbie Ehrmann Feldman, Jean-Marc Mac-Thiong. Requirement for tracheostomy and duration of mechanical ventilation support in patients with a complete cervical traumatic spinal cord injury: the influence of early management in a SCI-specialized center; Oral presentation at the 2016 ASIA Annual Scientific Meeting (international conference; Philadelphia, April 2016)

Thompson C, Richard-Denis A, Mac-Thiong JM. Expectations in chronic QOL following cervical traumatic spinal cord injury based on the initial severity of the neurological injury. Oral presentation at the 2017 ASIA Annual Scientific Meeting (international conference; Albuquerque, USA, April 2017)

Richard-Denis A, Thompson C, Mac-Thiong JM. Determining complete functional independence in patients with a traumatic cervical SCI: Proposal of a new 2-level scale based on the Spinal Cord Independence Measure (SCIM-III). Poster presentation at the 2017 ASIA Annual Scientific Meeting (international conference; Albuquerque, USA, April 2017)

Richard-Denis A, Rami Chatta, Mac-Thiong JM. Does the functional outcome 6 months after a traumatic spinal cord injury predict the chronic functional outcome 12 months after the injury? American Spinal Injury Association annual meeting, Rochester, Minnesota, USA (May 5th) (Podium)

Goulet J, Richard-Denis A, Thompson C, Mac-Thiong J-M. Relationships between Specific Functional Abilities and Health-Related Quality of Life in Chronic Spinal Cord Injury. 2018 Annual Scientific Meeting of the American Spinal Injury Association, Rochester, Minnesota, USA, May 2-4 (Podium)

Website(s) or other Internet site(s)

Nothing to report

Technologies or techniques

We started to work with the CART, a software to analyze data.

Inventions, patent applications, and/or licenses

Nothing to report

Other products

Nothing to report

7. PARTICIPANTS AND OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Please note that at our institution, a regular workday is 7 hours and the schedule is based on 35 hours of work per week. We however calculated the number of "person month" worked based on 160 hours of effort as indicated in the USAMRMC report guidelines.

Name Project role Researcher identifier Nearest person month worked Contribution to project Funding support	Dr Jean-Marc Mac-Thiong Principal investigator / director N/A 0.5 Supervision of staff and data collection; revision of documents No funding other than USAMRMC
Name Project role Researcher identifier Nearest person month worked Contribution to project Funding support	Geneviève Leblanc Research assistant N/A 1 Recruitment and enrollment of patients No funding other than USAMRMC
Name Project role Researcher identifier Nearest person month worked Contribution to project	Louisane Dupré Research nurse N/A 2 Follow-up of patients, data collection

Funding support	No funding other than USAMRMC
Name	Kim Grenier (since October 29)
Project role	Research nurse
Researcher identifier	N/A
Nearest person month worked	1
Contribution to project	Follow-up of patients, data collection
Funding support	N/A funding finished
Name	Laura Impériale (since July 2018)
Project role	Medical archivist
Researcher identifier	N/A
Nearest person month worked	1
Contribution to project	Data collection
Funding support	Other funding support

Has there been a change in the active other support of the PD / PI or senior / key personnel since the last reporting period?

Nothing to report

What other organizations were involved as partners?

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

Nothing to report

9. Appendix 1: Manuscript published in Journal of Spinal Cord Medicine (2017)

The Journal of Spinal Cord Medicine

Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization

--Manuscript Draft--

Manuscript Number:	JSCM-D-16-00077R1
Full Title:	Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization
Article Type:	Research Article
Section/Category:	Clinical Section
Keywords:	Spinal Cord Injuries; prediction; function; acute; trauma
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Abstract:	Objectives: To determine factors associated with functional status six months following a traumatic cervical and thoracic spinal cord injury (SCI), with a particular interest in factors related to the acute care hospitalization stay. Design and Methods: This prospective cohort study was conducted on 159 patients hospitalized in a single specialized Level I trauma center for an acute traumatic SCI between January 2010 and February 2015. Fifteen potential predictive variables were studied. Univariate regression analyses were first performed to determine the strength of association of each variable independently with the total SCIM score. Significant ones were then included in a General linear model in order to determine the most relevant predictive factors among them. Analyses were carried out separately for tetraplegia and paraplegia. Main outcome measure: Spinal Cord Independence Measure (SCIM III) score. Results: Motor-complete SCI (AIS-A,B) was the main predictive factor associated with decreased total SCIM score in tetraplegia and paraplegia. Longer acute care length of stay and the occurrence of acute medical complications were predictors of decreased functional outcome following tetraplegia, while increased body mass index and higher trauma severity were predictive of decreased functional outcome following paraplegia. Conclusions: This study supports previous work while adding information regarding the importance of optimizing acute care hospitalization as it may influence chronic functional status following traumatic SCI.

ver Letter

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Friday, November 18th, 2016

The Journal of Spinal Cord Medicine

Object: Submission of the REVISED manuscript entitled “**Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization**”

Dear Editors,

Enclosed is the revised manuscript by Andréane Richard-Denis, Debbie E. Feldman, Cynthia Thompson and Jean-Marc Mac-Thiong entitled “*Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization*”, which is being resubmitted for review and publication in your journal. This manuscript describes our own original work on properly conducted and documented research. It has never been published by any other journal, and will not be submitted to any other journal without prior written notification to the Editor that the manuscript is to be withdrawn.

Sincerely yours,



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sponse to Reviewers

Response to reviewers JSCM-D-16-00077

Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization

Reviewer 1 :

Title : Appropriate

Abstract :

The SCIM acronym is used before it is spelled out.

This was corrected in the revised manuscript.

Consider specifying the medical complications that were studied and/or found to be predictors.

This was also corrected in the revised manuscript.

Introduction: Adequate.

Methods:

It isn't clear whether the study protocol abstracted data from clinical charts, or whether their study protocol determined the data that was collected in a prospective manner.

This study used data from a prospective database from a single Level-1 trauma center specialized in spinal cord injury (SCI) care. In other words, this study consisted in a review of prospectively collected data. We agree that the information was not clear in the first version of the manuscript. The following modifications were bring to the revised manuscript:

- *“This study consisted in a review of a prospective database collected in a single Level-1 trauma center specialized in spinal cord injury (SCI) care. A total of 159 adult patients with acute T-SCI from C1 to L1 consecutively admitted between January 2010 and February 2015 (126 males and 33 females; 46.2±20.0 years old) were included.”(Lines 35 to 38, Introduction section).*

Consider providing a reference for the Injury Severity Score (ISS); define high velocity trauma and traumatic brain injury severity.

Information pertaining to the Injury Severity Score and reference was provided in the revised manuscript as follows:

- *“The ISS is a simple method describing patients with multiple traumatic injuries. It corresponds to an anatomical scoring system where each injury is assigned to a specific score according to its severity and location. The ISS takes values from 0 to 75.” (Baker et al. 1974-reference #18 in the text) (Lines 48 to 51, Methods section).*

High velocity trauma refers in this study to the occurrence of a SCI in the context of any motor vehicle accident (car, motorcycle, etc.). The severity of the traumatic brain injuries (TBI) was based on the Glasgow Coma Scale (GCS) in the first 48 hours following the injury. A GCS score of 9 to 12 refers to moderate TBI, while a GCS of 3 to 8 refers to severe TBI. This information was added to the revised manuscript as follows:

- *“Information pertaining to the age, gender, body mass index (BMI), trauma severity measured by the Injury Severity Score (ISS), presence of a high velocity trauma (defined as the occurrence of a SCI in the context of any motor vehicle accident), as well as presence of a concomitant traumatic brain injury (TBI) were collected (...) The presence of moderate and severe TBI was also specifically noted. The severity of the traumatic brain injuries (TBI) was based on the Glasgow Coma Scale (GCS) in the first 48 hours following the injury. A GCS score of 9 to 12 refers to moderate TBI, while a GCS of 3 to 8 refers to severe TBI.” (Lines 46 to 55. Methods section).*

It is confusing whether there were 2 or 4 groups studied - high and low tetra AND high and low para, or just tetra vs para?

All analyses (descriptive and linear regression analyses) were performed separately for tetraplegia and paraplegia. However, the level of the SCI (high vs. low) was also considered as a potential predictor variable. In other words, analyses were not carried for four groups, but only for tetraplegia and paraplegia.

The following modification was brought to the revised manuscript:

- *“All analyses were performed separately for individuals sustaining tetraplegia and paraplegia regardless of the level of the injury.” (Lines 97 and 98, Methods section).*

If possible, it would be useful to specify the medical complications in the analyses, is UTI, pressure ulcer, or pneumonia the culprit?

We agree with the reviewer. The incidence of the complications considered in this study (pneumonia, urinary tract infection and pressure ulcer) was added in the revised manuscript and in Table 2. We have also revised our regression analyses including each complication as an independent variable. However, the occurrence of medical complications, considered individually was not revealed as a significant predictor of functional outcome six-months post injury. Since it did not modified results of our prediction models, and rather decreased the R-square values, they were left sound with 16 independent variables regrouping complication occurrence.

The following modifications were brought to the revised manuscript:

- Table 2: The proportion of pneumonias, urinary tract infections and pressure ulcers for each group was added.
- *“According to Table 2, pneumonias were the most frequent complication in this group. The occurrence of pneumonia may prolonged the intensive care stay, interfere the rehabilitation process and delay the mechanical weaning process.” (Discussion section, lines 160 to 162).*

Is this a standard method of building a statistical prediction model? If so, a citation should be provided. Similarly, is the method used to assess collinearity typical?

A forward method used to select the independent variables included GLM. Selection process for multiple regression aims to reduce the set of predictor variables to those that are more relevant clinically and statistically. This method was used to help in determining the level of importance of each predictor variable. Our method allows entering variables of greater theoretical importance first in the GLM. It also allows assessing collinearity, which is an important assumption criteria to a valid prediction model using multivariate linear analyses.

Collinearity refers to a shared variance between predictors (independent variables). Collinearity

represents a statistical issue in multivariate regression analyses. Omitting collinearity issue may reduce the statistical power of the prediction model. It may be assessed using *tolerance* and *variance inflation factor*. Although these statistics only indicates how much information multicollinearity has cost the analysis. The best remedy for multicollinearity is to design a study to avoid it. To do so, there are three possible solutions: 1) dropping predictors, 2) combining or transforming predictors, 3) do nothing. Dropping predictors was reported to be a reasonable thing to do. However, this technic is limited by the fact that both predictors may jointly influence the outcome variable (dependent variable). In order to reduce the impact of this issue, collinearity was assessed after univariate linear analyses and the dropping process was then based on the strength of association of each predictor with the outcome variable (dependent variable). References are now added to the revised manuscript.

- Tabachnick BG, Fidell LS, Using multivariate statistic (Fifth edition). Pearson publisher. 2012, 1024 pages.

Results:

Table 1 suggests 16 variables were studies, whereas the abstract states 15. Perhaps level of injury should not be listed?

We agree with the reviewer that 16 potential predictor variables were included in our analyses. Information in the abstract was corrected.

It's not clear what the "X" signifies under input variable - does it mean significant associations in univariate linear regression?? Was spasticity a predictor in univariate analyses?? Perhaps the legend for Table 1 should explain what X signifies.

We agree with the reviewer that Table 1 was confusing. The “x” refers to variables that were finally included in the multivariate linear regression analyses (GLM) after reaching significance in the bivariate analysis and exclusion of collinearity. Therefore, the same variables were found as independent variables in their respective prediction model (general linear model using multivariate regression analyses) as shown in Table 4 and 5. For instance, presence of early spasticity was significantly associated with the functional score 6 months post injury in our univariate linear analysis (with a significance value set at 0.1 at this step- as explained in the method section-) and was not collinear for the tetraplegia and paraplegia group. Early spasticity was then included in both GLM. This information was added in the methods section and also in the legend of Table 1.

- *Table 1 (legend) “x” indicate that this variable was included in the multivariate linear analysis.*
- *Independent variables that were finally included in each GLMs (for paraplegia and tetraplegia) are indicated by an “x” in Table 1. (Methods section, lines 109-110).*

In Table 2, it isn't clear what the p-value is comparing, particularly for neurological level. What does the asterisk mean for spasticity? Should there be an asterisk for Motor score?

We want to thank the reviewer that has notice that an asterisk was missing in Table 2 (for motor score). We also agree that Table 2 should only presents characteristics of both groups without comparing them since individuals with paraplegia and tetraplegia are considered separately in this study. Comparative analyses between the two groups do not serve the objective of this study and was therefore excluded.

- Table 2 was therefore adjusted (p-values were erased)

Discussion:

In line 3 consider changing "decrease resource utilization" to "optimize resource utilization".

The suggestion was applied (*Line 145, discussion section*).

In second paragraph, "motor-sacral sparing" is confusing, does it mean "motor incomplete"?

This was also adjusted. (*Line 154, discussion section*).

In third paragraph, "relapse" is confusing. Also, it does not seem that number of medical complications was measured. Table 2 seems to compare the percentage of patients with multiple complications, not the actual number of complications per patient?

Table 2 now reports the proportion of pneumonia, urinary tract infection and pressure ulcer for each group. Comparison using chi-square tests were considered additional analyses and were then reported in the discussion section as follows.

- *"However, although severity of complications was not assessed in this study, additional analysis did not revealed any difference between in the number of complications between the two groups (p-values of 0.1, 0.4 and 0.3 for pneumonia, urinary tract infection and pressure ulcer respectively)." (Lines 172 to 175, Discussion section)*
- The word 'relapses' was replaced for "recurrences" (*Line 168, discussion section*).

Reviewer 2**The abstract:**

The abstract reflects the content of the paper. The objective: "To determine factors associated with functional status six months following a traumatic cervical and thoracic spinal cord injury (SCI), with a particular interest in factors related to the acute care hospitalization stay."

Introduction:

The introduction gives the background.

"Patients without overt spinal instability or central cord syndrome were excluded because these individuals typically present distinct outcome." - It may be of interest to determine factors associated with functional status six months post injury in this group.

We totally agree with the reviewer. This was added to the limitation section, since these patients (particularly individuals with central cord syndrome) represent a growing percentage of the population with traumatic SCI in our country (Thompson et al. 2015).

- *"Finally, a future study should investigate factors associated with functional outcome in individuals with central cord syndrome and without spinal instability since they were excluded from this study." (Lines 247-249, Study limitations section).*

Materials and Methods:

Please use ISNCSCI not ASIA.

- **Please replace reference no 18 with: "Kirshblum SC, Burns SP, Biering-Sorensen F, et al. International standards for neurological classification of spinal cord injury (Revised 2011). *The Journal of Spinal Cord Medicine*. 2011;34(6):535-546.»**

Thank you for the comment, we agree with the reviewer and the reference was replaced and AIS abbreviation was replaced by the ISNCSCI in the revised manuscript.

Results:

The results are clearly presented.

Discussion:

The discussion is sufficient.

Conclusion:

The conclusion is sound.

Figure and Tables:

The paper includes 1 Figure and 5 Tables which all add to the paper.

- **Please add an explanation to ISS at the end of Table 5**

The definition of ISS was add in the Table 5's legend.

References:

The references are up-to-date and relevant.

References

Baker SP, O'Neill B, Haddon W, Jr., Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma. 1974 Mar;14(3):187-96.

Thompson C, Mutch J, Parent S, Mac-Thiong JM. The changing demographics of traumatic spinal cord injury: An 11-year study of 831 patients. JSCM 2015; 38(2): 214-223.

Tabachnick BG, Fidell LS. Using multivariate statistic (Fifth edition). Pearson publisher. 2012, 1024 pages.

Running head: Prediction of function following spinal cord injury

Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization

ABSTRACT

Objectives: To determine factors associated with functional status six months following a traumatic cervical and thoracic spinal cord injury (SCI), with a particular interest in factors related to the acute care hospitalization stay.

Design: This is a prospective cohort study. Sixteen potential predictive variables were studied. Univariate regression analyses were first performed to determine the strength of association of each variable independently with the total Spinal Cord Independence Measure (SCIM) score. Significant ones were then included in a General linear model in order to determine the most relevant predictive factors among them. Analyses were carried out separately for tetraplegia and paraplegia.

Setting: A single specialized Level I trauma center.

Participants: 159 patients hospitalized for an acute traumatic SCI between January 2010 and February 2015.

Interventions: Not applicable.

Main outcome measure: The SCIM (version 3) functional score.

Results: Motor-complete SCI (AIS-A,B) was the main predictive factor associated with decreased total SCIM score in tetraplegia and paraplegia. Longer acute care length of stay and the occurrence of acute medical complications (either pneumonia, urinary tract infections or pressure ulcers) were predictors of decreased functional outcome following tetraplegia, while increased

body mass index and higher trauma severity were predictive of decreased functional outcome following paraplegia.

Conclusions: This study supports previous work while adding information regarding the importance of optimizing acute care hospitalization as it may influence chronic functional status following traumatic SCI.

Keywords

Spinal cord injuries; prediction; function; acute; trauma

Abbreviations

T-SCI, traumatic spinal cord injury

ISNCSCI, International Standards for Neurological Classification of Spinal Cord Injury

ASIA, American Spinal Injury Association

LOS, Length of stay

1 INTRODUCTION

2

3 The occurrence of traumatic spinal cord injury (T-SCI) may be devastating as it is associated with
 4 significant permanent functional disabilities. Prediction of function is important after a T-SCI in
 5 order to improve patient's care, plan rehabilitation and better optimize resources utilization.
 6 However, reliably predicting functional outcome following acute SCI remains difficult. Failure
 7 to consider various clinical factors influencing the acute care hospitalization and to underline the
 8 most relevant factors among them may contribute to that issue.

9

10 Previous studies agree that the severity of the T-SCI at initial presentation is the main factor
 11 associated with neurologic and functional outcomes, with complete SCI predicting worse
 12 outcome¹⁻⁵. The impact of other clinical and socio-demographic characteristics, such as the level
 13 of the SCI or age, is debated^{1, 2, 5, 6}. While most predictive factors of functional recovery
 14 following SCI are non-modifiable, potential modifiable predictors, such as clinical events
 15 occurring during the course of the acute care hospitalization may be of importance. In addition,
 16 the surgical planning⁷⁻¹¹, the development of early spasticity^{12, 13}, the occurrence of medical
 17 complications and the acute care length of stay (LOS)¹⁴ were suggested to influence the
 18 rehabilitation process and/or the neurological recovery. However, there is no study to date that
 19 has considered factors related to the acute care hospitalization process in a prediction model of
 20 functional outcome.

21

22 Previous studies predicting functional recovery are based on general functional outcome scales,
 23 such as the Functional Independence Measure (FIM) or the Glasgow Outcome Scale (GOS)^{1, 4, 15},
 24 ¹⁶. Unfortunately, these instruments were not designed for evaluating individuals sustaining T-

SCI. The Spinal Cord Independence Measure (SCIM) was created to specifically assess functional outcome in individuals with SCI ¹⁷ and is more sensitive to change as compared to the FIM scale ¹⁷. The SCIM scale is now widely used and has demonstrated its consistent reliability, consistency and sensitivity to change ¹⁷.

The purpose of this study was to determine the impact of various socio-demographic and clinical characteristics collected during the acute care hospitalization on functional recovery after a T-SCI, as measured by the total SCIM score. Because tetraplegia and paraplegia may be associated with distinct outcome predictors, analyses were performed separately.

METHODS

Patients

This study consisted in a review of a prospective database collected in a single Level-1 trauma center specialized in spinal cord injury (SCI) care. A total of 159 adult patients with acute T-SCI from C1 to L1 consecutively admitted between January 2010 and February 2015 (126 males and 33 females; 46.2 ± 20.0 years old) were included. Patients without overt spinal instability or central cord syndrome were excluded because these individuals typically present distinct outcome. This study was approved by the institutional review board and all patients were enrolled on a voluntary basis during the acute hospitalization. Patients were included in the study if they were seen at the routine follow-up visit planned 6 months after the trauma. Data collection was performed by researcher assistants not involved in the present study.

Data collection

Information pertaining to the age, gender, body mass index (BMI), trauma severity measured by the Injury Severity Score (ISS), presence of a high velocity trauma (defined as the occurrence of a SCI in the context of any motor vehicle accident), as well as presence of a concomitant traumatic brain injury (TBI) were collected. The ISS is a simple method describing patients with multiple traumatic injuries. It corresponds to an anatomical scoring system where each injury is assigned to a specific score according to its severity and location. The ISS takes values from 0 to 75.¹⁸ The presence of moderate and severe TBI was also specifically noted. The severity of the traumatic brain injuries (TBI) was based on the Glasgow Coma Scale (GCS) in the first 48 hours following the injury. A GCS score of 9 to 12 refers to moderate TBI, while a GCS of 3 to 8 refers to severe TBI.

The neurologic evaluation was performed based on the recommendation of the American Spinal Cord Injury Association (ASIA) upon admission for all patients and was characterized using the neurologic level of the injury (NLI) defined as the most caudal level with preserved normal sensation and motor function. Then, the NLI was dichotomized for tetraplegia as high (C1 to C4) vs. low cervical (C5 to T1) and for paraplegia as high (T2-T7) vs. low thoracic/lumbar (T8-L1).

The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) was used to determine the severity of the SCI and was dichotomized as motor-complete (AIS-A or B) or incomplete (AIS-C or D) injury. The ISNCSCI motor score was also noted, with a higher score designating higher motor strength¹⁹.

Clinical factors collected during the course of acute care hospitalization were also collected. First, the occurrence of non-neurological complications (pneumonias, urinary tract infections (UTI) and pressure ulcers (PU)) was noted, since they are the most prevalent complications occurring after a T-SCI¹⁰. Pneumonia was diagnosed using clinical features and confirmed by a radiologist using chest X-rays²⁰. UTI were diagnosed using criteria from the 2006 Consortium for Spinal Cord Medicine Guidelines for healthcare providers²¹; and PU were diagnosed using clinical guidelines defined by the National Pressure Ulcer Advisory Panel (NPUAP)²². The occurrence of any of these complications during the acute care hospitalization as well as the occurrence of multiple complications (two or more) was noted.

Then, the development of spasticity during the course of acute care hospitalization also was noted based on physical findings and symptoms reported by the patient^{23, 24}, and required two of the following three criteria: 1) presence of increased velocity-dependant muscle tone at physical examination (Modified Ashworth scale score >1), 2) spasm and/or clonus noted at physical

examination, and 3) spasm and/or clonus reported by the patient. The acute care LOS was defined as the number of days between admission and discharge from the acute care center. Finally, the delay of surgery designated the interval of time between the injury and time of incision (in hours) and was dichotomized into early (<24h post-trauma) and late surgery ($\geq$ 24h post-trauma).

Outcome variables

The functional outcome corresponds to the primary outcome in this study and was evaluated six months after the trauma using the Spinal Cord Independence Measure Scale (SCIM, version III)¹⁷. The SCIM evaluates three different areas of function: self-care (subscore 0-20), respiration and sphincter management (0-40) and mobility and transfers (0-40). The total score can reach 100 points with a higher score corresponding to a higher level of autonomy.

Analysis

IBM SPSS Statistics Version 19 software package was used for our statistical analyses. Our cohort was described using means $\pm$ standard deviation for continuous variables, and proportions or percentages for categorical variables.

All analyses were performed separately for individuals sustaining tetraplegia and paraplegia regardless of the level of the injury. Independent variables initially considered as potential outcome predictors are showed in Table 1. Univariate linear regression analyses were used to determine the strength of association between each independent variable and the total SCIM score (dependant variable), in order to reduce the number of variables to a smaller and relevant subset of outcome predictors to be introduced into the prediction model. Considering the high number of tests performed at this preliminary step, a level of significance was set at 0.1.

Considering that the reduced set of independent variables could contain collinear variables, Pearson correlations were used following the univariate regression analyses, and collinearity was confirmed when a level of significance of 0.7 was reached. In the presence of collinearity between two independent variables, the variable with the smallest p-value from the univariate regression analyses was included in the General linear model (GLM) as a potential predictor of the total SCIM score.²⁵ Independent variables that were finally included in each GLMs (for paraplegia and tetraplegia) are indicated by an “x” in Table 1. The association between the independent variables and the total SCIM score in the GLM was expressed in terms of beta (β) coefficients with 95% confidence interval (CI), and the R^2 was used as an indicator of the percentage of the variability explained by each model.

RESULTS

From the 159 patients initially enrolled in our study, 71 did not come to their 6-month follow-up or withdrew from the study. Thus, a total of 88 patients were included in our analyses (Figure 1), including 43 patients with tetraplegia and 45 patients with paraplegia. Table 2 presents the socio-demographic and clinical characteristics of patients with tetraplegia and paraplegia. Considering the high number of patients excluded from the study due to missing 6-month follow-up, comparisons were made between included and excluded patients to ensure that their baseline characteristics were similar, and rule out the presence of a major selection bias (Table 3).

Prediction of function for patients with tetraplegia

Four potential predictive factors were included in the GLM (Table 1): AIS grade, occurrence of complications, presence of early spasticity and LOS. The three following variables were excluded from the GLM for collinearity issue: presence of multiple complications, AIS motor score and the ISS. In the end, motor-complete SCI (AIS A or B), the occurrence of complications and longer acute care hospitalization stay were significantly associated with a decreased total SCIM score (Table 4). This model explained 67 percent of the variability of the total SCIM score ($R^2=0,671$).

Prediction of function for patients with paraplegia

Four independent variables were included in the GLM (Table 1): the AIS grade, BMI, trauma severity (ISS) and presence of early spasticity based on the simple regression linear analyses. The AIS motor score was excluded because of its collinearity with the AIS grade. Motor-complete SCI (AIS A or B), higher BMI and ISS were significantly associated with a decreased total SCIM

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score (Table 5). This model explained nearly 55 percent of the variability of the total SCIM score
($R^2=0,548$).

DISCUSSION

Health professionals working with individuals sustaining SCI should benefit from early identification of predictors of mid to long-term function to allow better communication with the patient and its relatives, promote efficient coordinated care and optimize resources utilization.

This study identified relevant acute clinical factors associated with function six-months after a T-SCI, accounting for various factors specific to individuals sustaining tetraplegia and paraplegia during acute care hospitalization.

The severity of the SCI remains the most important acute factor associated with chronic functional outcome following a cervical or thoracic SCI (Tables 4 and 5). The association of motor-complete SCI with total SCIM score was particularly strong, as shown by the beta coefficients in both models. This finding further supports previous work^{1, 5, 16} suggesting that a motor-complete SCI predicts limited neurological recovery²⁶, thereby leading to worst functional outcome^{2, 3}.

The occurrence of medical complications most frequently associated with T-SCI (pneumonia, UTI and PU) during the course of acute care hospitalization was also strongly associated with functional outcome six-months following tetraplegia. According to Table 2, pneumonias were the most frequent complication in this group. The occurrence of pneumonia may prolonged the intensive care stay, interfere the rehabilitation process and delay the mechanical weaning process.

It is recognized that the occurrence these complications in chronic SCI may interfere with the physical and social well-being²⁷. But this study also suggests that the occurrence of medical complications during the acute phase may still influence the functional outcome as far as six-

months post injury. Delay of the rehabilitation process and community reintegration may be possible consequences of acute care complications occurrence²⁸, particularly given that it also predisposes individuals with SCI at higher risk of chronic **recurrences**²⁹. However, it was not revealed as a predictive factor of function following paraplegia. Two hypotheses may be proposed to explain this. First, previous studies have suggested that individuals sustaining tetraplegia may suffer from a higher number and increased severity of complications compared to patients with paraplegia³⁰⁻³³, which could further limit their functional recovery. **However, although severity of complications was not assessed in this study, additional analysis did not revealed any difference between in the number of complications between the two groups (p-values of 0.1, 0.4 and 0.3 for pneumonia, urinary tract infection and pressure ulcer respectively).**

Then, it is possible that the timing of follow-up may explain our results. Indeed, as individuals with tetraplegia generally required longer acute care and inpatient rehabilitation hospitalization stay compared to paraplegic patients^{34, 35}, any significant delay in the process (such as the occurrence of medical complications) could therefore have underestimate functional results collected only six-months post-injury. It is therefore possible that a prolonged follow-up up to a point where the functional rehabilitation would be completed for all tetraplegic patients (e.g. at one year post-injury) would negate the impact of acute care medical complications on function. Nevertheless, early pro-active management towards the prevention of secondary conditions following SCI should not be overlook. As acute care specialized SCI-centers were showed to decrease the number and severity of complications³⁶, prompt transfer to SCI-centers, particularly following motor-complete tetraplegia, is recommended.

Longer acute care LOS was revealed as a significant factor associated with decreased total SCIM score following tetraplegia. However, describing the causal effect of longer acute care

hospitalization is tenuous as many confounding factors may interfere. Indeed, various variables such as the severity of the SCI, age, trauma severity, the occurrence of medical complications and surgical timing are some of the factors influencing the acute care LOS³⁷⁻³⁹. However, since these variables showed a weak correlation with the LOS, we might suggest that efficient transfer to inpatient rehabilitation facility following tetraplegia may optimize the long-term functional recovery independently of the factors studied in the present study, except for the trauma severity (ISS) which was significantly correlated (collinear) to the acute care LOS. But trauma severity was excluded from the general linear model because of its smaller significance with the outcome variable following the simple linear regression analysis. Therefore, higher trauma severity (ISS score) should be also considered as a potential factor associated with prolonged acute care LOS. Again, one efficient way to optimize the acute care LOS is early referral to a specialized SCI acute care center as shown in previous studies^{36, 40}.

While it is assumed that spasticity can alter functional outcome, it remains unproven¹³. Spasticity could potentially compensate for muscle weakness and ease mobility, but it can also interfere with movement, posture, sleeping, may be associated to pain and/or fatigue. Development of spasticity during the acute care stay was significantly associated with decreasing SCIM score in the univariate regression analyses, but it was not associated with the functional outcome when accounting for other covariates in our multivariate regression analyses, as showed in Table 4 and 5. However, the severity of the spasticity was not taken into account in this study, and investigating the association between the severity of spasticity and function should be addressed in a future study.

Increased BMI significantly decreased functional recovery in paraplegia, but not in tetraplegia (Tables 4 and 5). Overweight or obesity may represent an additional challenge for mobility and accomplishing activities of daily living. It is possible that BMI affects functional outcome specifically in patients with paraplegia as an increased body weight could limit the optimal use of upper extremities in tasks such as transfers, wheelchair propulsion or the use of technical aids. Moreover, obesity may increase respiratory dysfunction associated with SCI by aggravating restrictive pulmonary syndrome⁴¹, which in turn can alter general function. However, this variable had only a lower impact on the model as shown by its beta coefficient.

Finally, higher trauma severity (increased ISS) was significantly associated with decreased total SCIM score following paraplegia. Associated injuries may be associated with additional invasive treatments and functional limitations, which can delay rehabilitation and alter the functional recovery 6 months after the injury. Since the beta coefficient associated with trauma severity was relatively low for paraplegia and non significant for tetraplegia, it would also be interesting to assess the impact of ISS on function at later stage (1 year or more after injury), once all associated injuries have reached a chronic phase.

Study limitations

There are recognized limitations associated with this study. First, there was a significant loss to follow-up at 6 months. However, as shown in Table 3, baseline characteristics of patients lost to follow-up were similar to those completing the study, except for age. In addition to the SCI, older age is typically associated with decreased mobility, which may explain the difficulty to comply with scheduled postoperative visits for patients not seen at the 6-month follow-up. However, an interim analyses of 41 patients of the missing patients at 6 months but seen later at one year post-

injury showed that the results were similar, suggesting that there was no significant selection bias in the current study. The interval of six months was chosen in the present study as the vast majority of the recovery was shown to occur within the first three months following tetraplegia³ and generally reaches a plateau around six months post-injury to slow down thereafter^{2, 3, 42} and subsequently, the intensive functional rehabilitation is generally advanced or completed at this time⁴³. However, a future study evaluating predictors of functional outcome 12 months post injury will be done as soon as follow-up of patients will be completed.

Then, criteria used in the present study to define the occurrence of spasticity can be debated. Because the definition of spasticity and the agreement on clinical scales of spasticity vary widely, there is no reliable instrument to measure spasticity available. Although our criteria were based on the recent spasticity literature in terms of clinical measurement of spasticity^{23, 44} and the importance of patient's perception²⁴, strong validation studies are still lacking. Types of medical complications considered in this study are relatively small. Authors recognized that other complications and secondary conditions related or not to the SCI may have also influence outcome following SCI. Finally, a future study should investigate factors associated with functional outcome in individuals with central cord syndrome and without spinal instability since they were excluded from this study.

Conclusions

By using a specific functional outcome scale (SCIM scale) and by including various acute clinical factors potentially influencing the outcome, this study identifies relevant clinical predicting factors of functional outcome 6 months after the T-SCI causing tetraplegia and paraplegia. The severity of the SCI (ISNCSCI grade) remains the main predictive factor of global function six-months post injury regardless of the neurological level. Higher body mass index and increased burden of associated injuries (trauma severity) were predictive factors of worst functional outcome following paraplegia, while the occurrence of acute medical complications and longer acute care stay were significantly associated with worst functional outcome following tetraplegia. The optimization of acute care hospitalization may therefore significantly influence mid to long-term functional recovery and this might underline the importance of early referral to specialized SCI-centers particularly following acute traumatic cervical SCI.

References

1. Abdul-Sattar AB. Predictors of functional outcome in patients with traumatic spinal cord injury after inpatient rehabilitation: in Saudi Arabia. *NeuroRehabilitation*. 2014 Jan 1;35(2):341-7. PubMed PMID: 24990019.
2. Al-Habib AF, Attabib N, Ball J, Bajammal S, Casha S, Hurlbert RJ. Clinical predictors of recovery after blunt spinal cord trauma: systematic review. *Journal of neurotrauma*. 2011 Aug;28(8):1431-43. PubMed PMID: 19831845. Pubmed Central PMCID: 3143416.
3. Fawcett JW, Curt A, Steeves JD, Coleman WP, Tuszynski MH, Lammertse D, et al. Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. *Spinal cord*. 2007 Mar;45(3):190-205. PubMed PMID: 17179973.
4. Saboe LA, Darrah JM, Pain KS, Guthrie J. Early predictors of functional independence 2 years after spinal cord injury. *Archives of physical medicine and rehabilitation*. 1997 Jun;78(6):644-50. PubMed PMID: 9196473.
5. Wilson JR, Cadotte DW, Fehlings MG. Clinical predictors of neurological outcome, functional status, and survival after traumatic spinal cord injury: a systematic review. *Journal of neurosurgery Spine*. 2012 Sep;17(1 Suppl):11-26. PubMed PMID: 22985366.
6. Furlan JC, Bracken MB, Fehlings MG. Is age a key determinant of mortality and neurological outcome after acute traumatic spinal cord injury? *Neurobiol Aging*. 2010 Mar;31(3):434-46. PubMed PMID: 18550225.
7. Bourassa-Moreau E, Mac-Thiong JM, Li A, Ehrmann Feldman D, Gagnon DH, Thompson C, et al. Do Patients with Complete Spinal Cord Injury Benefit from Early Surgical Decompression? Analysis of Neurological Improvement in a Prospective Cohort Study. *Journal of neurotrauma*. 2016 Feb 1;33(3):301-6. PubMed PMID: 26494114.
8. van Middendorp JJ, Hosman AJ, Doi SA. The effects of the timing of spinal surgery after traumatic spinal cord injury: a systematic review and meta-analysis. *Journal of neurotrauma*. 2013 Nov 1;30(21):1781-94. PubMed PMID: 23815524.
9. Del Curto D, Tamaoki MJ, Martins DE, Puertas EB, Belloti JC. Surgical approaches for cervical spine facet dislocations in adults. *Cochrane Database Syst Rev*. 2014;10:CD008129. PubMed PMID: 25354696.
10. Bourassa-Moreau E, Mac-Thiong JM, Feldman DE, Thompson C, Parent S. Non-neurological outcomes after complete traumatic spinal cord injury: the impact of surgical timing. *Journal of neurotrauma*. 2013 Sep 15;30(18):1596-601. PubMed PMID: 23829420.
11. Luo J, Cao K, Huang S, Li L, Yu T, Cao C, et al. Comparison of anterior approach versus posterior approach for the treatment of multilevel cervical spondylotic myelopathy. *Eur Spine J*. 2015 Aug;24(8):1621-30. PubMed PMID: 25840781.
12. Bhimani R, Anderson L. Clinical understanding of spasticity: implications for practice. *Rehabil Res Pract*. 2014;2014:279175. PubMed PMID: 25276432. Pubmed Central PMCID: 4168242.
13. Pandyan AD, Gregoric M, Barnes MP, Wood D, Van Wijck F, Burrridge J, et al. Spasticity: clinical perceptions, neurological realities and meaningful measurement. *Disability and rehabilitation*. 2005 Jan 7-21;27(1-2):2-6. PubMed PMID: 15799140.
14. Street JT, Noonan VK, Cheung A, Fisher CG, Dvorak MF. Incidence of acute care adverse events and long-term health-related quality of life in patients with TSCI. *Spine J*. 2015 May 1;15(5):923-32. PubMed PMID: 23981816.

15. Tee JW, Chan PC, Fitzgerald MC, Liew SM, Rosenfeld JV. Early predictors of functional disability after spine trauma: a level 1 trauma center study. *Spine (Phila Pa 1976)*. 2013 May 20;38(12):999-1007. PubMed PMID: 23459136.
16. Wilson JR, Grossman RG, Frankowski RF, Kiss A, Davis AM, Kulkarni AV, et al. A clinical prediction model for long-term functional outcome after traumatic spinal cord injury based on acute clinical and imaging factors. *Journal of neurotrauma*. 2012 Sep;29(13):2263-71. PubMed PMID: 22709268. Pubmed Central PMCID: 3430477.
17. Catz A, Itzkovich M, Agranov E, Ring H, Tamir A. SCIM--spinal cord independence measure: a new disability scale for patients with spinal cord lesions. *Spinal cord*. 1997 Dec;35(12):850-6. PubMed PMID: 9429264.
18. Baker SP, O'Neill B, Haddon W, Jr., Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *J Trauma*. 1974 Mar;14(3):187-96. PubMed PMID: 4814394.
19. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, et al. International standards for neurological classification of spinal cord injury (revised 2011). *The journal of spinal cord medicine*. 2011 Nov;34(6):535-46. PubMed PMID: 22330108. Pubmed Central PMCID: 3232636.
20. Medicine CfSC. Respiratory management following spinal cord injury: a clinical practice guideline for health-care professionals. *J Spinal cord Med*. 2005;28:259-93.
21. Medicine CfSC. Bladder management for adults with adults with spinal cord injury: a clinical practice guideline for health-care providers. *J Spinal cord Med*. 2006;29(5):527-73.
22. NPUAP-EPUAP I. NPUAP pressure ulcer stages/categories. 2007.
23. Bhimani RH, Anderson LC, Henly SJ, Stoddard SA. Clinical measurement of limb spasticity in adults: state of the science. *J Neurosci Nurs*. 2011 Apr;43(2):104-15. PubMed PMID: 21488584.
24. Bhimani RH, McAlpine CP, Henly SJ. Understanding spasticity from patients' perspectives over time. *J Adv Nurs*. 2012 Nov;68(11):2504-14. PubMed PMID: 22339651.
25. Tabachnick BG, Fidell, Linda S. *Using Multivariate Statistics* (6th Edition): Pearson; 2012. 1024 p.
26. Kirshblum S, Botticello A, Lammertse DP, Marino RJ, Chiodo AE, Jha A. The impact of sacral sensory sparing in motor complete spinal cord injury. *Archives of physical medicine and rehabilitation*. 2011 Mar;92(3):376-83. PubMed PMID: 21353822. Pubmed Central PMCID: 3698852.
27. Consortium for Spinal Cord Medicine Clinical Practice G. Pressure ulcer prevention and treatment following spinal cord injury: a clinical practice guideline for health-care professionals. *The journal of spinal cord medicine*. 2001 Spring;24 Suppl 1:S40-101. PubMed PMID: 11958176.
28. Houghton PE CKaCP. Canadian Best Practice Guidelines for the Prevention and Management of Pressure Ulcers in People with Spinal Cord Injury. A resource handbook for Clinicians. <http://www.onf.org>2013.
29. Salzberg CA, Byrne DW, Cayten CG, van Niewerburgh P, Murphy JG, Viehbeck M. A new pressure ulcer risk assessment scale for individuals with spinal cord injury. *American journal of physical medicine & rehabilitation / Association of Academic Physiatrists*. 1996 Mar-Apr;75(2):96-104. PubMed PMID: 8630201.

30. Grossman RG, Frankowski RF, Burau KD, Toups EG, Crommett JW, Johnson MM, et al. Incidence and severity of acute complications after spinal cord injury. *Journal of neurosurgery Spine*. 2012 Sep;17(1 Suppl):119-28. PubMed PMID: 22985378.
31. Hagen EM. Acute complications of spinal cord injuries. *World journal of orthopedics*. 2015 Jan 18;6(1):17-23. PubMed PMID: 25621207. Pubmed Central PMCID: 4303786.
32. Consortium for Spinal Cord M. Early acute management in adults with spinal cord injury: a clinical practice guideline for health-care professionals. *The journal of spinal cord medicine*. 2008;31(4):403-79. PubMed PMID: 18959359. Pubmed Central PMCID: 2582434.
33. Ropper AE, Neal MT, Theodore N. Acute management of traumatic cervical spinal cord injury. *Practical neurology*. 2015 Aug;15(4):266-72. PubMed PMID: 25986457.
34. Information ClfH. Life after traumatic spinal cord injury: From inpatient rehabilitation back to the community. *Analysis in Brief*. 2006.
35. Information ClfH. Inpatient rehabilitation in Canada 2004-2005. 2006.
36. Parent S, Barchi S, LeBreton M, Casha S, Fehlings MG. The impact of specialized centers of care for spinal cord injury on length of stay, complications, and mortality: a systematic review of the literature. *Journal of neurotrauma*. 2011 Aug;28(8):1363-70. PubMed PMID: 21410318. Pubmed Central PMCID: 3143414.
37. Radhakrishna M, Makriyianni I, Marcoux J, Zhang X. Effects of injury level and severity on direct costs of care for acute spinal cord injury. *Int J Rehabil Res*. 2014 Dec;37(4):349-53. PubMed PMID: 25192008.
38. Mac-Thiong JM, Feldman DE, Thompson C, Bourassa-Moreau E, Parent S. Does timing of surgery affect hospitalization costs and length of stay for acute care following a traumatic spinal cord injury? *Journal of neurotrauma*. 2012 Dec 10;29(18):2816-22. PubMed PMID: 22920942.
39. Tator CH, Duncan EG, Edmonds VE, Lapczak LI, Andrews DF. Complications and costs of management of acute spinal cord injury. *Paraplegia*. 1993 Nov;31(11):700-14. PubMed PMID: 8295780.
40. Tator CH, Duncan EG, Edmonds VE, Lapczak LI, Andrews DF. Neurological recovery, mortality and length of stay after acute spinal cord injury associated with changes in management. *Paraplegia*. 1995 May;33(5):254-62. PubMed PMID: 7630650.
41. Gater DR, Jr. Obesity after spinal cord injury. *Physical medicine and rehabilitation clinics of North America*. 2007 May;18(2):333-51, vii. PubMed PMID: 17543776.
42. Ditunno JF, Jr. The John Stanley Coulter Lecture. Predicting recovery after spinal cord injury: a rehabilitation imperative. *Archives of physical medicine and rehabilitation*. 1999 Apr;80(4):361-4. PubMed PMID: 10206595.
43. Eastwood EA, Hagglund KJ, Ragnarsson KT, Gordon WA, Marino RJ. Medical rehabilitation length of stay and outcomes for persons with traumatic spinal cord injury--1990-1997. *Archives of physical medicine and rehabilitation*. 1999 Nov;80(11):1457-63. PubMed PMID: 10569441.
44. Fleuren JF, Voerman GE, Erren-Wolters CV, Snoek GJ, Rietman JS, Hermens HJ, et al. Stop using the Ashworth Scale for the assessment of spasticity. *J Neurol Neurosurg Psychiatry*. 2010 Jan;81(1):46-52. PubMed PMID: 19770162.

Table 1: Potential predictive variable associated with function six-months posttraumatic SCI

<i>Potential predictive variable</i>	<i>Input variable for multivariate analysis</i>		<i>Coding</i>
	<i>Tetraplegia</i>	<i>Paraplegia</i>	
1. Surgical delay			<24h post-trauma >24h post-trauma
2. Early spasticity	x	x	Presence or not
3. Gender			Male or female
4. Age			As continuous data
5. Body mass index		x	As continuous data
6. Smoking status			Active smoker Past or non-smoker
7. Mechanism of traumatic injury			High-velocity trauma Non-high velocity trauma
8. Occurrence of medical complications	x		Presence or not
9. Occurrence of multiple complications			Presence or not
10. Initial ASIA Impairment Scale (AIS) grade	x	x	AIS grade A or B; no motor function is preserved in the sacral segments AIS grade C or D; motor function is preserved below the neurological level
11. Initial ASIA motor score			As continuous data
12. Acute care LOS	x		As continuous data
13. Presence of TBI			Presence or not
14. Presence of moderate or severe TBI			Presence or not
15. Initial neurologic level of the injury			High level <i>Tetraplegia: C1 to C4</i> <i>Paraplegia: T2 to T7</i> Low level <i>Tetraplegia: C4 to T1</i> <i>Paraplegia: T8 to L1</i>
16. Injury severity score (ISS)		x	Continuous data

ASIA, American Spinal Injury Association; TBI, Traumatic brain injury; LOS, Length of stay
 “x” indicates that this variable was included in the multivariate linear analysis.

Table 2: Socio-demographic and clinical characteristics at hospital admission for individuals with tetraplegia and paraplegia (N=88)

<i>Characteristics</i>	<i>Tetraplegia N=43</i>	<i>Paraplegia N=45</i>
ASIA grade		
<i>AIS-A,B</i>	65,1%	82,2%
<i>AIS-C,D</i>	34,9%	17,8%
Neurologic level		
<i>High tetraplegia (C1-C4)</i>	39,5%	---
<i>Low tetraplegia (C5-T1)</i>	60,5%	---
<i>High paraplegia (T2-T7)</i>	--	22,2%
<i>Low paraplegia (T8-L1)</i>	--	77,8%
ASIA motor score (<i>mean +/-SD</i>)	38,1 (30,1)	59,0 (16,7)
Age (<i>mean +/-SD</i>)	44,3 (17,2)	40,0 (15,6)
Gender (% Male)	74,4%	86,7%
ISS (<i>mean +/-SD</i>)	25,7 (14,1)	27,2 (7,7)
BMI (<i>mean +/-SD</i>)	27,4 (10,2)	25,5 (4,0)
Presence of TBI	53,5%	37,8%
Presence of moderate or severe TBI	2,3%	6,7%
Early surgery (<24h post-trauma)	97,7%	97,8%
Acute care LOS (<i>in days</i>) (<i>mean +/-SD</i>)	32,7 (26,0)	27,9 (16,8)
Presence of medical complications	58,5%	40,0%
Pneumonia	37.2%	20.0%
Urinary tract infection	23.3%	15.6%
Pressure ulcer	30.2%	20.0%
Presence of multiple complications	23,3%	15,6%
Presence of early spasticity	74,4%	48,9%
Smoking status (% active smoker)	25,6%	31,1%
High-velocity trauma mechanism	41,9%	33,3%

ISS: Injury Severity Score; BMI, Body Mass Index; TBI: Traumatic brain injury; LOS: Length of stay

Table 3: Comparison of socio-demographic and clinical characteristics at hospital admission between individuals that have and have not completed follow-up six-months post injury (N=164).

<i>Characteristics</i>	<i>Patients with 6 months FU N=88</i>	<i>Patients excluded N=71</i>	<i>p-value</i>
ASIA grade			
<i>AIS-A,B</i>	73,9%	61,4%	0,12
<i>AIS-C,D</i>	26,1%	38,6%	
Neurologic level			
<i>High tetraplegia (C1-C4)</i>	19,3%	26,8%	0,34
<i>Low tetraplegia (C5-T1)</i>	29,5%	31,0%	0,86
<i>High paraplegia (T2-T7)</i>	11,4%	9,9%	0,80
<i>Low paraplegia (T8-L1)</i>	39,8%	32,4%	0,41
ASIA motor score (<i>mean +/-SD</i>)	49,2 (26,0)	51,1 (26,0)	0,99
Age (<i>mean +/-SD</i>)	42,1 (16,5)	51,2 (22,7)	<10 ⁻³ *
Gender (% Male)	80,7%	77,5%	0,70
ISS (<i>mean +/-SD</i>)	26,5 (11,1)	26,3 (10,7)	0,83
BMI (<i>mean +/-SD</i>)	26,4 (7,7)	26,8 (5,8)	0,99
Presence of TBI	45,5%	54,9%	0,27
Presence of moderate or severe TBI	4,5%	1,4%	0,38
Early surgery (<24h post-trauma)	100%	97,7%	0,50
Acute care LOS (<i>in days</i>) (<i>mean +/-SD</i>)	30,2 (21,8)	35,4 (30,1)	0,07
Presence of medical complications	53,2%	46,8%	0,63
Presence of multiple complications	19,3%	16,9%	0,84
Presence of early spasticity	61,4%	67,8%	0,49
Smoking status (% active smoker)	31,3%	22,6%	0,26
High-velocity trauma mechanism	37,5%	29,6%	0,32

ISS: Injury Severity Score; BMI, Body Mass Index; TBI: Traumatic brain injury; LOS: Length of stay

Table 4: Factors associated with the total SCIM score six-months post injury for patients with acute traumatic **tetraplegia** (N=43)

<i>Predictive variable</i>	Total SCIM score		
	β coefficient	95%CI	P-value
ASIA grade			
<i>AIS A-B</i>	-27,3	(-42,9;-11,8)	<10 ⁻³ *
<i>AIS C-D</i>	0 ^d		
Occurrence of complications	-22,7	(-37,6;-7,8)	<10 ⁻³ *
Acute care LOS	-0,3	(-0,6; -0,1)	0,02*
Presence of early spasticity	-2,5	(-19,3; 14,3)	0,77
R ² = 0.671			

0^d Reference category

ASIA, American Spinal Injury Association

LOS, Length of stay

Table 5: Factors associated with the total SCIM score six-months post injury for patients with acute traumatic **paraplegia** (N=45)

<i>Predictive variable</i>	Total SCIM score		
	β coefficient	95%CI	P-value
ASIA grade			
<i>AIS A-B</i>	-19,1	(-31,3;-6,9)	<10 ⁻³ *
<i>AIS C-D</i>	0 ^d		
BMI	-1,3	(-2,3;-0,4)	<10 ⁻³ *
ISS	-0,8	(-1,4; -0,2)	0,01*
Presence of early spasticity	-6,3	(-13,9;1,4)	0,11
R ² = 0.548			

0^d Reference category

ASIA, American Spinal Injury Association

BMI, Body Mass Index

ISS, Injury Severity Score

Running head: Prediction of function following spinal cord injury

Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization

ABSTRACT

Objectives: To determine factors associated with functional status six months following a traumatic cervical and thoracic spinal cord injury (SCI), with a particular interest in factors related to the acute care hospitalization stay.

Design: This is a prospective cohort study. Sixteen potential predictive variables were studied. Univariate regression analyses were first performed to determine the strength of association of each variable independently with the total Spinal Cord Independence Measure (SCIM) score. Significant ones were then included in a General linear model in order to determine the most relevant predictive factors among them. Analyses were carried out separately for tetraplegia and paraplegia.

Setting: A single specialized Level I trauma center.

Participants: 159 patients hospitalized for an acute traumatic SCI between January 2010 and February 2015.

Interventions: Not applicable.

Main outcome measure: The SCIM (version 3) functional score.

Results: Motor-complete SCI (AIS-A,B) was the main predictive factor associated with decreased total SCIM score in tetraplegia and paraplegia. Longer acute care length of stay and the occurrence of acute medical complications (either pneumonia, urinary tract infections or pressure ulcers) were predictors of decreased functional outcome following tetraplegia, while increased

body mass index and higher trauma severity were predictive of decreased functional outcome following paraplegia.

Conclusions: This study supports previous work while adding information regarding the importance of optimizing acute care hospitalization as it may influence chronic functional status following traumatic SCI.

Keywords

Spinal cord injuries; prediction; function; acute; trauma

Abbreviations

T-SCI, traumatic spinal cord injury

ISNCSCI, International Standards for Neurological Classification of Spinal Cord Injury

ASIA, American Spinal Injury Association

LOS, Length of stay

1 INTRODUCTION

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3 The occurrence of traumatic spinal cord injury (T-SCI) may be devastating as it is associated with
 4 significant permanent functional disabilities. Prediction of function is important after a T-SCI in
 5 order to improve patient's care, plan rehabilitation and better optimize resources utilization.
 6 However, reliably predicting functional outcome following acute SCI remains difficult. Failure
 7 to consider various clinical factors influencing the acute care hospitalization and to underline the
 8 most relevant factors among them may contribute to that issue.

9

10 Previous studies agree that the severity of the T-SCI at initial presentation is the main factor
 11 associated with neurologic and functional outcomes, with complete SCI predicting worse
 12 outcome¹⁻⁵. The impact of other clinical and socio-demographic characteristics, such as the level
 13 of the SCI or age, is debated^{1, 2, 5, 6}. While most predictive factors of functional recovery
 14 following SCI are non-modifiable, potential modifiable predictors, such as clinical events
 15 occurring during the course of the acute care hospitalization may be of importance. In addition,
 16 the surgical planning⁷⁻¹¹, the development of early spasticity^{12, 13}, the occurrence of medical
 17 complications and the acute care length of stay (LOS)¹⁴ were suggested to influence the
 18 rehabilitation process and/or the neurological recovery. However, there is no study to date that
 19 has considered factors related to the acute care hospitalization process in a prediction model of
 20 functional outcome.

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22 Previous studies predicting functional recovery are based on general functional outcome scales,
 23 such as the Functional Independence Measure (FIM) or the Glasgow Outcome Scale (GOS)^{1, 4, 15},
 24 ¹⁶. Unfortunately, these instruments were not designed for evaluating individuals sustaining T-

SCI. The Spinal Cord Independence Measure (SCIM) was created to specifically assess functional outcome in individuals with SCI¹⁷ and is more sensitive to change as compared to the FIM scale¹⁷. The SCIM scale is now widely used and has demonstrated its consistent reliability, consistency and sensitivity to change¹⁷.

The purpose of this study was to determine the impact of various socio-demographic and clinical characteristics collected during the acute care hospitalization on functional recovery after a T-SCI, as measured by the total SCIM score. Because tetraplegia and paraplegia may be associated with distinct outcome predictors, analyses were performed separately.

METHODS

Patients

This study consisted in a review of a prospective database collected in a single Level-1 trauma center specialized in spinal cord injury (SCI) care. A total of 159 adult patients with acute T-SCI from C1 to L1 consecutively admitted between January 2010 and February 2015 (126 males and 33 females; 46.2 ± 20.0 years old) were included. Patients without overt spinal instability or central cord syndrome were excluded because these individuals typically present distinct outcome. This study was approved by the institutional review board and all patients were enrolled on a voluntary basis during the acute hospitalization. Patients were included in the study if they were seen at the routine follow-up visit planned 6 months after the trauma. Data collection was performed by researcher assistants not involved in the present study.

Data collection

Information pertaining to the age, gender, body mass index (BMI), trauma severity measured by the Injury Severity Score (ISS), presence of a high velocity trauma (defined as the occurrence of a SCI in the context of any motor vehicle accident), as well as presence of a concomitant traumatic brain injury (TBI) were collected. The ISS is a simple method describing patients with multiple traumatic injuries. It corresponds to an anatomical scoring system where each injury is assigned to a specific score according to its severity and location. The ISS takes values from 0 to 75.¹⁸ The presence of moderate and severe TBI was also specifically noted. The severity of the traumatic brain injuries (TBI) was based on the Glasgow Coma Scale (GCS) in the first 48 hours following the injury. A GCS score of 9 to 12 refers to moderate TBI, while a GCS of 3 to 8 refers to severe TBI.

The neurologic evaluation was performed based on the recommendation of the American Spinal Cord Injury Association (ASIA) upon admission for all patients and was characterized using the neurologic level of the injury (NLI) defined as the most caudal level with preserved normal sensation and motor function. Then, the NLI was dichotomized for tetraplegia as high (C1 to C4) vs. low cervical (C5 to T1) and for paraplegia as high (T2-T7) vs. low thoracic/lumbar (T8-L1).

The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) was used to determine the severity of the SCI and was dichotomized as motor-complete (AIS-A or B) or incomplete (AIS-C or D) injury. The ISNCSCI motor score was also noted, with a higher score designating higher motor strength¹⁹.

Clinical factors collected during the course of acute care hospitalization were also collected. First, the occurrence of non-neurological complications (pneumonias, urinary tract infections (UTI) and pressure ulcers (PU)) was noted, since they are the most prevalent complications occurring after a T-SCI¹⁰. Pneumonia was diagnosed using clinical features and confirmed by a radiologist using chest X-rays²⁰. UTI were diagnosed using criteria from the 2006 Consortium for Spinal Cord Medicine Guidelines for healthcare providers²¹; and PU were diagnosed using clinical guidelines defined by the National Pressure Ulcer Advisory Panel (NPUAP)²². The occurrence of any of these complications during the acute care hospitalization as well as the occurrence of multiple complications (two or more) was noted.

Then, the development of spasticity during the course of acute care hospitalization also was noted based on physical findings and symptoms reported by the patient^{23, 24}, and required two of the following three criteria: 1) presence of increased velocity-dependant muscle tone at physical examination (Modified Ashworth scale score >1), 2) spasm and/or clonus noted at physical

examination, and 3) spasm and/or clonus reported by the patient. The acute care LOS was defined as the number of days between admission and discharge from the acute care center. Finally, the delay of surgery designated the interval of time between the injury and time of incision (in hours) and was dichotomized into early (<24h post-trauma) and late surgery ($\geq$ 24h post-trauma).

Outcome variables

The functional outcome corresponds to the primary outcome in this study and was evaluated six months after the trauma using the Spinal Cord Independence Measure Scale (SCIM, version III)¹⁷. The SCIM evaluates three different areas of function: self-care (subscore 0-20), respiration and sphincter management (0-40) and mobility and transfers (0-40). The total score can reach 100 points with a higher score corresponding to a higher level of autonomy.

Analysis

IBM SPSS Statistics Version 19 software package was used for our statistical analyses. Our cohort was described using means $\pm$ standard deviation for continuous variables, and proportions or percentages for categorical variables.

All analyses were performed separately for individuals sustaining tetraplegia and paraplegia regardless of the level of the injury. Independent variables initially considered as potential outcome predictors are showed in Table 1. Univariate linear regression analyses were used to determine the strength of association between each independent variable and the total SCIM score (dependant variable), in order to reduce the number of variables to a smaller and relevant subset of outcome predictors to be introduced into the prediction model. Considering the high number of tests performed at this preliminary step, a level of significance was set at 0.1.

RESULTS

From the 159 patients initially enrolled in our study, 71 did not come to their 6-month follow-up or withdrew from the study. Thus, a total of 88 patients were included in our analyses (Figure 1), including 43 patients with tetraplegia and 45 patients with paraplegia. Table 2 presents the socio-demographic and clinical characteristics of patients with tetraplegia and paraplegia. Considering the high number of patients excluded from the study due to missing 6-month follow-up, comparisons were made between included and excluded patients to ensure that their baseline characteristics were similar, and rule out the presence of a major selection bias (Table 3).

Prediction of function for patients with tetraplegia

Four potential predictive factors were included in the GLM (Table 1): AIS grade, occurrence of complications, presence of early spasticity and LOS. The three following variables were excluded from the GLM for collinearity issue: presence of multiple complications, AIS motor score and the ISS. In the end, motor-complete SCI (AIS A or B), the occurrence of complications and longer acute care hospitalization stay were significantly associated with a decreased total SCIM score (Table 4). This model explained 67 percent of the variability of the total SCIM score ($R^2=0,671$).

Prediction of function for patients with paraplegia

Four independent variables were included in the GLM (Table 1): the AIS grade, BMI, trauma severity (ISS) and presence of early spasticity based on the simple regression linear analyses. The AIS motor score was excluded because of its collinearity with the AIS grade. Motor-complete SCI (AIS A or B), higher BMI and ISS were significantly associated with a decreased total SCIM

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4 106 Considering that the reduced set of independent variables could contain collinear variables,
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6 107 Pearson correlations were used following the univariate regression analyses, and collinearity was
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9 108 confirmed when a level of significance of 0.7 was reached. In the presence of collinearity
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11 109 between two independent variables, the variable with the smallest p-value from the univariate
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14 110 regression analyses was included in the General linear model (GLM) as a potential predictor of
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16 111 the total SCIM score.²⁵ Independent variables that were finally included in each GLMs (for
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19 112 paraplegia and tetraplegia) are indicated by an “x” in Table 1. The association between the
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21 113 independent variables and the total SCIM score in the GLM was expressed in terms of beta (β)
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24 114 coefficients with 95% confidence interval (CI), and the R^2 was used as an indicator of the
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26 115 percentage of the variability explained by each model.
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score (Table 5). This model explained nearly 55 percent of the variability of the total SCIM score
($R^2=0,548$).

DISCUSSION

Health professionals working with individuals sustaining SCI should benefit from early identification of predictors of mid to long-term function to allow better communication with the patient and its relatives, promote efficient coordinated care and optimize resources utilization.

This study identified relevant acute clinical factors associated with function six-months after a T-SCI, accounting for various factors specific to individuals sustaining tetraplegia and paraplegia during acute care hospitalization.

The severity of the SCI remains the most important acute factor associated with chronic functional outcome following a cervical or thoracic SCI (Tables 4 and 5). The association of motor-complete SCI with total SCIM score was particularly strong, as shown by the beta coefficients in both models. This finding further supports previous work^{1, 5, 16} suggesting that a motor-complete SCI predicts limited neurological recovery²⁶, thereby leading to worst functional outcome^{2, 3}.

The occurrence of medical complications most frequently associated with T-SCI (pneumonia, UTI and PU) during the course of acute care hospitalization was also strongly associated with functional outcome six-months following tetraplegia. According to Table 2, pneumonias were the most frequent complication in this group. The occurrence of pneumonia may prolonged the intensive care stay, interfere the rehabilitation process and delay the mechanical weaning process. It is recognized that the occurrence these complications in chronic SCI may interfere with the physical and social well-being²⁷. But this study also suggests that the occurrence of medical complications during the acute phase may still influence the functional outcome as far as six-

months post injury. Delay of the rehabilitation process and community reintegration may be possible consequences of acute care complications occurrence²⁸, particularly given that it also predisposes individuals with SCI at higher risk of chronic recurrences²⁹. However, it was not revealed as a predictive factor of function following paraplegia. Two hypotheses may be proposed to explain this. First, previous studies have suggested that individuals sustaining tetraplegia may suffer from a higher number and increased severity of complications compared to patients with paraplegia³⁰⁻³³, which could further limit their functional recovery. However, although severity of complications was not assessed in this study, additional analysis did not revealed any difference between in the number of complications between the two groups (p-values of 0.1, 0.4 and 0.3 for pneumonia, urinary tract infection and pressure ulcer respectively). Then, it is possible that the timing of follow-up may explain our results. Indeed, as individuals with tetraplegia generally required longer acute care and inpatient rehabilitation hospitalization stay compared to paraplegic patients^{34,35}, any significant delay in the process (such as the occurrence of medical complications) could therefore have underestimate functional results collected only six-months post-injury. It is therefore possible that a prolonged follow-up up to a point where the functional rehabilitation would be completed for all tetraplegic patients (e.g. at one year post-injury) would negate the impact of acute care medical complications on function. Nevertheless, early pro-active management towards the prevention of secondary conditions following SCI should not be overlook. As acute care specialized SCI-centers were showed to decrease the number and severity of complications³⁶, prompt transfer to SCI-centers, particularly following motor-complete tetraplegia, is recommended.

Longer acute care LOS was revealed as a significant factor associated with decreased total SCIM score following tetraplegia. However, describing the causal effect of longer acute care

hospitalization is tenuous as many confounding factors may interfere. Indeed, various variables such as the severity of the SCI, age, trauma severity, the occurrence of medical complications and surgical timing are some of the factors influencing the acute care LOS³⁷⁻³⁹. However, since these variables showed a weak correlation with the LOS, we might suggest that efficient transfer to inpatient rehabilitation facility following tetraplegia may optimize the long-term functional recovery independently of the factors studied in the present study, except for the trauma severity (ISS) which was significantly correlated (collinear) to the acute care LOS. But trauma severity was excluded from the general linear model because of its smaller significance with the outcome variable following the simple linear regression analysis. Therefore, higher trauma severity (ISS score) should be also considered as a potential factor associated with prolonged acute care LOS. Again, one efficient way to optimize the acute care LOS is early referral to a specialized SCI acute care center as shown in previous studies^{36, 40}.

While it is assumed that spasticity can alter functional outcome, it remains unproven¹³. Spasticity could potentially compensate for muscle weakness and ease mobility, but it can also interfere with movement, posture, sleeping, may be associated to pain and/or fatigue. Development of spasticity during the acute care stay was significantly associated with decreasing SCIM score in the univariate regression analyses, but it was not associated with the functional outcome when accounting for other covariates in our multivariate regression analyses, as showed in Table 4 and 5. However, the severity of the spasticity was not taken into account in this study, and investigating the association between the severity of spasticity and function should be addressed in a future study.

Increased BMI significantly decreased functional recovery in paraplegia, but not in tetraplegia (Tables 4 and 5). Overweight or obesity may represent an additional challenge for mobility and accomplishing activities of daily living. It is possible that BMI affects functional outcome specifically in patients with paraplegia as an increased body weight could limit the optimal use of upper extremities in tasks such as transfers, wheelchair propulsion or the use of technical aids. Moreover, obesity may increase respiratory dysfunction associated with SCI by aggravating restrictive pulmonary syndrome⁴¹, which in turn can alter general function. However, this variable had only a lower impact on the model as shown by its beta coefficient.

Finally, higher trauma severity (increased ISS) was significantly associated with decreased total SCIM score following paraplegia. Associated injuries may be associated with additional invasive treatments and functional limitations, which can delay rehabilitation and alter the functional recovery 6 months after the injury. Since the beta coefficient associated with trauma severity was relatively low for paraplegia and non significant for tetraplegia, it would also be interesting to assess the impact of ISS on function at later stage (1 year or more after injury), once all associated injuries have reached a chronic phase.

Study limitations

There are recognized limitations associated with this study. First, there was a significant loss to follow-up at 6 months. However, as shown in Table 3, baseline characteristics of patients lost to follow-up were similar to those completing the study, except for age. In addition to the SCI, older age is typically associated with decreased mobility, which may explain the difficulty to comply with scheduled postoperative visits for patients not seen at the 6-month follow-up. However, an interim analyses of 41 patients of the missing patients at 6 months but seen later at one year post-

injury showed that the results were similar, suggesting that there was no significant selection bias in the current study. The interval of six months was chosen in the present study as the vast majority of the recovery was shown to occur within the first three months following tetraplegia³ and generally reaches a plateau around six months post-injury to slow down thereafter^{2, 3, 42} and subsequently, the intensive functional rehabilitation is generally advanced or completed at this time⁴³. However, a future study evaluating predictors of functional outcome 12 months post injury will be done as soon as follow-up of patients will be completed.

Then, criteria used in the present study to define the occurrence of spasticity can be debated. Because the definition of spasticity and the agreement on clinical scales of spasticity vary widely, there is no reliable instrument to measure spasticity available. Although our criteria were based on the recent spasticity literature in terms of clinical measurement of spasticity^{23, 44} and the importance of patient's perception²⁴, strong validation studies are still lacking. Types of medical complications considered in this study are relatively small. Authors recognized that other complications and secondary conditions related or not to the SCI may have also influence outcome following SCI. Finally, a future study should investigate factors associated with functional outcome in individuals with central cord syndrome and without spinal instability since they were excluded from this study.

Conclusions

By using a specific functional outcome scale (SCIM scale) and by including various acute clinical factors potentially influencing the outcome, this study identifies relevant clinical predicting factors of functional outcome 6 months after the T-SCI causing tetraplegia and paraplegia. The severity of the SCI (ISNCSCI grade) remains the main predictive factor of global function six-months post injury regardless of the neurological level. Higher body mass index and increased burden of associated injuries (trauma severity) were predictive factors of worst functional outcome following paraplegia, while the occurrence of acute medical complications and longer acute care stay were significantly associated with worst functional outcome following tetraplegia. The optimization of acute care hospitalization may therefore significantly influence mid to long-term functional recovery and this might underline the importance of early referral to specialized SCI-centers particularly following acute traumatic cervical SCI.

References

1. Abdul-Sattar AB. Predictors of functional outcome in patients with traumatic spinal cord injury after inpatient rehabilitation: in Saudi Arabia. *NeuroRehabilitation*. 2014 Jan 1;35(2):341-7. PubMed PMID: 24990019.
2. Al-Habib AF, Attabib N, Ball J, Bajammal S, Casha S, Hurlbert RJ. Clinical predictors of recovery after blunt spinal cord trauma: systematic review. *Journal of neurotrauma*. 2011 Aug;28(8):1431-43. PubMed PMID: 19831845. Pubmed Central PMCID: 3143416.
3. Fawcett JW, Curt A, Steeves JD, Coleman WP, Tuszynski MH, Lammertse D, et al. Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. *Spinal cord*. 2007 Mar;45(3):190-205. PubMed PMID: 17179973.
4. Saboe LA, Darrah JM, Pain KS, Guthrie J. Early predictors of functional independence 2 years after spinal cord injury. *Archives of physical medicine and rehabilitation*. 1997 Jun;78(6):644-50. PubMed PMID: 9196473.
5. Wilson JR, Cadotte DW, Fehlings MG. Clinical predictors of neurological outcome, functional status, and survival after traumatic spinal cord injury: a systematic review. *Journal of neurosurgery Spine*. 2012 Sep;17(1 Suppl):11-26. PubMed PMID: 22985366.
6. Furlan JC, Bracken MB, Fehlings MG. Is age a key determinant of mortality and neurological outcome after acute traumatic spinal cord injury? *Neurobiol Aging*. 2010 Mar;31(3):434-46. PubMed PMID: 18550225.
7. Bourassa-Moreau E, Mac-Thiong JM, Li A, Ehrmann Feldman D, Gagnon DH, Thompson C, et al. Do Patients with Complete Spinal Cord Injury Benefit from Early Surgical Decompression? Analysis of Neurological Improvement in a Prospective Cohort Study. *Journal of neurotrauma*. 2016 Feb 1;33(3):301-6. PubMed PMID: 26494114.
8. van Middendorp JJ, Hosman AJ, Doi SA. The effects of the timing of spinal surgery after traumatic spinal cord injury: a systematic review and meta-analysis. *Journal of neurotrauma*. 2013 Nov 1;30(21):1781-94. PubMed PMID: 23815524.
9. Del Curto D, Tamaoki MJ, Martins DE, Puertas EB, Belloti JC. Surgical approaches for cervical spine facet dislocations in adults. *Cochrane Database Syst Rev*. 2014;10:CD008129. PubMed PMID: 25354696.
10. Bourassa-Moreau E, Mac-Thiong JM, Feldman DE, Thompson C, Parent S. Non-neurological outcomes after complete traumatic spinal cord injury: the impact of surgical timing. *Journal of neurotrauma*. 2013 Sep 15;30(18):1596-601. PubMed PMID: 23829420.
11. Luo J, Cao K, Huang S, Li L, Yu T, Cao C, et al. Comparison of anterior approach versus posterior approach for the treatment of multilevel cervical spondylotic myelopathy. *Eur Spine J*. 2015 Aug;24(8):1621-30. PubMed PMID: 25840781.
12. Bhimani R, Anderson L. Clinical understanding of spasticity: implications for practice. *Rehabil Res Pract*. 2014;2014:279175. PubMed PMID: 25276432. Pubmed Central PMCID: 4168242.
13. Pandyan AD, Gregoric M, Barnes MP, Wood D, Van Wijck F, Burridge J, et al. Spasticity: clinical perceptions, neurological realities and meaningful measurement. *Disability and rehabilitation*. 2005 Jan 7-21;27(1-2):2-6. PubMed PMID: 15799140.
14. Street JT, Noonan VK, Cheung A, Fisher CG, Dvorak MF. Incidence of acute care adverse events and long-term health-related quality of life in patients with TSCI. *Spine J*. 2015 May 1;15(5):923-32. PubMed PMID: 23981816.

15. Tee JW, Chan PC, Fitzgerald MC, Liew SM, Rosenfeld JV. Early predictors of functional disability after spine trauma: a level 1 trauma center study. *Spine (Phila Pa 1976)*. 2013 May 20;38(12):999-1007. PubMed PMID: 23459136.
16. Wilson JR, Grossman RG, Frankowski RF, Kiss A, Davis AM, Kulkarni AV, et al. A clinical prediction model for long-term functional outcome after traumatic spinal cord injury based on acute clinical and imaging factors. *Journal of neurotrauma*. 2012 Sep;29(13):2263-71. PubMed PMID: 22709268. Pubmed Central PMCID: 3430477.
17. Catz A, Itzkovich M, Agranov E, Ring H, Tamir A. SCIM--spinal cord independence measure: a new disability scale for patients with spinal cord lesions. *Spinal cord*. 1997 Dec;35(12):850-6. PubMed PMID: 9429264.
18. Baker SP, O'Neill B, Haddon W, Jr., Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *J Trauma*. 1974 Mar;14(3):187-96. PubMed PMID: 4814394.
19. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, et al. International standards for neurological classification of spinal cord injury (revised 2011). *The journal of spinal cord medicine*. 2011 Nov;34(6):535-46. PubMed PMID: 22330108. Pubmed Central PMCID: 3232636.
20. Medicine CfSC. Respiratory management following spinal cord injury: a clinical practice guideline for health-care professionals. *J Spinal cord Med*. 2005;28:259-93.
21. Medicine CfSC. Bladder management for adults with adults with spinal cord injury: a clinical practice guideline for health-care providers. *J Spinal cord Med*. 2006;29(5):527-73.
22. NPUAP-EPUAP I. NPUAP pressure ulcer stages/categories. 2007.
23. Bhimani RH, Anderson LC, Henly SJ, Stoddard SA. Clinical measurement of limb spasticity in adults: state of the science. *J Neurosci Nurs*. 2011 Apr;43(2):104-15. PubMed PMID: 21488584.
24. Bhimani RH, McAlpine CP, Henly SJ. Understanding spasticity from patients' perspectives over time. *J Adv Nurs*. 2012 Nov;68(11):2504-14. PubMed PMID: 22339651.
25. Tabachnick BG, Fidell, Linda S. *Using Multivariate Statistics* (6th Edition): Pearson; 2012. 1024 p.
26. Kirshblum S, Botticello A, Lammertse DP, Marino RJ, Chiodo AE, Jha A. The impact of sacral sensory sparing in motor complete spinal cord injury. *Archives of physical medicine and rehabilitation*. 2011 Mar;92(3):376-83. PubMed PMID: 21353822. Pubmed Central PMCID: 3698852.
27. Consortium for Spinal Cord Medicine Clinical Practice G. Pressure ulcer prevention and treatment following spinal cord injury: a clinical practice guideline for health-care professionals. *The journal of spinal cord medicine*. 2001 Spring;24 Suppl 1:S40-101. PubMed PMID: 11958176.
28. Houghton PE CKaCP. Canadian Best Practice Guidelines for the Prevention and Management of Pressure Ulcers in People with Spinal Cord Injury. A resource handbook for Clinicians. <http://www.onf.org>2013.
29. Salzberg CA, Byrne DW, Cayten CG, van Niewerburgh P, Murphy JG, Viehbeck M. A new pressure ulcer risk assessment scale for individuals with spinal cord injury. *American journal of physical medicine & rehabilitation / Association of Academic Physiatrists*. 1996 Mar-Apr;75(2):96-104. PubMed PMID: 8630201.

30. Grossman RG, Frankowski RF, Burau KD, Toups EG, Crommett JW, Johnson MM, et al. Incidence and severity of acute complications after spinal cord injury. *Journal of neurosurgery Spine*. 2012 Sep;17(1 Suppl):119-28. PubMed PMID: 22985378.
31. Hagen EM. Acute complications of spinal cord injuries. *World journal of orthopedics*. 2015 Jan 18;6(1):17-23. PubMed PMID: 25621207. Pubmed Central PMCID: 4303786.
32. Consortium for Spinal Cord M. Early acute management in adults with spinal cord injury: a clinical practice guideline for health-care professionals. *The journal of spinal cord medicine*. 2008;31(4):403-79. PubMed PMID: 18959359. Pubmed Central PMCID: 2582434.
33. Ropper AE, Neal MT, Theodore N. Acute management of traumatic cervical spinal cord injury. *Practical neurology*. 2015 Aug;15(4):266-72. PubMed PMID: 25986457.
34. Information ClfH. Life after traumatic spinal cord injury: From inpatient rehabilitation back to the community. *Analysis in Brief*. 2006.
35. Information ClfH. Inpatient rehabilitation in Canada 2004-2005. 2006.
36. Parent S, Barchi S, LeBreton M, Casha S, Fehlings MG. The impact of specialized centers of care for spinal cord injury on length of stay, complications, and mortality: a systematic review of the literature. *Journal of neurotrauma*. 2011 Aug;28(8):1363-70. PubMed PMID: 21410318. Pubmed Central PMCID: 3143414.
37. Radhakrishna M, Makriyianni I, Marcoux J, Zhang X. Effects of injury level and severity on direct costs of care for acute spinal cord injury. *Int J Rehabil Res*. 2014 Dec;37(4):349-53. PubMed PMID: 25192008.
38. Mac-Thiong JM, Feldman DE, Thompson C, Bourassa-Moreau E, Parent S. Does timing of surgery affect hospitalization costs and length of stay for acute care following a traumatic spinal cord injury? *Journal of neurotrauma*. 2012 Dec 10;29(18):2816-22. PubMed PMID: 22920942.
39. Tator CH, Duncan EG, Edmonds VE, Lapczak LI, Andrews DF. Complications and costs of management of acute spinal cord injury. *Paraplegia*. 1993 Nov;31(11):700-14. PubMed PMID: 8295780.
40. Tator CH, Duncan EG, Edmonds VE, Lapczak LI, Andrews DF. Neurological recovery, mortality and length of stay after acute spinal cord injury associated with changes in management. *Paraplegia*. 1995 May;33(5):254-62. PubMed PMID: 7630650.
41. Gater DR, Jr. Obesity after spinal cord injury. *Physical medicine and rehabilitation clinics of North America*. 2007 May;18(2):333-51, vii. PubMed PMID: 17543776.
42. Ditunno JF, Jr. The John Stanley Coulter Lecture. Predicting recovery after spinal cord injury: a rehabilitation imperative. *Archives of physical medicine and rehabilitation*. 1999 Apr;80(4):361-4. PubMed PMID: 10206595.
43. Eastwood EA, Hagglund KJ, Ragnarsson KT, Gordon WA, Marino RJ. Medical rehabilitation length of stay and outcomes for persons with traumatic spinal cord injury--1990-1997. *Archives of physical medicine and rehabilitation*. 1999 Nov;80(11):1457-63. PubMed PMID: 10569441.
44. Fleuren JF, Voerman GE, Erren-Wolters CV, Snoek GJ, Rietman JS, Hermens HJ, et al. Stop using the Ashworth Scale for the assessment of spasticity. *J Neurol Neurosurg Psychiatry*. 2010 Jan;81(1):46-52. PubMed PMID: 19770162.

Table 1: Potential predictive variable associated with function six-months posttraumatic SCI

<i>Potential predictive variable</i>	<i>Input variable for multivariate analysis</i>		<i>Coding</i>
	<i>Tetraplegia</i>	<i>Paraplegia</i>	
1. Surgical delay			<24h post-trauma >24h post-trauma
2. Early spasticity	x	x	Presence or not
3. Gender			Male or female
4. Age			As continuous data
5. Body mass index		x	As continuous data
6. Smoking status			Active smoker Past or non-smoker
7. Mechanism of traumatic injury			High-velocity trauma Non-high velocity trauma
8. Occurrence of medical complications	x		Presence or not
9. Occurrence of multiple complications			Presence or not
10. Initial ASIA Impairment Scale (AIS) grade	x	x	AIS grade A or B; no motor function is preserved in the sacral segments AIS grade C or D; motor function is preserved below the neurological level
11. Initial ASIA motor score			As continuous data
12. Acute care LOS	x		As continuous data
13. Presence of TBI			Presence or not
14. Presence of moderate or severe TBI			Presence or not
15. Initial neurologic level of the injury			High level <i>Tetraplegia: C1 to C4</i> <i>Paraplegia: T2 to T7</i> Low level <i>Tetraplegia: C4 to T1</i> <i>Paraplegia: T8 to L1</i>
16. Injury severity score (ISS)		x	Continuous data

ASIA, American Spinal Injury Association; TBI, Traumatic brain injury; LOS, Length of stay
 “x” indicates that this variable was included in the multivariate linear analysis.

Table 2: Socio-demographic and clinical characteristics at hospital admission for individuals with tetraplegia and paraplegia (N=88)

<i>Characteristics</i>	<i>Tetraplegia N=43</i>	<i>Paraplegia N=45</i>
ASIA grade		
<i>AIS-A,B</i>	65,1%	82,2%
<i>AIS-C,D</i>	34,9%	17,8%
Neurologic level		
<i>High tetraplegia (C1-C4)</i>	39,5%	---
<i>Low tetraplegia (C5-T1)</i>	60,5%	---
<i>High paraplegia (T2-T7)</i>	--	22,2%
<i>Low paraplegia (T8-L1)</i>	--	77,8%
ASIA motor score (<i>mean +/-SD</i>)	38,1 (30,1)	59,0 (16,7)
Age (<i>mean +/-SD</i>)	44,3 (17,2)	40,0 (15,6)
Gender (% Male)	74,4%	86,7%
ISS (<i>mean +/-SD</i>)	25,7 (14,1)	27,2 (7,7)
BMI (<i>mean +/-SD</i>)	27,4 (10,2)	25,5 (4,0)
Presence of TBI	53,5%	37,8%
Presence of moderate or severe TBI	2,3%	6,7%
Early surgery (<24h post-trauma)	97,7%	97,8%
Acute care LOS (<i>in days</i>) (<i>mean +/-SD</i>)	32,7 (26,0)	27,9 (16,8)
Presence of medical complications	58,5%	40,0%
Pneumonia	37.2%	20.0%
Urinary tract infection	23.3%	15.6%
Pressure ulcer	30.2%	20.0%
Presence of multiple complications	23,3%	15,6%
Presence of early spasticity	74,4%	48,9%
Smoking status (% active smoker)	25,6%	31,1%
High-velocity trauma mechanism	41,9%	33,3%

ISS: Injury Severity Score; BMI, Body Mass Index; TBI: Traumatic brain injury; LOS: Length of stay

Table 3: Comparison of socio-demographic and clinical characteristics at hospital admission between individuals that have and have not completed follow-up six-months post injury (N=164).

<i>Characteristics</i>	<i>Patients with 6 months FU N=88</i>	<i>Patients excluded N=71</i>	<i>p-value</i>
ASIA grade			
<i>AIS-A,B</i>	73,9%	61,4%	0,12
<i>AIS-C,D</i>	26,1%	38,6%	
Neurologic level			
<i>High tetraplegia (C1-C4)</i>	19,3%	26,8%	0,34
<i>Low tetraplegia (C5-T1)</i>	29,5%	31,0%	0,86
<i>High paraplegia (T2-T7)</i>	11,4%	9,9%	0,80
<i>Low paraplegia (T8-L1)</i>	39,8%	32,4%	0,41
ASIA motor score (<i>mean +/-SD</i>)	49,2 (26,0)	51,1 (26,0)	0,99
Age (<i>mean +/-SD</i>)	42,1 (16,5)	51,2 (22,7)	<10 ⁻³ *
Gender (% Male)	80,7%	77,5%	0,70
ISS (<i>mean +/-SD</i>)	26,5 (11,1)	26,3 (10,7)	0,83
BMI (<i>mean +/-SD</i>)	26,4 (7,7)	26,8 (5,8)	0,99
Presence of TBI	45,5%	54,9%	0,27
Presence of moderate or severe TBI	4,5%	1,4%	0,38
Early surgery (<24h post-trauma)	100%	97,7%	0,50
Acute care LOS (<i>in days</i>) (<i>mean +/-SD</i>)	30,2 (21,8)	35,4 (30,1)	0,07
Presence of medical complications	53,2%	46,8%	0,63
Presence of multiple complications	19,3%	16,9%	0,84
Presence of early spasticity	61,4%	67,8%	0,49
Smoking status (% active smoker)	31,3%	22,6%	0,26
High-velocity trauma mechanism	37,5%	29,6%	0,32

ISS: Injury Severity Score; BMI, Body Mass Index; TBI: Traumatic brain injury; LOS: Length of stay

Table 4: Factors associated with the total SCIM score six-months post injury for patients with acute traumatic **tetraplegia** (N=43)

<i>Predictive variable</i>	Total SCIM score		
	β coefficient	95%CI	P-value
ASIA grade			
<i>AIS A-B</i>	-27,3	(-42,9;-11,8)	<10 ⁻³ *
<i>AIS C-D</i>	0 ^d		
Occurrence of complications	-22,7	(-37,6;-7,8)	<10 ⁻³ *
Acute care LOS	-0,3	(-0,6; -0,1)	0,02*
Presence of early spasticity	-2,5	(-19,3; 14,3)	0,77
R ² = 0.671			

0^d Reference category

ASIA, American Spinal Injury Association

LOS, Length of stay

Table 5: Factors associated with the total SCIM score six-months post injury for patients with acute traumatic **paraplegia** (N=45)

<i>Predictive variable</i>	Total SCIM score		
	β coefficient	95%CI	P-value
ASIA grade			
<i>AIS A-B</i>	-19,1	(-31,3;-6,9)	<10 ⁻³ *
<i>AIS C-D</i>	0 ^d		
BMI	-1,3	(-2,3;-0,4)	<10 ⁻³ *
ISS	-0,8	(-1,4; -0,2)	0,01*
Presence of early spasticity	-6,3	(-13,9;1,4)	0,11
R ² = 0.548			

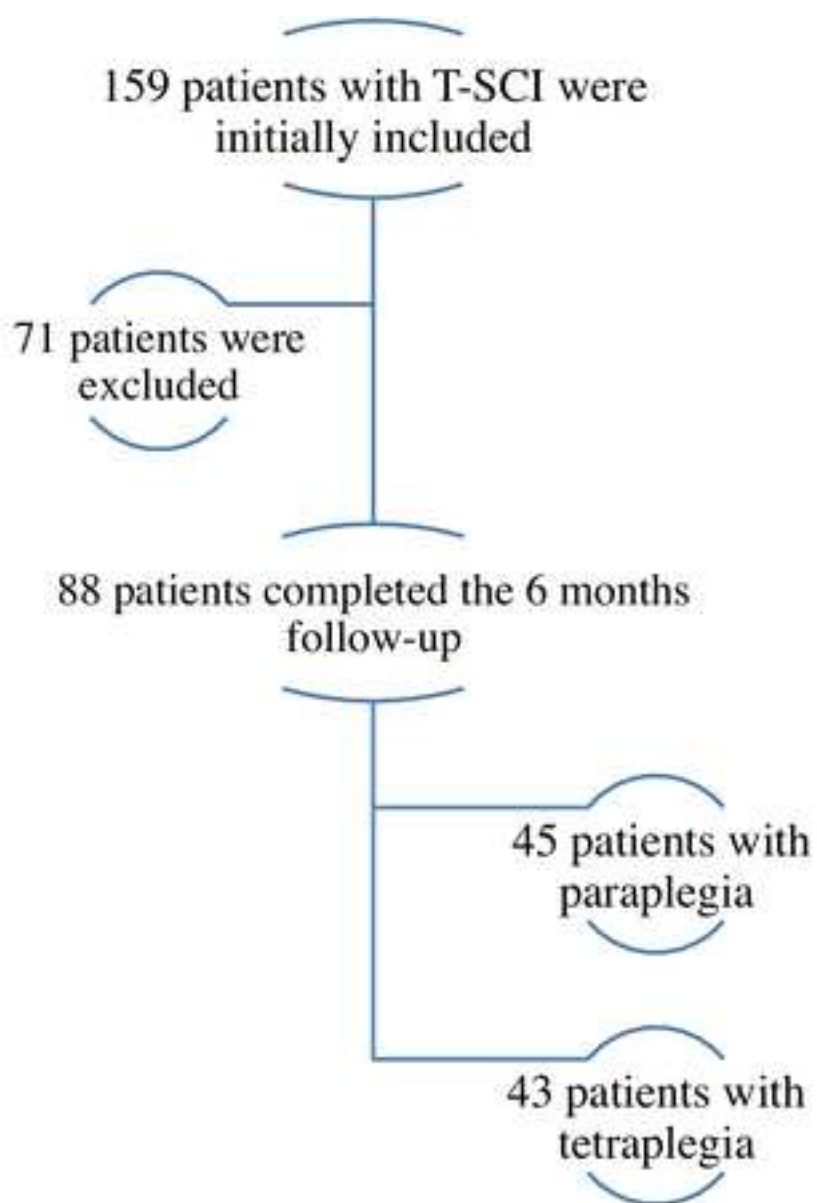
0^d Reference category

ASIA, American Spinal Injury Association

BMI, Body Mass Index

ISS, Injury Severity Score

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10. Appendix 2: Manuscript published in American Journal of Physical Medicine and Rehabilitation (2017)

CME

Costs and Length of Stay for the Acute Care of Patients with Motor-Complete Spinal Cord Injury Following Cervical Trauma

The Impact of Early Transfer to Specialized Acute SCI Center

Andréane Richard-Denis, MD, Debbie Ehrmann Feldman, PhD, Cynthia Thompson, PhD,
Étienne Bourassa-Moreau, MD, MSc, and Jean-Marc Mac-Thiong, MD, PhD

Objective: Acute spinal cord injury (SCI) centers aim to optimize outcome following SCI. However, there is no timeframe to transfer patients from regional to SCI centers in order to promote cost-efficiency of acute care. Our objective was to compare costs and length of stay (LOS) following early and late transfer to the SCI center.

Design: A retrospective cohort study involving 116 individuals was conducted. Group 1 (n = 87) was managed in an SCI center promptly after the trauma, whereas group 2 (n = 29) was transferred to the SCI center only after surgery. Direct comparison and multivariate linear regression analyses were used to assess the relationship between costs, LOS, and timing to transfer to the SCI center.

Results: Length of stay was significantly longer for group 2 (median, 93.0 days) as compared with group 1 (median, 40.0 days; $P < 10^{-3}$), and average costs were also higher (median, Canadian \$17,920.0 vs. \$10,521.6; $P = 0.004$) for group 2, despite similar characteristics. Late transfer to the SCI center was the main predictive factor of longer LOS and increased costs.

Conclusions: Early admission to the SCI center was associated with shorter LOS and lower costs for patients sustaining tetraplegia. Early referral to an SCI center before surgery could lower the financial burden for the health care system.

Key Words: Costs, Length of Stay, Specialized Centers, Spinal Cord Injury

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CME Objectives: Upon completion of this article, the reader should be able to: (1) Determine the optimal timing for transfer of individuals with cervical traumatic spinal cord injury (SCI) in order to decrease acute care resource utilization; (2) Determine benefits of a complete perioperative management in a specialized SCI center; and (3) Identify factors that may influence resource utilization for acute care following motor-complete tetraplegia.

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The incidence of traumatic spinal cord injuries (SCIs) in Quebec, Canada, ranged between 11 and 23 cases per million in the last 13 years.¹ Although this number is relatively

low as compared with other musculoskeletal traumatic injuries, an SCI is associated with extensive economic costs, mostly due to substantial health care burden.^{2,3} This is particularly true for individuals who are more severely affected. Motor-complete cervical SCI requires additional load of care, as this condition is associated with severe respiratory and cardiovascular dysfunction and a greater occurrence of complications.^{4–6} In addition, the cost per acute day of hospitalization in Canada for patients with tetraplegia reaches Canadian \$1124 (CA \$), and the annual economic burden associated with new cases of traumatic SCI (TSCI) was estimated as CA \$2.67 billion in 2011.⁷ Therefore, improving the efficiency and the use of optimal resources is necessary.

Managing motor-complete cervical SCI remains a clinical challenge and requires the integration skills of many specialists and urgent medical stabilization care.⁸ Once medical stabilization is reached, prompt transfer to the SCI center is recommended.^{9,10}

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In Canada, specialized acute care centers are tertiary care–designated centers developed to help patients with acute SCI and were shown to improve recovery and decrease the occurrence of complications.^{10–12} In this way, early transfer is recommended (<48 hours), but this recommendation relies on limited evidence (level V, panel opinion).⁹ On the other hand, recent studies have suggested that emergent spinal surgery could improve neurological recovery,^{13,14} decrease the incidence of complications,^{15,16} and reduce costs and length of stay (LOS).¹⁷ Thus, after stabilizing of a patient with acute cervical TSCI, a decision has to be made whether a prompt surgery at the nonspecialized (NS) regional center or direct transfer to the SCI center should be prioritized. So, optimal timing for transfer to the SCI center should also be established with respect to the spinal surgical procedure and the amount of specialized perioperative care provided. This is particularly important for motor-complete cervical SCI, as this condition is associated with limited neurological recovery and a high risk of complications.¹⁸ Thus, our hypothesis is that complete perioperative care at a specialized SCI center will decrease costs and LOS. Accordingly, the purpose of this study was to compare the LOS and costs of care between patients managed perioperatively at an NS versus SCI center following a traumatic motor-complete cervical SCI.

MATERIALS AND METHODS

Patients

We conducted a retrospective cohort study of prospectively collected data including 116 consecutive adult patients (92 men, 24 women) aged 46.0 ± 19.3 years admitted to a single level I SCI-specialized trauma center between April 2008 and November 2014 for a motor-complete cervical TSCI. A motor-complete SCI was defined as a grade A or B severity on the ASIA (American Spinal Injury Association) Impairment Scale (AIS). All subjects were treated surgically to decompress and stabilize the spine in order to minimize the secondary injury to the spinal cord. Because subjects treated nonsurgically or sustaining a cervical SCI with milder neurological deficits (AIS-C or AIS-D, including central cord syndrome) are recognized to experience better outcomes,¹⁸ they were excluded from this study. The institutional review board approved this study.

Our cohort was subdivided into 2 groups based on the timing of admission to the specialized center. Group 1 included 87 individuals “early” transferred to the SCI center, whereas group 2 included 29 patients “late” transferred to the SCI center. “Early” transfer was defined as transfer and admission to the SCI center prior to the surgical management in order to receive complete perioperative management by a specialized multidisciplinary team, whereas group 2 consisted of 29 patients transferred to the SCI center for postoperative management only. More clearly, patients from group 2 received preoperative, surgical, and immediate postoperative management in an NS center before being transferred to the SCI center. Patients from group 1 could also be first transported to an NS center after their trauma, but were all surgically managed in the SCI center. The term “perioperative period” refers in the present work to 3 phases: (1) the preoperative period (period between the trauma and surgical management), (2) surgical

procedure, and (3) postoperative management (period from the surgical procedure to the discharge from acute care setting).

The organization of SCI care may vary from one province and one country to another. In Quebec, Canada, all patients sustaining a TSCI should be directed to 1 of the 2 designated acute care centers (SCI center) according to its location: 1 center serving the eastern, whereas the other serves the western part of the province. This system was established in the late 1970s in order to allow centralization of patients and improve standard of care. Although there are no specific requirements to define these centers in Canada, they are all based on similar characteristics in terms of medical management and rehabilitation resources. Also, in our province, many patients are first transported to NS centers following their SCI in order to stabilize patients and confirm the diagnosis of an SCI. Even if our provincial government strongly encourages prompt transfer to the SCI center in the preoperative phase, some NS centers may choose to transfer patients only after surgical management. It is important to note that all patients were transported by ambulance. No helicopter service or else was used. The level I trauma center involved in this study was designated in 1977 as 1 of the 2 acute care specialized SCI reference centers of our province.^{19,20} Since this designation, our hospital center has managed 70 to 100 patients with TSCI per year.²⁰ It comprises a multidisciplinary health care professional team specialized in SCI care, including, but not limited to, a specialized SCI trauma unit, a dedicated multidisciplinary acute rehabilitation team, and a collaborative intensive functional rehabilitation facility system for the establishment of viable community integration.^{9,10} The team ensured complete perioperative care for patients in group 1 and postoperative care for group 2. All patients were admitted and initially managed in the intensive care unit (ICU). When their condition was judged stable by the ICU team, patients were transferred to the ward while continuing rehabilitation therapies. The perioperative care in the specialized SCI center follows the evidence-based recommendations for the acute care of SCI patients.⁹ Hospital clinical protocols and interdisciplinary team work are used to systematically manage bowel and bladder care and prevent venous thrombosis, pressure ulcers (PUs), contractures, malnourishment, and aspiration and improve cardiovascular and respiratory outcomes. Cardiovascular management and respiratory management were individualized based on the clinical judgment of the medical team and involved daily respiratory rehabilitation therapies. A physical medicine and rehabilitation specialist directed the acute rehabilitation process, applied interventions to promote functional and neurological recovery, and coordinated the transfer to a functional rehabilitation facility with a liaison nurse, once the patient’s condition does not require additional active medical or surgical management.

Data Collection and Outcomes

Sociodemographic and clinical data pertaining to the hospitalization at the level I SCI-specialized acute center were collected prospectively through the Quebec Trauma Registry. This prospective database includes all patients admitted at our institution following a traumatic event. Administrative data such as the costs of acute hospitalization were collected directly from the hospital database. Although patients from group 2 were

TABLE 1. Demographic and clinical characteristics of patients early and lately transferred to an SCI center following a motor-complete cervical SCI

		Early Transfer (SCI Center [Group 1])	Late Transfer (NS Center [Group 2])	P
n	—	87	29	—
Age	Median (interquartile range)	46.0 (28.6–62.0)	48.0 (23.5–64.5)	0.97
Sex	% Male	78.2	82.8	0.60
ISS	% ≥ 29	39.1	58.6	0.053
ASIA grade	% A	65.5	82.8	0.08
	% B	34.5	17.2	
Neurological level	% C1–C4	51.7	62.1	0.33
Traumatic brain injury	% TBI	51.3	27.6	0.02 ^a
In-hospital death	% Deceased	9.2	6.9	0.70
Surgical delay	% >24 h after injury	54.0	51.7	0.83
Respiratory complications	%	54.0	51.7	0.83
Pneumonia	%	47.1	41.4	0.67
Pressure ulcer	%	36.8	34.5	1.00
UTI	%	20.7	31.0	0.31
At least 1 complication (≥ 1)	%	71.3	72.1	1.00
Multiple complications (≥ 2)	%	44.8	37.9	0.67

prospectively enrolled into the Quebec Trauma Registry upon arrival to our institution, chart review was required for acquiring the surgical delay and the LOS in the NS center.

Collected data (Table 1) included age, sex, and trauma severity as measured by the Injury Severity Score (ISS). The ISS score was dichotomized according to Bull's method²¹ using the LD₅₀, meaning the ISS score representing a "lethal dose of injuries" for 50% of the patients injured. The suggested LD₅₀ score was 40 for individuals 15 to 44 years old and 29 for those aged 45 to 64 years. Because the median ages of our 2 groups were 46 and 48 years, we dichotomized the ISS into less than 29 or greater. The neurological level was defined as the most caudal segment with normal motor and sensory function bilaterally and was used to discriminate between high cervical levels (C1 to C4) and lower cervical levels (C5 to C8). The severity of the SCI was assessed at arrival to the SCI center using the AIS and was reported using the AIS grade A or B. The presence of a concomitant traumatic brain injury (TBI) was also noted. The proportion of mortality during the SCI center stay was compared between the 2 groups. Then, the surgical delay was defined as the time (in hours) between the trauma and the spinal surgery (time of skin incision) and was dichotomized in 2 categories (<24 or ≥ 24 hours after trauma). Finally, the following complications were considered: overall respiratory complications (e.g., pneumonia, acute respiratory distress syndrome, pulmonary embolism, bronchitis, atelectasis, pulmonary edema, pneumothorax, etc.), urinary tract infections (UTIs), and PUs. The occurrence of respiratory complications was diagnosed using clinical features and confirmed by a radiologist using chest radiographs.²² Urinary tract infections were diagnosed using criteria from the 2006 Consortium for Spinal Cord Medicine Guidelines for health care providers, using significant bacteriuria, pyuria, and signs and symptoms of UTI.²³ Finally, the presence of PU was diagnosed based on the clinical guidelines defined by the National Pressure Ulcer Advisory Panel.²⁴ The complication rate refers to the proportion of patients who developed one of the previously

mentioned complications during their stay at the specialized SCI center and was expressed as a percentage. The same was performed for the occurrence of multiple complications, where we considered patients having experienced more than 1 complication (≥ 2 complications) during the SCI center stay.

The main outcome variables were hospital LOS and costs related to hospitalization in the SCI center (in CA \$). Details are provided in the following sections.

Length of Stay and Costs

The total LOS was defined as the number of days from arrival at the emergency room of either NS hospital or SCI center after the trauma until discharge from the SCI center to the rehabilitation center. For group 2, the total LOS comprised 2 distinct portions: (1) LOS in the NS hospital (days between arrival at the emergency room and transfer to the SCI center) and (2) LOS in the SCI center. Length of stay in an NS hospital was also collected for patients in group 1, as most of these patients were first transported from the site of trauma to a community hospital prior to being transferred to the SCI center. Data on LOS in the ICU of the SCI center were also collected for both groups.

In our system of care, urgent and acute care such as that required for TSCI is covered by our universal health care system, as well as for all fees related to the care of the patients. All the costs of hospitalization are paid from the hospital's budget, except for the physicians who are self-employed private entities receiving a fixed salary for every working day, in addition to a fee-for-service scale similar for all physicians of the same specialty throughout the province. Costs related to hospital care at the SCI center (excluding costs for prior care at NS center) were estimated using the "Niveau d'Intensité Relative des Ressources Utilisées" (NIRRU) index corresponding to the relative intensity level of resources used. This NIRRU index is specific to the province of Quebec but is similar to the Resource Intensity Weights used in the rest of Canada and is

based on the Maryland cost index adjusted for conditions specific to the province of Quebec. The NIRRU index encompasses all resources involved during hospitalization but excludes physician fees. However, because the spine surgery and, on some occasions, the tracheostomy were performed in the NS center for individuals later transferred to the SCI center (group 2), all costs related to the spine surgery and tracheostomy placement were excluded for both groups. All other procedures such as the rehabilitation therapies, wound care, and any additional surgeries occurring in the specialized SCI center were included in the estimation of costs. Costs in Canadian dollars were then derived from the partial NIRRU index after adjusting for patients' clinical conditions, risk of mortality, and resources used, as well as for additional costs related to the teaching involved in our university-affiliated SCI center. Costs were then adjusted according to the Canadian average rate of inflation between the year of hospitalization for each patient and 2014. It should also be mentioned that transportation fees were not included in the partial NIRRU index for cost estimation in the present study. The costs for transportation by ambulance typically depend on the distance and time required for transfer because it is provided by the public health care system. Considering that all patients have been ultimately transferred to our specialized SCI center, it is not likely that the costs for transportation will differ significantly for each specific patient whether he/she is transferred preoperatively or postoperatively.

Statistical Methods

In order to compare the 2 groups, we first used nonparametrical analyses (Mann-Whitney *U* tests for continuous variables and χ^2 tests for categorical variables). We used IBM SPSS Statistics version 21 software (SPSS version 21.0, IBM, Chicago, IL) package for all statistical analyses.

In order to account for discrepancies in patient characteristics and complications, which can strongly influence the LOS and costs,^{10,11} multiple linear regression models were used to determine the impact of the timing of admission to the SCI center. A backward stepwise method was used with a level of significance of 0.05. Two different models were performed, with the LOS at the SCI center and costs (excluding surgery and tracheostomy involved during the acute care hospitalization) as dependent variables, respectively. The main independent variable was the timing of admission to the SCI center (early transfer [group 1] vs. late transfer [group 2]). Thirteen independent variables were included in each model as covariables: (a) age, (b) sex, (c) ISS (<29 and $\geq$ 29), (d) surgical

delay (<24 or $\geq$ 24 hours after trauma), (e) ASIA grade (A or B), (f) neurological level (high cervical [C1 to C4] or low cervical [C5 to C8]), (g) presence of concomitant TBI, (h) occurrence of respiratory complications, (i) occurrence of pneumonia, (j) occurrence of PU, (k) occurrence of UTI, (l) occurrence of at least 1 complication; (m) occurrence of multiple complications ($\geq$ 2).

RESULTS

Patients' Characteristics

The entire cohort for our study consisted of 116 subjects who sustained a traumatic motor-complete cervical SCI. There were 87 patients in group 1, whereas 29 patients were in group 2. Patient sociodemographic and clinical characteristics are shown in Table 1. There were no significant differences between the 2 groups in terms of age, sex, and trauma severity as measured by the ISS, but there was a tendency toward higher trauma severity in group 2 ($P = 0.053$). Fifty-three percent of patients from group 1 had a TBI, which was nearly twice as large as for group 2 (28%; $P = 0.015$). Eight individuals in group 1 died during their acute hospital stay (9.2%), whereas 2 individuals in group 2 died prior to discharge (6.9%) ($P = 0.70$). The surgical delay was similar in both groups.

Length of Stay

Ninety-four percent of patients from group 1 (82 of 87 patients) were transported from the site of trauma to a community hospital prior to their transfer to the specialized SCI center. However, the delay between the trauma and admission to the specialized SCI center, including the time spent in the community hospital, was short (median, 0.2 days) (Table 2). On the other hand, patients in group 2 spent more than 2 weeks (median, 18.8 days; $P < 0.001$) in an NS hospital prior to their transfer to the SCI center. Once transferred to the SCI center, patients in group 2 remained hospitalized longer in comparison with group 1, particularly in the ICU, as shown in Table 2. Ultimately, the total hospital LOS between the trauma and discharge to the rehabilitation center was nearly twice as long for subjects in group 2 as compared with group 1 (Table 2). Table 3 shows that results were similar when matching individuals according to their trauma severity (ISS <29 vs. $\geq$ 29).

The multiple linear regression analysis showed that late transfer to the SCI center (group 2), presence of multiple complications, and older age were significantly associated with longer LOS in the SCI center (Table 4).

TABLE 2. Hospitalization LOS in patients with a motor-complete cervical spine injury early and later transferred to the SCI center (Group 1 and 2)

Hospitalization Stay, d			Early Transfer (SCI Center [Group 1])	Late Transfer (NS Center [Group 2])	<i>P</i>
Prior to the SCI center admission	Regional center (NS center)	Median (interquartile range)	0.2 (0.1–0.3)	18.8 (8.2–36.3)	<0.001 ^a
From admission to discharge of the SCI center	In the ICU	Median (interquartile range)	14.0 (8.0–37.0)	34.0 (12.5–89.0)	0.04 ^a
	In the ward	Median (interquartile range)	40.0 (24.0–67.0)	68.0 (35.5–119.0)	<0.001 ^a
Total acute care hospitalization		Median (interquartile range)	40.0 (24.0–67.0)	93.0 (61.0–149.0)	<0.001 ^a

TABLE 3. Comparison of LOS and costs of care between individuals early and lately transferred to the SCI center after matching for trauma severity (ISS <29 vs. ≥29) (N = 116)

		Early Transfer (SCI Center [Group 1])	Late Transfer (NS Center [Group 2])	P
ISS ≥29				
n	—	34	17	—
LOS	Median (interquartile range)	57.0 (32.3–101.3)	107.0 (65.5–149.0)	0.007 ^a
Costs of care	Median (interquartile range)	19928.5 (10845.1–21191.6)	25555.4 (15572.8–30605.8)	0.058
ISS <29				
n	—	53	12	—
LOS	Median (interquartile range)	32.0 (23.5–55.5)	86.0 (60.0–149.55)	<0.001 ^a
Costs of care	Median (interquartile range)	10144.2 (6478.5–17332.7)	17028.3 (8523.1–20776.3)	0.13

Hospitalization Costs

Total costs related to the acute care management were similar for both groups. However, costs using partial NIRRU indices excluding surgery and tracheostomy for both groups were nearly CA \$6000 lower for group 1 than for group 2 patients ($P = 0.004$) (Table 5).

The multiple linear regression analysis for SCI center hospitalization costs (excluding tracheostomy and spine surgery) revealed that higher costs were significantly associated with 2 factors: late transfer to the SCI center (group 2) and the occurrence of respiratory complications (Table 6).

DISCUSSION

Prompt transfer to the SCI center was shown to be beneficial on many levels following an SCI. However, there is no study to date that has proposed specific timeframe for regional (NS) hospital centers to transfer patients to the SCI centers upon medical stabilization following SCI. Results of this study therefore support previous work while adding the information that presurgical referral to the SCI center in order to benefit from a complete specialized perioperative management may decrease acute care resource utilization in terms of LOS and costs of care. Moreover, the timing of admission to the SCI center (based on where the surgical procedure and perioperative management were undertaken) was revealed as an important independent significant factor associated with LOS and costs of care accounting for potential confounding factors.

TABLE 4. Factors associated with total hospitalization LOS at the SCI center in individuals sustaining a severe cervical TSCI: results of the multiple linear regression analysis (N = 116)

Factors Associated With Hospital LOS in the SCI Center		
	β Coefficient (95% CI)	P
Timing of SCI center admission (group 2 [NS center] vs. group 1 [SCI])	50.5 (30.8–70.2)	<0.001 ^a
Occurrence of multiple complications	50.2 (33.0–67.4)	<0.001 ^a
Age	0.6 (0.1–1.0)	0.014 ^a
$R^2 = 0.358$ (percentage of the response variable variation that is explained by our linear model).		
CI indicates confidence interval.		

Determining factors specific to the SCI centers that may influence the LOS and costs of care is, however, complex. In theory, there are 3 aspects of patient care that differ between the 2 groups in this study: (1) preoperative management, (2) surgical procedure, and (3) early postoperative care and prevention of complications. In practice, coordinated and continuum of care between the trauma and surgical teams and particularly between the surgical and early rehabilitation teams also differs significantly between the 2 groups. In a specialized SCI center such as ours, the rehabilitation team (physical rehabilitation doctors, physiotherapists, occupational therapists, clinical nurses, social workers, liaison nurse, etc.) is involved as soon as the patient is admitted in order to prevent complications that could delay the intensive functional rehabilitation. Immediately after surgery, management of the patients is primarily under the responsibility of the rehabilitation team in order to prepare the patient for intensive functional rehabilitation: (1) prevent/reduce complications, (2) achieve medical stabilization before transfer to the rehabilitation facility, (3) determine the potential for neurological/functional recovery, (4) evaluate the resources and goals required in terms of chronic rehabilitation, (5) increase function and promote neurological recovery, and (6) determine when patients are ready for discharge from the acute care facility. Timely initiating protocols for early rehabilitation is also a crucial aspect of our rehabilitation team that will facilitate the orientation of the patients in the chronic phase. Accordingly, the main reason raised by the NS centers for transferring patients in group 2 after the surgery is the lack of a rehabilitation team in their hospital. As an end result, early coordinated and continuum of care throughout the perisurgical management may reduce the time, costs, and resources required during the acute hospitalization in order to undertake early rehabilitation and prepare patients for intensive functional rehabilitation in the rehabilitation facility, and this will likely be increased if patients are transferred to an SCI center only after surgery. This is supported by previous studies that have suggested that prompt transfer to the SCI center optimizes outcomes following SCI.^{10,12} Because the level and severity of the SCI are recognized as the main predictive factors of outcome following SCI^{11,25} and were fixed in the present study, this study proposes relevant information given the fact that timing of referral to the SCI center is a modifiable factor.

One may ask if a potential higher complexity of cases may justify why some patients were sent to the SCI center later and therefore explain results of this study. However, this hypothesis

TABLE 5. Costs related to the hospitalization in the SCI center for patients with a motor-complete cervical spine injury based on the timing of admission to the SCI center

Costs (CA \$)		Timing of Admission to the SCI Center		P
		Early Transfer (SCI Center [Group 1])	Late Transfer (NS Center [Group 2])	
Total	Median (interquartile range)	15,552.2 (14,406.9–38,578.1)	21 630.4 (11,582.5–32,539.0)	0.47
Surgery and tracheostomy excluded	Median (interquartile range)	10,521.6 (6 840.2–18,895.5)	17,920.0 (11,159.3–24,500.4)	0.004 ^a

is somehow counterintuitive and is not supported by the following observations. First, as NS centers typically do not involve health care providers specialized in the management of TSCI and because they receive low volume of patients for this condition, it is not likely that NS centers would prefer to delay transfer to a specialized SCI center for complex patients requiring more complex management. While this study specifically pertains to the costs and resources for treating TSCI, we can also add that in our public system there is no incentive whatsoever for NS centers to treat more complex patients with TSCI, because it will increase the local costs and use of resources. But more importantly, we would like to highlight that all patients sustained a similar injury involving a cervical motor-complete SCI, which somehow involves a complex surgical and postoperative course for all patients. Individuals sustaining a motor-complete SCI, whether AIS-A or AIS-B, represent a relatively homogenous group of patients with regard to the acute management, because both cervical AIS-A and AIS-B injuries lead to severe motor, autonomic, and respiratory dysfunctions requiring particular care in the ICU following the injury, when deficits are at their peak.^{9,26,27} We also want to highlight that Table 1 shows that even if the number of AIS-A in group 2 was higher this difference was not significant. Although recent studies have demonstrated that sensitive sacral sparing (AIS-B) is associated to distinct long-term neurological and functional outcomes in comparison with complete SCI (AIS-A),^{28,29} there is no study to our knowledge that has specifically compared those 2 levels of severity on acute care outcomes. But again, when looking at the total acute care LOS, individuals from group 2 may have had a significantly longer period to recover (Table 2), particularly knowing that the neurological recovery is more rapid within the first 3 months after injury.¹⁸

Table 1 also shows a tendency toward higher trauma severity in group 2 (NS center). However, outcome comparison after

matching the participants according to their trauma severity (ISS) still showed a significantly longer LOS and a tendency toward higher costs for group 2 (NS center) as shown in Table 3. On the other hand, the higher percentage of TBI in group 1 (patients entirely treated in the SCI center) may rather suggest a higher complexity in this group and therefore further reinforce the results of this study.

Regarding results of the regression analysis, 2 factors were predictive of the LOS with the timing of admission to the SCI center: the occurrence of multiple complications and older age. These findings are not only intuitive but also well supported by previous studies.^{11,30–32} The presence of complications, such as UTI, PUs, and pneumonia, was demonstrated to increase costs of acute care hospitalization in SCI patients¹¹ and is also recognized as a frequent and major cause of morbidity^{5,33–37} associated with longer LOS.^{11,25} Older age may be a factor associated with increased duration of acute care LOS for many reasons. Older age may be associated with higher comorbidity burden and increase the risk of complication occurrence, which may put them at higher vulnerability following an SCI,^{31,32} although according to the results of this study (β coefficient) the age does not seem to have an important impact for patients with cervical motor-complete SCI.

The occurrence of respiratory complications was revealed as an important factor influencing costs of acute care with the timing of transfer to the SCI center. Indeed, respiratory complications such as acute respiratory distress syndrome and atelectasis may frequently occur in patients with higher levels of cervical SCI³⁸ and particularly in individuals under mechanical ventilation support. Mechanical ventilation support requires substantial hospital resources and important costs,^{11,39,40} which may explain our result. Moreover, the occurrence of respiratory complication may also prolong the intensive care duration, which may also be very costly.

It should be finally mentioned that even if this study suggests that early admission to the SCI center might enhance cost-effectiveness of acute care, initial evaluation and medical stabilization in a community NS center may be still required. For instance, confirmation of the presence of an SCI and/or, most importantly, early medical stabilization may be needed. This study does not intend to question the importance of medical stabilization following an SCI as soon as possible in any NS hospital center if the SCI center is not closely located. This study rather supports our provincial legislation and suggests that prompt management in a specialized hospital center for complete surgical and perioperative management upon medical stabilization following a TSCI may decrease costs of care. In the context where the NIRR index considered in this study did not include physician fees or transportation fees that could

TABLE 6. Factors associated with costs related to hospitalization at the SCI center in individuals sustaining a severe cervical TSCI (N = 116)

Factors Associated With Higher Hospitalization Costs (CA \$)		
	β Coefficient (95% CI)	P
Timing of SCI center admission (group 2 [NS center] vs. group 1 [SCI])	7070.4 (1589.8–12,551.0)	0.013 ^a
Respiratory complications	5796.0 (125.8–11,466.2)	0.045 ^a
$R^2 = 0.186$.		

highly vary from one health care system to another, costs evaluated essentially reflect inpatient acute care stay, which may be directly proportional to the acute care LOS. Therefore, because all patients sustaining a TSCI will require hospitalization in an acute care setting, this study could apply elsewhere. In fact, every health care system treating patients with acute TSCI should aim to decrease resource utilization and acute care LOS, and specialized centers may be an important way to achieve this.

Limitations

The main limitations of this study are the small number of patients and its retrospective nature. Group 2 included only 29 patients arriving from many different hospital centers. Patient management may vary between centers, and some of these differences may account for the disparities in LOS and costs.

Potential biases during data acquisition may have occurred because of the retrospective nature of this study. However, it is important to mention that all variables included in this study are collected routinely for all patients sustaining a TSCI at our institution and performed by a medical archivist who was not involved in the present study. The inclusion of inpatient rehabilitation fees could have been an interesting feature to add to our analyses as it also represents an important cost driver following an SCI in Canada.³ However, it is also important to mention that we have strict criteria for transferring patients to intensive functional rehabilitation facilities that were exactly the same between the 2 groups. Consequently, it is assumed that the costs of intensive functional rehabilitation would be similar between the 2 groups. This is indeed related to a major finding of our study because we suggest that increased costs and resources are required for patients in group 2 to reach the same discharge milestones and to prepare them for transfer to intensive functional rehabilitation. It should be also noted that there was a tendency toward higher severity of complete SCI in group 2. Although this difference was not significant, additional comparative nonparametrical subanalyses showed that the LOS and costs of care were similar for patients with AIS grades A and B in each group. Moreover, considering that multivariate analysis also takes into account this potential confounding variable, it is unlikely that this issue had influenced the results of this study.

Travel distances and costs related to transportation were not considered in this study. First, it is important to note that all patients included in this study were transported by ambulance, and no helicopter or other expensive means of transport were used. Then, considering that both groups were at some point directed to their respective SCI center, travel distances and costs related to transportation are likely to be similar between the 2 groups. However, if other means of transport are used in a health care system, this should be added in the estimation of costs of acute care.

Finally, even if this study does not address clinical outcome (such as the neurological and functional outcomes), economic impact and resource utilization are outcome variables of great importance in the current political context in Canada, where health costs have greatly increased over the last years.

CONCLUSIONS

Length of stay and costs were decreased with early admission to a specialized SCI center for complete perioperative care

following a motor-complete cervical SCI. Furthermore, LOS and costs were also significantly associated with the timing of admission to the SCI center.

Thus, this study strengthens current recommendations of prompt transfer of patients to an SCI center following a TSCI, but may also add that transfer prior to surgical management is beneficial on acute care resource utilization, even if medical stabilization was first performed in a regional NS center. Many factors could be beneficial to the SCI centers, such as the early introduction of specialized rehabilitation and optimization of coordination of care, but characteristics of SCI centers still need to be studied. Even if this study was performed in a specific public health care system, results still can be applied elsewhere. In fact, the present study has mainly evaluated costs of care based on the LOS (by the exclusion of fees that may vary from one system to another, such as physician and surgical fees). And, all patients sustaining cervical TSCI generally require long acute care hospitalization. Therefore, its optimization by prompt admission to an SCI center prior to surgical management may be an efficient way, applicable to any health care system, to decrease resource utilization that may be an important issue worldwide.

REFERENCES

1. Thompson C, Mutch J, Parent S, et al: The changing demographics of traumatic spinal cord injury: an 11-year study of 831 patients. *J Spinal Cord Med* 2015;38:214–23
2. Mahabaleshwarkar R, Khanna R: National hospitalization burden associated with spinal cord injuries in the United States. *Spinal Cord* 2014;52:139–44
3. Munce SE, Wodchis WP, Guilcher SJ, et al: Direct costs of adult traumatic spinal cord injury in Ontario. *Spinal Cord* 2013;51:64–9
4. Wilson JR, Arnold PM, Singh A, et al: Clinical prediction model for acute inpatient complications after traumatic cervical spinal cord injury: a subanalysis from the Surgical Timing in Acute Spinal Cord Injury Study. *J Neurosurg Spine* 2012;17(1 suppl):46–51
5. Haisma JA, van der Woude LH, Stam HJ, et al: Complications following spinal cord injury: occurrence and risk factors in a longitudinal study during and after inpatient rehabilitation. *J Rehabil Med* 2007;39:393–8
6. Radhakrishna M, Makriyanni I, Marcoux J, et al: Effects of injury level and severity on direct costs of care for acute spinal cord injury. *Int J Rehabil Res* 2014;37:349–53
7. Krueger H, Noonan VK, Trenaman LM, et al: The economic burden of traumatic spinal cord injury in Canada. *Chronic Dis Inj Can* 2013;33:113–22
8. Ryken TC, Hurlbert RJ, Hadley MN, et al: The acute cardiopulmonary management of patients with cervical spinal cord injuries. *Neurosurgery* 2013;72(suppl 2):84–92
9. Consortium for Spinal Cord Medicine: Early acute management in adults with spinal cord injury: a clinical practice guideline for health-care professionals. *J Spinal Cord Med* 2008;31:403–79
10. Parent S, Barchi S, LeBreton M, et al: The impact of specialized centers of care for spinal cord injury on length of stay, complications, and mortality: a systematic review of the literature. *J Neurotrauma* 2011;28:1363–70
11. Tator CH, Duncan EG, Edmonds VE, et al: Complications and costs of management of acute spinal cord injury. *Paraplegia* 1993;31:700–14
12. Bagnall AM, Jones L, Richardson G, et al: Effectiveness and cost-effectiveness of acute hospital-based spinal cord injuries services: systematic review. *Health Technol Assess* 2003;7:iii, 1–92
13. Wilson JR, Singh A, Craven C, et al: Early versus late surgery for traumatic spinal cord injury: the results of a prospective Canadian cohort study. *Spinal Cord* 2012;50:840–3
14. Wilson JR, Grossman RG, Frankowski RF, et al: A clinical prediction model for long-term functional outcome after traumatic spinal cord injury based on acute clinical and imaging factors. *J Neurotrauma* 2012;29:2263–71
15. Bourassa-Moreau É, Mac-Thiong JM, Ehrmann Feldman D, et al: Complications in acute phase hospitalization of traumatic spinal cord injury: does surgical timing matter? *J Trauma Acute Care Surg* 2013;74:849–54
16. McKinley W, Meade MA, Kirshblum S, et al: Outcomes of early surgical management versus late or no surgical intervention after acute spinal cord injury. *Arch Phys Med Rehabil* 2004;85:1818–25
17. Mac-Thiong JM, Feldman DE, Thompson C, et al: Does timing of surgery affect hospitalization costs and length of stay for acute care following a traumatic spinal cord injury? *J Neurotrauma* 2012;29:2816–22
18. Fawcett JW, Curt A, Steeves JD, et al: Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. *Spinal Cord* 2007;45:190–205

19. Moutquin Jean-Marie: Lésions médullaires traumatiques et non-traumatiques: analyse comparative des caractéristiques et de l'organisation des soins et services de réadaptation au Québec. l'Institut national d'excellence en santé et en services sociaux. *ETMIS* 2013;9(no. 1):iii
20. Nord-de-l'île-de-Montréal Ciuadssed: Centre d'expertise pour les personnes blessées médullaires de l'Ouest du Québec (CEBMOQ): Hôpital du Sacré-Coeur de Montreal; 2013. Available at: <http://www.hscm.ca/soins-et-services/les-soins-et-services-medicaux-chirurgicaux-psychiatriques-et-professionnel/t/centre-de-traumatologie/cebmoq/index.html>. Accessed May 1, 2016
21. Baker SP, O'Neill B, Haddon W Jr, et al: The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *J Trauma* 1974;14:187–96
22. Consortium for Spinal Cord Medicine: Respiratory management following spinal cord injury: a clinical practice guideline for health-care professionals. *J Spinal Cord Med* 2005; 28:259–93
23. Consortium for Spinal Cord Medicine: Bladder management for adults with spinal cord injury: a clinical practice guideline for health-care providers. *J Spinal Cord Med* 2006;29:527–73
24. National Pressure Ulcer Advisory Panel (NPUAP): Educational and clinical resources; 2016. Available at: <http://www.npuap.org/resources/educational-and-clinical-resources/>. Accessed April 28, 2016
25. Donovan WH, Carter RE, Bedbrook GM, et al: Incidence of medical complications in spinal cord injury: patients in specialised, compared with non-specialised centres. *Paraplegia* 1984;22:282–90
26. Furlan JC, Fehlings MG: Cardiovascular complications after acute spinal cord injury: pathophysiology, diagnosis, and management. *Neurosurg Focus* 2008;25:E13
27. Ropper AE, Neal MT, Theodore N: Acute management of traumatic cervical spinal cord injury. *Pract Neurol* 2015;15:266–72
28. Kirshblum S, Botticello A, Lammertse DP, et al: The impact of sacral sensory sparing in motor complete spinal cord injury. *Arch Phys Med Rehabil* 2011;92:376–83
29. Kirshblum SC, Botticello AL, Dyson-Hudson TA, et al: Patterns of sacral sparing components on neurologic recovery in newly injured persons with traumatic spinal cord injury. *Arch Phys Med Rehabil* 2016;97:1647–55
30. Wu Q, Ning GZ, Li YL, et al: Factors affecting the length of stay of patients with traumatic spinal cord injury in Tianjin, China. *J Spinal Cord Med* 2013;36:237–42
31. Franceschini M, Cerrel Bazo H, Lauretani F, et al: Age influences rehabilitative outcomes in patients with spinal cord injury (SCI). *Aging Clin Exp Res* 2011;23:202–8
32. DeVivo MJ, Kartus PL, Rutt RD, et al: The influence of age at time of spinal cord injury on rehabilitation outcome. *Arch Neurol* 1990;47:687–91
33. Vickrey BG, Shekelle P, Morton S, et al: Prevention and management of urinary tract infections in paralyzed persons. *Evid Rep Technol Assess (Summ)* 1999:1–3
34. Grossman RG, Frankowski RF, Burau KD, et al: Incidence and severity of acute complications after spinal cord injury. *J Neurosurg Spine* 2012;17(1 suppl):119–28
35. Richard-Denis A, Thompson C, Bourassa-Moreau É, et al: Does the acute care spinal cord injury setting predict the occurrence of pressure ulcers at arrival to intensive rehabilitation centers? *Am J Phys Med Rehabil* 2016;95:300–8
36. Allman RM: Pressure ulcer prevalence, incidence, risk factors, and impact. *Clin Geriatr Med* 1997;13:421–36
37. Berney S, Bragge P, Granger C, et al: The acute respiratory management of cervical spinal cord injury in the first 6 weeks after injury: a systematic review. *Spinal Cord* 2011;49:17–29
38. Aarabi B, Harrop JS, Tator CH, et al: Predictors of pulmonary complications in blunt traumatic spinal cord injury. *J Neurosurg Spine* 2012;17(1 suppl):38–45
39. Cooke CR: Economics of mechanical ventilation and respiratory failure. *Crit Care Clin* 2012;28:39–55 vi
40. Berly M, Shem K: Respiratory management during the first five days after spinal cord injury. *J Spinal Cord Med* 2007;30:309–18

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The impact of acute management in a specialized spinal cord injury center on the occurrence of medical complications following motor-complete cervical spinal cord injury

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ABSTRACT

Objective: To determine the impact of pre-surgical admission to a specialized spinal cord injury (SCI) trauma center (SCI-center) on the occurrence of non-neurological complications following tetraplegia.

Methods: A retrospective comparative cohort study of prospectively collected data involving 116 individuals was conducted. Group 1 (N=87) was managed in a SCI-center promptly after the trauma, whereas Group 2 (N=29) was pre-operatively and surgically managed in a non-specialized (NS) acute care center before being transferred to the SCI-center. The occurrence of pressure ulcers, urinary tract infections, pneumonia and respiratory complications during the SCI-center stay as well as the total length of stay (LOS) were compared between the two groups.

Bivariate analyses were used to determine the relationship between complication occurrence and individual socio-demographic and clinical variables. Significant covariates were included in a binary logistic model in order to analyze the relationship between the timing of admission to the SCI-center and the occurrence of complications, while accounting for other variables. A subanalysis was performed for the occurrence of respiratory complications only.

Results: There was a similar rate of complications regardless of the timing of admission to the SCI-center ($p=1.00$). However, the LOS was greater in Group 2 ($p=0.004$). High cervical injuries (C1-C4) and obesity increased the odds of developing a complication, while high cervical injuries and increased trauma severity increased the odds of developing respiratory complications following the SCI-center admission.

Conclusion: Previous studies have shown that the risk of complications is increased for SCI patients treated in non-specialized centers. Management by a specialized SCI team even at a later stage during the acute hospitalization will limit the rate of complications. However, efforts to

limit the rate of complications following late transfer to a specialized SCI-center after surgery results in an increased LOS.

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Key words: spinal cord injury, complications, specialized centers, cervical.

INTRODUCTION

Spinal cord injury (SCI) is a devastating event causing significant long-term neurological and functional impacts. Although the incidence of SCI is relatively low as compared to other traumatic injuries, it is estimated that nearly 86,000 persons are currently living with a SCI and half of this number sustain tetraplegia[1]. Patients with tetraplegia are particularly prone to complications as they may suffer from multisystem impairments and severe mobility limitation. This is particularly true during the acute care hospitalization as the neurologic deficit is at its peak, while associated to traumatic injuries and surgical procedures that may delay the rehabilitation process and promote the development of complications.

The occurrence of medical complications following SCI is associated with increased hospital length of stay, costs of care and mortality rate [2, 3], and may also impact the neurological and functional outcomes [4]. While the occurrence of acute complications remains frequent[5], studies towards the improvement of SCI care led to the establishment of specialized acute care centers. Although there are no clear requirements to define them, SCI-centers usually comprise multidisciplinary coordinated care with the objective of optimizing the neurological and functional outcomes as well as promoting social reintegration [6, 7]. By providing the latest recommendations in SCI care, SCI-centers have demonstrated their effectiveness by decreasing hospital resources utilization and overall mortality rate [3, 6-9].

Recommendations for early transfer to SCI-centers following a traumatic SCI are based on low-quality studies. Furthermore, current recommendations do not determine the optimal timing for transfer to the acute SCI-center following the injury. Finally, considering that recent studies

suggest that emergent surgery could improve neurological recovery[10-12] and decrease risks of complications[13, 14], a decision has to be made whether a prompt surgery at the non-specialized (NS) regional center or direct transfer to the SCI-center should be prioritized. This question is particularly important for motor-complete cervical SCI, as this condition is associated with limited neurological recovery and a high risk of complications[15].

Some studies in the past have focused on the impact of specialized acute SCI-centers on the occurrence of medical complications[2, 16, 17]. However, these studies have either compared individuals managed in a NS or a SCI-center for the total acute care hospitalization stay, or by comparing individuals regardless of the amount of peri-operative management received in the SCI-center. In addition, patients sustaining severe tetraplegia were not specifically examined. Thus, the hypothesis underlying the current study is that complete peri-operative and surgical care in a specialized SCI-center will decrease the occurrence of medical complications.

Accordingly, the purpose of this study was to compare the occurrence of complications between patients surgically managed in a non-specialized center (NS) before being transferred to the SCI-center as compared to individuals promptly transferred to a SCI-center for complete peri-operative management.

METHODS

Patients

We conducted a retrospective cohort study including 116 adult patients (92 males; 24 females) aged 46.0 ± 19.3 years old, consecutively admitted to a single Level I SCI-specialized trauma center between April 2008 and November 2014. All subjects sustained a motor-complete cervical traumatic SCI, which was defined as a grade A or B severity on the ASIA (American Spinal Injury Association) impairment scale (AIS). All patients were treated surgically to decompress and stabilize the spine in order to minimize secondary injury to the spinal cord. Individuals treated non-surgically or sustaining a cervical SCI with milder neurological deficits (AIS-C or D, including central cord syndrome) were excluded, as they are recognized to experience better neurological and functional outcomes.

Our cohort was subdivided into two groups. Group 1 included 87 individuals who received complete peri-operative management (including surgery) provided by a specialized multidisciplinary team in a SCI-center. These patients were either transported directly from the trauma site to the SCI-center or evaluated initially in a NS center and then transferred to the SCI-center before the surgery. Group 2 consisted of 29 patients surgically and peri-operatively managed in one of ten non-specialized (NS) acute care centers before being transferred to the SCI center for postoperative management only.

The SCI-center involved in the current study comprises a specialized multidisciplinary approach that addresses medical, functional, psychological, and social issues. This team is composed of, but not limited to trauma, intensive care, spine surgery and physical medicine and rehabilitation

specialists, as well as many therapists and clinical nurses experienced in SCI care. The team ensured a complete peri-operative care for patients in Group 1 and post-operative care for Group 2. All patients were admitted and initially managed in the intensive care unit. Patients were transferred to the ward after their condition was deemed stable by the medical team.

Rehabilitation therapies were provided continuously throughout the hospitalization stay. The peri-operative care in the specialized SCI-center follows evidence-based recommendations for the acute care of SCI patients[7]. Clinical protocols are used to systematically manage bowel and bladder care and prevent venous thrombosis, pressure ulcers, contractures, malnourishment and aspiration. Cardiovascular and respiratory management is individualized based on the clinical judgement of the medical team and involved daily respiratory rehabilitation therapies. A physical medicine and rehabilitation specialist directs the acute rehabilitation process, applies interventions to promote functional and neurological recovery and coordinates transfer to a functional rehabilitation facility, once the patient's condition does not require additional active medical or surgical management.

Data collection and outcomes

All socio-demographic and clinical data pertaining to the hospitalization at the Level I SCI-specialized acute center was prospectively collected through the Quebec Trauma Registry. This prospective database includes all patients admitted at our institution following a traumatic event. Patients from Group 2 were also prospectively enrolled into the Quebec Trauma Registry upon arrival to our institution, but chart review was required to collect information pertaining to the presence of complications at admission to the SCI-center.

Collected data included age, gender and trauma severity as measured by the Injury Severity Score (ISS)[18]. The ISS was dichotomized as higher (≥ 26) and lower trauma severity (<26), based on the total cohort's median (median =26). The neurological level was defined as the most caudal segment with normal motor and sensory function bilaterally and was used to discriminate between high cervical levels (C1 to C4) and lower cervical levels (C5 to C8). The severity of the SCI was assessed at arrival to the SCI-center using the ASIA Impairment Scale (AIS) and dichotomized as AIS grades A or B. The presence of a concomitant traumatic brain injury (TBI) was also noted as well as the smoking status (past or active smoking vs. non-smoking). The surgical delay was defined as the time (in hours) between the trauma and the spinal surgery (time of skin incision) and was dichotomized as $<24\text{h}$ or $\geq 24\text{h}$ post-trauma.

The main outcome variable was the occurrence of non-neurological complications during the hospitalization at the SCI-center. Details are provided below.

Non-neurologic complications

In order to be considered as a complication, the secondary condition had to develop and be diagnosed in the course of the acute hospitalization in the SCI-center. However, complications developed previously in the NS center and still present at admission to the SCI-center were also considered for both groups, since these complications may influence the acute rehabilitation process in the SCI-center. Complications that may have occurred previously in the NS center but resolved prior to the SCI-center admission were not included. We did not have information on the majority of patients from Group 2 regarding respiratory complications at admission to the SCI-center; thus, we could not include respiratory complication at admission in our analysis.

However, respiratory complications during the course of stay at the SCI-center were included. Only complications occurring in more than 10% of patients were retrieved.

We considered the following complications: overall respiratory complications (e.g. pneumonia, acute respiratory distress syndrome; pulmonary embolism; bronchitis; atelectasis; pulmonary oedema; pneumothorax; etc.) urinary tract infections (UTI) and pressure ulcers (PU). Since the occurrence of pneumonia is frequent in patients with acute tetraplegia, pneumonia was also analyzed independently. The occurrence of respiratory complications were diagnosed using clinical features and were confirmed by a radiologist using chest X-rays[19]. UTI were diagnosed using criteria from the 2006 Consortium for Spinal Cord Medicine Guidelines for healthcare providers, using significant bacteriuria, pyuria, and signs and symptoms of UTI[20]. Finally, the presence of PU was diagnosed based on the clinical guidelines defined by the National Pressure Ulcer Advisory Panel (NPUAP)[21]. The complication rate refers to the proportion of patients who developed one of the above-mentioned complications during their stay at the specialized SCI center, and was expressed as a percentage.

In order to better evaluate the impact of the occurrence of complications, the length of stay (LOS) in the SCI-center was also compared between both groups.

Analysis

In order to compare characteristics of the two groups, we first used bivariate analysis (t- tests for continuous variables and chi-square tests for categorical variables). Normality of the distribution was assessed using the Kolmogorov-Smirnov test with a significance level set at 0.05.

In order to account for discrepancies in patient clinical and socio-demographic characteristics, a binary logistic regression model was used to determine the impact of timing of admission to the SCI-center on the occurrence of medical complications. The main dependent variable was the occurrence of at least one complication. The main independent variable was the time of admission to the SCI-center (Group 1- pre-surgery, or Group 2 –post-surgery). We included in the logistic model those covariates that were associated with having at least one complication in the bivariate analysis, with a p-value <0.2 , using chi-square and t-tests for categorical and continuous variables respectively. The level of significance for the logistic regression model was set at 0.05. IBM SPSS Statistics Version 21 software package was used for all statistical analyses.

RESULTS

Patient's characteristics

The entire cohort for our study consisted of 116 subjects who sustained a traumatic motor-complete cervical SCI. There were 87 patients in Group 1, while 29 were in Group 2. Patient socio-demographic and clinical characteristics are shown in Table 1. There were no significant differences between the two groups in terms of age, gender, ASIA grade, neurologic level of injury, severity of trauma as measured by the ISS, surgical delay and mortality rate. However, 52.9% patients from Group 1 had a TBI, which was nearly twice as many as for Group 2 (27.6%; $p=0.02$).

Approximately 70% of individuals experienced at least one complication during the SCI-center's stay, which was similar for both groups ($p=1.00$) (Table 2). When looking at individual types of complications, there were no differences between the two groups with respect to respiratory complications (54% vs 51.7%, $p=0.83$), pneumonia (47.1% vs 41.4%, $p=0.67$), UTI (20.7% vs 31.0%, $p=0.31$) and PU (36.8% vs 34.5% $p=1.00$).

Patients who were completely managed in the SCI-center (Group 1) were sent sooner to the intensive rehabilitation facility as compared to patients who had surgery in a NS center (Table 2). Indeed, following a median stay of 18.8 days (IQR 8.2-36.3) in the NS center prior to their transfer to the SCI-center, Group 2 were hospitalized in the SCI-center for a 20-day longer period than Group 1 (mean of 77.3 and 56.6 days, for Groups 2 and 1 respectively). Ultimately, transfer

to the SCI-center after surgical management was associated with longer acute care LOS following a motor-complete cervical SCI.

Four variables were associated with the occurrence of medical complications following bivariate analyses and were included in the binary regression model (Table 3). Therefore, timing of admission to the SCI-center (Group 1 or 2), neurologic level of injury, presence of obesity and trauma severity (ISS) were included as potential predictive factors of the occurrence of complications in our logistic regression model (Table 3). Higher level of cervical injury (C1 to C4) and presence of obesity increased the odds of developing a medical complication during the SCI-center's stay, with odds ratios of 2.5 and 11.7 respectively. The timing of admission to the SCI-center was not significantly associated to the occurrence of medical complications. However, the confidence interval showed a discrete tendency towards an odds ratio of greater than 1 (Table 3).

Finally, four variables were associated with the occurrence of respiratory complications following bivariate analyses and were subsequently included in the binary regression model (Table 4). Timing of admission to the SCI-center (Group 1 or 2), neurologic level of injury, age and trauma severity (ISS) were included as potential predictive factors of the occurrence of respiratory complications in our logistic regression model. Higher level of cervical injury (C1 to C4) and higher trauma severity were significantly associated with the occurrence of respiratory complications, with an odd ratio of 3.3 and 2.6 respectively. Timing of admission to the SCI-center was not associated with our outcome and its confidence interval was rather centered around the value of 1.

Pourquoi tu as pas fait la meme chose pour PU, pneumo, UTI et complic multiples? Je me doute que ça sortira pas mais je pense qu'il faudrait au moins justifier pourquoi on l'a fait juste avec les complic respiratoires et pas les autres...

DISCUSSION

The results of this study indicate that the rate of medical complications was similar following early and late management in a specialized SCI-center in individuals sustaining severe tetraplegia. It also suggests that late transfer to the SCI-center may be associated with prolonged acute care LOS. This study is the first to assess the occurrence of complications during the SCI-center hospitalization with respect to the amount of peri-operative management in a SCI-center following a motor-complete cervical SCI.

The rate of medical complications in this study was nearly 70% for both groups, which is at the higher end of previously reported data, ranging from 20% to 77% worldwide[5, 22, 23]. This great variability may be attributed to the different methods and definitions employed. Because specialized acute care SCI-centers were shown to improve outcomes and aim to decrease the occurrence of complications following a SCI [6], one would expect a lower occurrence of medical complications in Group 1. A potential explanation might be the fact that individuals from Group 1 suffered from a significant higher rate of concomitant traumatic brain injuries, which may be a risk factor for complications[24, 25]. This may explain the higher than expected rate of complications obtained in Group 1. On the other hand, 10.3% of patients from Group 2 were admitted to the SCI-center with medical complications. The presence of complications at admission to the SCI-center requires additional care from the SCI-center team in order to promote the healing process but also to prevent reoccurrence[26]. However, this was achieved at the expense of longer LOS. It is therefore possible that surgical management in a NS center and subsequent referral to a SCI-center for post-surgical management may not significantly impact

the occurrence of medical complications following the admission to the SCI-center, but may rather require additional resources in order to prepare individuals with severe tetraplegia to be discharged to an intensive functional rehabilitation setting.

The occurrence of medical complications during the SCI-center stay was associated with high cervical SCI and presence of obesity. Motor-complete SCI (AIS-A and B) are recognized as the main predictor of worst neurological and functional outcome[15, 27]. They are also recognized as a predictive factor for the occurrence of acute medical complications[5]. Since only motor-complete tetraplegia has been included in this study, it is not surprising that the level of injury was revealed as a predictive factor of the occurrence of medical complications during the SCI-center stay. Indeed, individuals sustaining higher level of cervical SCI (C1-C4) may suffer from severe respiratory and cardiovascular dysfunction as well as severe mobility restriction and dependency for activities of daily living, bed mobility and transfers[28, 29], which may ultimately lead to medical complications. The impact of obesity on functional outcomes has been reported in the SCI literature[30], but its impact on the occurrence of acute care medical complication remains unknown. However, it can be hypothesised that the addition of an obesity problem to severe cervical SCI may further deteriorate the respiratory and mobility functions, and may explain an increased vulnerability of these individuals to acute care complications[30, 31]. The differentiation between AIS-A and B grade was not revealed as a predictive factor of acute care complication. Since their differentiation lies in the sensitive sacral sparing which is recognized to influence the long-term neurological and functional outcomes, sensitive sacral sparing may not significantly influence the occurrence of complications during the acute care hospitalization.

Although the burden of associated injuries was individually associated with the occurrence of medical complications and previously associated to the occurrence of complications[5], it was not revealed as a significant predictor in our final logistic model. Associated traumatic injuries may reflect high-energy injury mechanism, additional surgery, prolonged immobilization as well as longer acute care length of stay. We may therefore conclude that individuals sustaining higher trauma severity are probably more vulnerable to acute care complications and further precaution should be undertaken for these individuals.

Although early management in a specialized SCI-center was showed to decrease the severity and number of medical complications following a SCI, timing of admission to the SCI-center was not revealed as a significant predictive factor of complication occurrence in our logistic regression model. Since the comparative analyses of this study demonstrated a similar rate of complications regardless of the timing of admission to the SCI-center, results of the regression analyses are not surprising. However, when looking at the confidence interval of Table 3, this one was a little skewed towards a value larger than one.

The occurrence of respiratory complications during the SCI-center's stay was significantly associated with the level of cervical injury and higher trauma severity. As expected, high cervical motor-complete SCI (C1-C4) being associated with severe respiratory, cardiovascular and mobility dysfunction. More particularly, C1-C4 patients may sustain a combined dysfunction of the inhalation and exhalation muscles, leading to respiratory insufficiency, increased airway resistance and impaired secretion clearance[32]. Moreover, dysphagia is also frequently diagnosed in the acute and subacute period following the injury[33]. As a result, these individuals

are particularly prone to respiratory infection and respiratory complications; they also may require mechanical ventilation assistance and prolonged intensive care stay[34].

As previously mentioned, increased burden of associated traumatic injuries may be a specific predictive factor of respiratory complications. Although the age was significantly associated to the occurrence of medical complications in our bivariate analysis, it was not revealed as a predictive factor in our logistic model accounting for other covariates. As older age was previously demonstrated as a predictive factor of acute care complications, it is therefore recommended to consider elderly patients as vulnerable individuals.

Finally, the LOS in the SCI-center was significantly longer for individuals lately transferred to the SCI-center. Many factors could influence the acute care LOS, and early admission to specialized SCI-center was shown to be one of them[6, 35]. Indeed, early management by a specialized multidisciplinary team may decrease hospital resources and optimize transfer to the functional rehabilitation [2, 3] , although the specific reasons why specialized acute care centers may decrease the acute care LOS remain imprecise. Specialized SCI-centers comprise skilled clinical professionals and caregivers that may assess risk factors of secondary condition related to SCI and positively affect outcome in SCI acute care management.

Limitations

The main limitations of this study are the small number of patients and its retrospective nature. Group 2 included only 29 patients arriving from many different hospital centers. Patient

management may vary between centers and some of these differences may account for the disparities in the complication rate.

Potential biases during data acquisition may have occurred due to the retrospective nature of this study. However, it is important to mention that all variables included in this study are collected routinely for all patients sustaining a traumatic SCI at our institution, and is performed by a medical archivist who was not involved in the present study.

Another limitation of this study relates to the occurrence of medical complications that may have developed and healed prior to the SCI-center admission. The inclusion of these complications would have allowed us to compare the occurrence of medical complications for the total acute care hospitalization and should be addressed in a future study.

Conclusion

Our study suggests that individuals sustaining severe tetraplegia who are transferred to an SCI-center from a NS center either pre-surgery or post-surgery developed a similar rate of medical complications during the SCI center stay. However, those transferred after surgical management in a NS center required longer stay in the SCI acute care hospital. Early referral to a SCI-center for complete management by a specialized multidisciplinary team following a motor-complete cervical SCI may optimize the acute care LOS, which is associated with the occurrence of medical complications. Previous studies have shown that the risk of complications is increased for SCI patients treated in non-specialized centers. From their arrival to the SCI-center, patients developed a similar rate of medical complications regardless of the timing of their admission. However, efforts to manage them and limit the rate of complications following late transfer to the SCI-center likely results in an increased acute care LOS.

References

1. Noonan, V.K., et al., *Incidence and prevalence of spinal cord injury in Canada: a national perspective*. Neuroepidemiology, 2012. **38**(4): p. 219-26.
2. Tator, C.H., et al., *Complications and costs of management of acute spinal cord injury*. Paraplegia, 1993. **31**(11): p. 700-14.
3. Richard-Denis, A., *Costs and length of stay for the acute care of patients with motor-complete spinal cord injury (SCI) following cervical trauma: the impact of early peri-operative management in a specialized acute SCI center*. Submitted in Journal of Neurotrauma, 2015.
4. Haisma, J.A., et al., *Complications following spinal cord injury: occurrence and risk factors in a longitudinal study during and after inpatient rehabilitation*. J Rehabil Med, 2007. **39**(5): p. 393-8.
5. Wilson, J.R., et al., *Clinical prediction model for acute inpatient complications after traumatic cervical spinal cord injury: a subanalysis from the Surgical Timing in Acute Spinal Cord Injury Study*. J Neurosurg Spine, 2012. **17**(1 Suppl): p. 46-51.
6. Parent, S., et al., *The impact of specialized centers of care for spinal cord injury on length of stay, complications, and mortality: a systematic review of the literature*. J Neurotrauma, 2011. **28**(8): p. 1363-70.
7. Consortium for Spinal Cord, M., *Early acute management in adults with spinal cord injury: a clinical practice guideline for health-care professionals*. J Spinal Cord Med, 2008. **31**(4): p. 403-79.
8. Wong, S.L., K. Shem, and J. Crew, *Specialized respiratory management for acute cervical spinal cord injury: a retrospective analysis*. Top Spinal Cord Inj Rehabil, 2012. **18**(4): p. 283-90.
9. Richard-Denis, A., et al., *Does the Acute Care Spinal Cord Injury Setting Predict the Occurrence of Pressure Ulcers at Arrival to Intensive Rehabilitation Centers?* Am J Phys Med Rehabil, 2015.
10. Fehlings, M.G., et al., *Early versus delayed decompression for traumatic cervical spinal cord injury: results of the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS)*. PLoS One, 2012. **7**(2): p. e32037.
11. Wilson, J.R., et al., *Early versus late surgery for traumatic spinal cord injury: the results of a prospective Canadian cohort study*. Spinal Cord, 2012. **50**(11): p. 840-3.
12. Cengiz, S.L., et al., *Timing of thoracolumbar spine stabilization in trauma patients; impact on neurological outcome and clinical course. A real prospective (rct) randomized controlled study*. Arch Orthop Trauma Surg, 2008. **128**(9): p. 959-66.
13. Bourassa-Moreau, E., et al., *Complications in acute phase hospitalization of traumatic spinal cord injury: does surgical timing matter?* J Trauma Acute Care Surg, 2013. **74**(3): p. 849-54.
14. McKinley, W., et al., *Outcomes of early surgical management versus late or no surgical intervention after acute spinal cord injury*. Arch Phys Med Rehabil, 2004. **85**(11): p. 1818-25.
15. Fawcett, J.W., et al., *Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials*. Spinal Cord, 2007. **45**(3): p. 190-205.

16. Donovan, W.H., et al., *Incidence of medical complications in spinal cord injury: patients in specialised, compared with non-specialised centres*. Paraplegia, 1984. **22**(5): p. 282-90.
17. DeVivo, M.J., et al., *Benefits of early admission to an organised spinal cord injury care system*. Paraplegia, 1990. **28**(9): p. 545-55.
18. Baker, S.P., et al., *The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care*. J Trauma, 1974. **14**(3): p. 187-96.
19. Medicine, C.f.S.C., *Respiratory management following spinal cord injury: a clinical practice guideline for health-care professionals*. J Spinal cord Med, 2005. **28**: p. 259-93.
20. Medicine, C.f.S.C., *Bladder management for adults with adults with spinal cord injury: a clinical practice guideline for health-care providers*. J Spinal cord Med, 2006. **29**(5): p. 527-573.
21. NPUAP-EPUAP, I., *NPUAP pressure ulcer stages/categories*, 2007.
22. Ackery, A., C. Tator, and A. Krassioukov, *A global perspective on spinal cord injury epidemiology*. J Neurotrauma, 2004. **21**(10): p. 1355-70.
23. Dryden, D.M., et al., *The epidemiology of traumatic spinal cord injury in Alberta, Canada*. Can J Neurol Sci, 2003. **30**(2): p. 113-21.
24. Bradbury, C.L., et al., *Traumatic brain injury in patients with traumatic spinal cord injury: clinical and economic consequences*. Arch Phys Med Rehabil, 2008. **89**(12 Suppl): p. S77-84.
25. Godbolt, A.K., et al., *Subacute complications during recovery from severe traumatic brain injury: frequency and associations with outcome*. BMJ Open, 2015. **5**(4): p. e007208.
26. Salzberg, C.A., et al., *A new pressure ulcer risk assessment scale for individuals with spinal cord injury*. Am J Phys Med Rehabil, 1996. **75**(2): p. 96-104.
27. Wilson, J.R., et al., *A clinical prediction model for long-term functional outcome after traumatic spinal cord injury based on acute clinical and imaging factors*. J Neurotrauma, 2012. **29**(13): p. 2263-71.
28. Burns, A.S. and J.F. Ditunno, *Establishing prognosis and maximizing functional outcomes after spinal cord injury: a review of current and future directions in rehabilitation management*. Spine (Phila Pa 1976), 2001. **26**(24 Suppl): p. S137-45.
29. Aito, S. and G.G. Gruppo Italiano Studio Epidemiologico Mielolesioni, *Complications during the acute phase of traumatic spinal cord lesions*. Spinal Cord, 2003. **41**(11): p. 629-35.
30. Hatchett, P.E., et al., *Body mass index changes over 3 years and effect of obesity on community mobility for persons with chronic spinal cord injury*. J Spinal Cord Med, 2016.
31. Gater, D.R., Jr., *Obesity after spinal cord injury*. Phys Med Rehabil Clin N Am, 2007. **18**(2): p. 333-51, vii.
32. Brown, R., et al., *Respiratory dysfunction and management in spinal cord injury*. Respir Care, 2006. **51**(8): p. 853-68;discussion 869-70.
33. Kirshblum, S., et al., *Predictors of dysphagia after spinal cord injury*. Arch Phys Med Rehabil, 1999. **80**(9): p. 1101-5.
34. Aarabi, B., et al., *Predictors of pulmonary complications in blunt traumatic spinal cord injury*. J Neurosurg Spine, 2012. **17**(1 Suppl): p. 38-45.

35. Bagnall, A.M., et al., *Effectiveness and cost-effectiveness of acute hospital-based spinal cord injuries services: systematic review*. Health Technol Assess, 2003. 7(19): p. iii, 1-92.

Table 1

Demographic and clinical characteristics of patients early and lately transferred to a SCI-center following a motor-complete cervical SCI.

Characteristics		SCI center (Group 1)	NS center (Group 2)	p-value
<i>N</i>	---	87	29	---
Age	Mean (SD)	46.0 (19.4)	48.1 (19.3)	0.95
Gender	% Male	78.2	82.8	0.79
ISS	% Higher trauma severity (≥ 26)	50.6	58.6	0.52
ASIA grade	A	65.5	82.8	0.10
	B	34.5	17.2	
Neurological level	% C1-C4	51.7	62.1	0.39
TBI	% TBI	52.9	27.6	0.02*
In-hospital death	% Deceased	9.2	6.9	0.70
Surgical delay	% <24h post injury	46.0	31.0	0.20
Smoking status	% active or previous smoking	47.1%	44.8%	1.00
Obesity	# of patients with BMI ≥ 30	3	1	1.00

ISS, Injury severity score

TBI, Traumatic brain injury

Table 2

Comparison of medical complications and length of stay according to timing of admission to the specialized SCI-center following a traumatic SCI.

Occurrence of complications		Time of admission to the SCI-center		p-value
		Pre-surgery (Group 1)	Post-surgery (Group 2)	
At least one (one or more)	%	71.3	72.4	1.00
Overall respiratory	%	54.0	51.7	0.83
Pneumonia	%	47.1	41.4	0.67
Pressure ulcer	%	36.8	34.5	1.00
Urinary track infection	%	20.7	31.0	0.31
LOS in the SCI-center	Mean (SD)	56.6(+/- 51.5)	77.3 (+/- 44.2)	0.04*

LOS, length of stay in the SCI-center (in days)

Table 3

Factors associated with the occurrence of medical complication during the acute care hospitalization using binary logistic regression analyses.

Variable	Odd ratio	95%CI	p-value
Time of admission to the SCI-center			
Group 1 (pre-surgery)	0 ^d		
Group 2 (post-surgery)	1.1	(0.4 ; 3.0)	0.85
Neurologic level of injury			
<i>C1-C4</i>	2.5	(1.0 ; 5.9)	0.04*
<i>C5-C8</i>	0 ^d		
Presence of obesity	11.7	(1.1 ; 129.4)	0.05*
ISS			
<26	0 ^d		
≥26	2.0	(0.84 ; 4.7)	0.12

$R^2 = 0.134$

ISS, Injury severity score

Table 4

Factors associated with the occurrence of respiratory complications during the acute care hospitalization using binary logistic regression analyses.

Variable	Odd ratio	95%CI	p-value
Time of admission to the SCI-center			
Group 1 (pre-surgery)	0 ^d		
Group 2 (post-surgery)	0.7	(0.3 ; 1.8)	0.50
Neurologic level of injury			
<i>C1-C4</i>	3.3	(1.5 ; 7.4)	<0.01*
<i>C5-C8</i>	0 ^d		
Age	0.99	(0.9 ; 1.0)	0.60
ISS			
<26	0 ^d		
≥26	2.6	(1.2 ; 5.8)	0.02*

$R^2 = 0.178$

ISS, Injury severity score

12 **12. Appendix 4: Manuscript published in Journal of Neurotrauma (2017)**

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Functional Outcome Prediction after Traumatic Spinal Cord Injury Based on Acute Clinical Factors

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Abstract

Spinal cord injury (SCI) is a devastating condition that affects patients on both a personal and societal level. The objective of the study is to improve the prediction of long-term functional outcome following SCI based on the acute clinical findings. A total of 76 patients with acute traumatic SCI were prospectively enrolled in a cohort study in a single Level I trauma center. Spinal Cord Independence Measure (SCIM) at 1 year after the trauma was the primary outcome. Potential predictors of functional outcome were recorded during the acute hospitalization: age, sex, level and type of injury, comorbidities, American Spinal Injury Association (ASIA) Impairment Scale (AIS), ASIA Motor Score (AMS), ASIA Light Touch score (LT), ASIA Pin Prick score (PP), Injury Severity Score (ISS), traumatic brain injury, and delay from trauma to surgery. A linear regression model was created with the primary outcome modeled relative to the acute clinical findings. Only four variables were selected in the model, with performance averaging an R-square value of 0.57. In descending order, the best predictors for SCIM at 1 year were: LT, AIS grade, ISS, and AMS. One-year functional outcome (SCIM) can be estimated by a simple equation that takes into account four parameters of the initial physical examination. Estimating the patient long-term outcome early after traumatic SCI is important in order to define the management strategies that might diminish the costs and to give the patient and family a better view of the long-term expectations.

Keywords: ASIA impairment scale; clinical prediction model; functional outcome; spinal cord injury

Introduction

WITH AN ANNUAL INCIDENCE in the United States estimated between 27.11 and 77.0² per million people, or roughly 12,000 to 20,000 new cases per year,² spinal cord injury (SCI) is a severe and debilitating condition. Around the world, the incidence of traumatic SCI ranges from 3.6 to 195.4 patients per million people.³ Australia, Canada, the U.S., and high-income European countries have various valuable reports of SCI, while African and Asian countries lack the appropriate epidemiologic data on it.³

Costs associated with SCI are greatly influenced by the patient's severity of injury and resultant degree of disability.⁴ In 2011, average per-person yearly expenses in the U.S. were \$523,089 in the first year and \$79,759 in each subsequent year.⁵ In Canada, the estimated lifetime economic burden per individual with SCI ranges from \$1.5 million for incomplete paraplegia to \$3.0 million for

complete tetraplegia. The annual economic burden associated with 1389 new persons with SCI surviving their initial hospitalization is estimated at \$2.67 billion.⁶

Prognosticating the patient functional outcome early after traumatic SCI is important in order to guide the management strategies that might diminish the costs and to give the patient and family a better view of the long-term expectations. The meta-analysis published by van Middendorp and colleagues in 2013 showed that despite the fact that "early" spinal surgery was significantly associated with improved neurological outcome and decreased length of stay, the evidence supporting early spinal surgery after SCI lacks robustness as a result of different sources of heterogeneity within and between original studies.⁷ The prediction model published by Wilson and colleagues in 2012 did not include the time to decompressive surgery that may influence patient outcomes.⁸ In addition, they

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used the Functional Independence Measure (FIM), which is not specific to patients with spinal cord injuries. Indeed, the Spinal Cord Independence Measure (SCIM) is the only functional recovery outcome measure designed specifically for SCI and the latest version of the SCIM (SCIM III) is recommended to be implemented worldwide as the primary functional recovery outcome measure for SCI.⁹ Moreover, SCIM has the most appropriate performance regarding the instrument's psychometric properties¹⁰ and is more responsive to change than the FIM for the respiration and sphincter management subscale¹¹ and mobility indoors and outdoors.¹²

The AMS (American Spinal Injury Association [ASIA] Motor Score) has been shown to be a predictor of the outcome for SCI,⁸ while being an integral part of the basic neurological examination, along with the light touch (LT) and pin prick (PP) sensory examination. Preservation of PP sensation below the zone of injury is associated with excellent prognosis for regaining functional ambulation.¹³ LT has a tendency to score higher than PP in SCI subjects. The discrepancies between LT and PP could relate to the greater complexity of the PP testing or to a difference in the extent of injury to the posterior columns (LT) and spinothalamic (PP) tracts.¹⁴

The Injury Severity Score (ISS) is an anatomical scoring system that provides an overall score for patients with multiple injuries. This scale is an independent predictor of death following severe trauma and correlates well with disability and hospitalization. In patients with SCI treated in Level I trauma centers, the severity of injury was significantly associated with an unfavorable outcome.¹⁵ There also are reports supporting the negative impact of the brain injury on the functional outcome and community integration.¹⁶ Given the incidence of combined traumatic brain injury (TBI) and SCI,¹⁷ one must take into account the former parameter.

With regard to the delay to surgery, there are reports that suggest that the patients with SCI who undergo surgical decompression (SD) within 8 h after injury have superior neurological outcomes than patients who undergo SD 8–24 h after injury, without any increase in the rate of adverse effects.^{18,19} Previous data also suggest that patients with traumatic SCI should be promptly operated on earlier than 24 h following the injury to reduce complications while optimizing neurologic recovery.^{20,21}

Older individuals with SCI have a substantially increased mortality rate during the first year, compared with younger patients. Among survivors, for a similar neurological improvement after the SCI, the functional gain is lower for older patients, compared with young patients.²²

The aim of this study is to examine whether different clinical parameters obtained in the acute period post-SCI, including the demographic factors and delay to surgery are predictors of the functional outcome at 1 year, evaluated with SCIM III.

Methods

Data source

A prospective cohort of 76 patients with a cervical or thoracolumbar traumatic SCI consecutively admitted to a single Level I SCI-specialized trauma center between April 2010 and November 2013 was studied. Patients entered the cohort at the time of admission after consent and were followed until discharge from the SCI-center. They were included if they sustained an acute traumatic SCI at the cervical (C1 to C8) or thoracolumbar (T1 to L1) requiring surgical management, which was performed in our institution, were aged 16 years or older and

TABLE 1. VARIABLES

Predictor variables (preoperative)

ASIA Impairment Scale (AIS)
ASIA Motor Score (AMS)
ASIA Light Touch score (LT)
ASIA Pin Prick score (PP)
Injury Severity Score (ISS)
Traumatic brain injury (TBI)
Delay to surgery (h)
Age (years)
Sex
Comorbidity
Type of injury
Level of injury

Dependent variables

Spinal Cord Independence Measure (SCIM)

ASIA, American Spinal Injury Association.

presented at their 1-year post-trauma follow-up visit. Patients were excluded if they had a penetrating trauma, received non-surgical management, had a diagnosis of central cord syndrome or neurological deficit without evidence of spinal instability, or did not come to the 1-year follow-up visit. The study was approved by the institutional review board and all patients were enrolled on a voluntary basis. Neurological status was assessed systematically at arrival to the hospital prior to surgery, in accordance with ASIA recommendations by a trained physician or nurse. No patient received steroids before or after the decompressive surgery.

Predictor variables

Independent variables consisted of variables that have been described in the literature as outcome predictors (Table 1). These

TABLE 2. SPINAL CORD INDEPENDENCE MEASURE (SCIM) VERSION III (ITZKOVICH AND COLLEAGUES 2007)

Self care	
1. Feeding	/3
2. Bathing	
A. Upper body	/3
B. Lower body	/3
3. Dressing	
A. Upper body	/4
B. Lower body	/4
4. Grooming	/3
Respiration and sphincter	
5. Respiration	/10
6. Sphincter management - bladder	/15
7. Sphincter management - bowel	/10
8. Use of toilet	/5
Mobility (room and toilet)	
9. Mobility in bed and action to prevent pressure sores	/6
10. Transfers: bed-wheelchair	/2
11. Transfers: wheelchair-toilet-tub	/2
Mobility (indoors and outdoors)	
12. Mobility indoors	/8
13. Mobility for moderate distances (10–100 meters)	/8
14. Mobility outdoors (more than 100 meters)	/8
15. Stair management	/3
16. Transfers: wheelchair-car	/2
17. Transfers: ground-wheelchair	/1

TABLE 3. PATIENT CHARACTERISTICS (SCALE VARIABLES)

	Total (missing)	Mean (SD)	Median	[P25 – P75]
Age (years)	76 (0)	43 (18)	40.0	[26 – 60]
Delay (hours)	76 (0)	57.8 (110)	20.7	[15.2 – 36.2]
ISS* (%)	75 (1)	26 (10)	26	[18 – 30]
Hospital LoS* (days)	76 (0)	28 (21)	22	[16 – 35]
ASIA motor score* (/100)	71 (5)	56 (25)	50.0	[46 – 78]
ASIA light touch score* (/112)	67 (9)	75 (30)	78.0	[52 – 100]
ASIA pin prick score* (/112)	60 (16)	73 (30)	78.0	[52 – 97]
Self-care score (/20)	76 (0)	17 (5)	18.0	[17 – 20]
Respiration and sphincter score (/40)	76 (0)	31 (10)	33.0	[24 – 40]
Mobility score (/40)	76 (0)	25 (12)	22.0	[17 – 39]
SCIM (%)	76 (0)	72 (25)	71.0	[59 – 97]

Bold* for significant correlation with SCIM (p value <0.05 were calculated using Spearman's rho).

Bold for normal distribution according to Kolmogorov-Smirnov test.

SD, standard deviation; LoS, length of stay; ASIA, American Spinal Injury Association; SCIM, Spinal Cord Independence Measure.

independent variables were collected prospectively during the early acute period after the SCI and describe the baseline characteristics of the patient and trauma, as well as the delay to surgery. For neurological classification, 28 dermatomes were assessed bilaterally using PP and LT sensation (0: absent; 1: impaired or 2: normal) and 10 key muscles (from 0 [total paralysis] to 5 [full

range of motion against resistance]) were assessed bilaterally for AMS. The results were summed to produce overall sensory and motor scores. LT and PP each scored out of 112 (28 locations bilaterally with a maximum score of 2 at each location) while AMS scored out of 100 (10 locations bilaterally with a maximum score of 5 at each location).

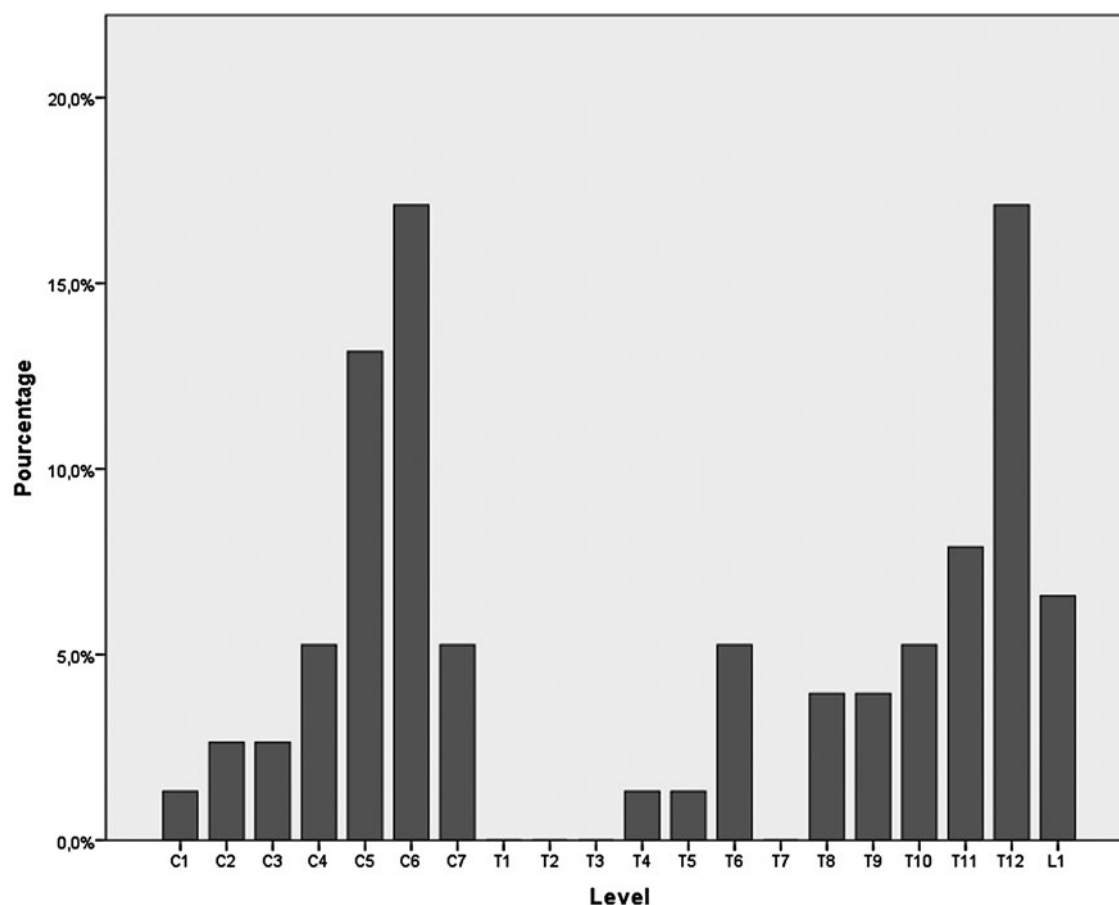


FIG. 1. Bimodal distribution of the level of anatomical lesions.

15 Outcome and follow-up

We quantified the outcome using the SCIM III score at 1 year (Table 2). The SCIM score consists in 19 items that take into account three domains: self-care (six items, scores range from 0–20); respiration and sphincter management (four items, scores range from 0–40); and mobility (nine items, scores range from 0–40). The total SCIM score ranges from 0 to 100.¹²

Statistical analysis

To explore the data, we performed a univariate and bivariate analysis, and then focused on inference and modeling. Central tendency, dispersion, and frequency of variables were analyzed. For continuous variables, their normal distribution was tested using a Kolmogorov-Smirnov test. Most variables did not have a Gaussian distribution. Therefore, we occasionally used median for central tendency and non-parametric tests for statistical inference. All categorical data were bilaterally tested on SCIM with a level of significance of 0.05 using *t*-tests or one-way analysis of variance. The statistical modeling for SCIM was based on a linear regression model with forward stepwise method, which met conditions of independence of errors and approached a studentized distribution of residues. Collinearity problems were tested using variance inflation factors. To account for missing data, a multiple imputation analysis was performed with 10 imputation iterations using Markov chain Monte Carlo method. Internal validation was obtained using a bootstrap re-sampling procedure of the imputed dataset. All statistics were performed using SPSS software (v.20, SPSS, Inc., Chicago, IL).

Results

Study population

The mean age was 43 years (± 18 ; Table 3) and most patients presented with fractures (64.5%) or fracture-dislocation injuries (27.6%). Remaining patients had acute traumatic disc and soft tissue injury causing overt spinal instability. There was a peak incidence for the levels C5-C7 (40.7%) and T11-L1 (31.6%) in terms of anatomical lesions (Fig. 1).

We found a male/female distribution ratio of 3/1. The most common causes of injury in our series are falls (36.8%), motor vehicle accidents (34.2%), and sport-related injuries (19.7%). Most patients were healthy with no comorbidities (75%) and almost half of them (46.1%) presented with TBI (Table 4).

Functional outcome and modeling

The functional outcome tested using the SCIM III had a mean value of 72% (± 25) at 12 months. As expected, the SCIM was significantly correlated with the AIS grade ($p < 0.001$).

In our model, the most powerful predictor variables proved to be, in descending order, the ASIA LT score, AIS grade, ISS, and the AMS score, all collected at the admission.

The pre-operative LT score was available for 67 patients while the AIS grade, the ISS and the AMS were respectively available for 75, 75, and 71 patients. To account for missing data, multiple imputations with 10 iterations was performed, resulting in a complete dataset of 760 patients in order to perform a linear regression less susceptible to bias. For the linear regression model, the performance was reflected by an R-squared value of 0.573.

The relative importance of the significant predictors were explained in terms of standardized coefficients (Table 5), reflecting the contribution of each variable in the prediction model.

TABLE 4. PATIENT CHARACTERISTICS
(CATEGORICAL VARIABLES)

	Total (missing)	No.	%	SCIM (%)	p value
Sex	76 (0)				0.58
Man		58	76.3	74	
Woman		18	23.7	69	
Comorbidity	76 (0)				0.79
Yes		19	25.0	74	
No		57	75.0	72	
TBI	76 (0)				0.96
Yes		35	46.1	72	
No		41	53.9	73	
Type of injury	76 (0)				0.82
Sport		15	19.7	69	
Assault (closed)		4	5.3	67	
Assault (penetrating)		1	1.3	99	
Fall		28	36.8	71	
Transport		26	34.2	76	
Other		2	2.6	75	
AIS grade*	75 (1)				<0.001
A		40	53.3	59	
B		8	10.7	71	
C		7	9.3	82	
D		20	26.7	98	
Level of injury	76 (0)				0.32
C1-C7		35	46.1	69	
T1-L1		41	53.9	75	

Bold *for significant association with SCIM (p value <0.05 according to Student's *t*-test or one way analysis of variance).

SCIM, Spinal Cord Independence Measure; TBI, traumatic brain injury; AIS, American Spinal Injury Association Impairment Scale.

The pre-operative LT score had a statistical predictive value of 0.382 (which reflect the participation of the variable in the model). The second most powerful predictor, the AIS grade, had a predictive value of 0.281 while the third predictor, the ISS, had a value of 0.272. The fourth predictor in order of importance was the AMS, with a predictive value of 0.068.

TABLE 5. PARAMETER ESTIMATES FOR MODEL PREDICTING
SCIM SCORE AT 1 YEAR FOLLOW-UP ($R^2=0.573$)

Prognostic variable	Standard. coefficient	Parameter estimate	95% CI	p value
Intercept		69.2	[62.1 – 76.3]	<0.001
ASIA light touch score	0.382	0.283	[0.221 – 0.346]	<0.001
AIS grade	0.281			<0.001
A		–15.0	[–18.9 – –11.1]	
B		–12.4	[–17.3 – –7.57]	
C		–7.01	[–11.6 – –2.42]	
D		0		
ISS	0.272	–0.589	[–0.743 – –0.434]	<0.001
ASIA motor score	0.065	0.134	[0.062 – 0.206]	<0.001

SCIM, Spinal Cord Independence Measure; CI, confidence interval; ASIA, American Spinal Injury Association; AIS, American Spinal Injury Association Impairment Scale; ISS, Injury Severity Score.

TABLE 6. PREDICTIVE MODEL EQUATION

SCIM score (1 year follow-up, %) = $69.2 + 0.283(\text{LT}) + (\text{AIS})$
 $- 0.589(\text{ISS}) + 0.134(\text{AMS})$

With:

LT = American Spinal Injury Association Light Touch score

AIS = American Spinal Injury Association Impairment Scale

ASIA A = -15

ASIA B = -12.4

ASIA C = -7.01

ASIA D = 0

ISS = Injury Severity Score

AMS = ASIA Motor Score

SCIM, Spinal Cord Independence Measure.

The other predictor variables with statistical significance were: the pre-operative ASIA PP scores and the hospital length of stay ($p < 0.05$). We found no predictive value for the sex, age, comorbidities, TBI, and type of injury or level of injury. Moreover, there was no significant correlation between the delay to surgery and the SCIM at 1 year.

According to the findings, we created a predictive equation of the SCIM score at 1 year after the SCI, based on the four most

powerful predictive variables: LT, AIS, ISS, and AMS (Table 6). The effect of LT score in predicting SCIM at 1 year is highlighted in Figure 2.

Discussion

This is the first study in the literature proposing a predictive model of the SCIM III total score based on acute predictors. By using only four predictors (LT, AIS grade, ISS and AMS), the model was associated with an R-squared value of 0.573, thereby explaining 57% of the variance in SCIM III total score.

Many studies have utilized walking as the primary measure of long-term functional outcome but if mobility function is highly important to individuals with paraplegia, restoration of arm and hand function is a specific priority for individuals with tetraplegia that needs to be taken into account.²³ Some authors⁸ have measured functional outcome using the FIM, which is not specific to patients with SCI. Moreover, many authors underscore the importance of incorporating outcome tools that include multi-dimensional assessments of functional status. In our series, the outcome is measured using the SCIM III. The choice was based on the fact that SCIM is the only functional recovery outcome measure designed specifically for

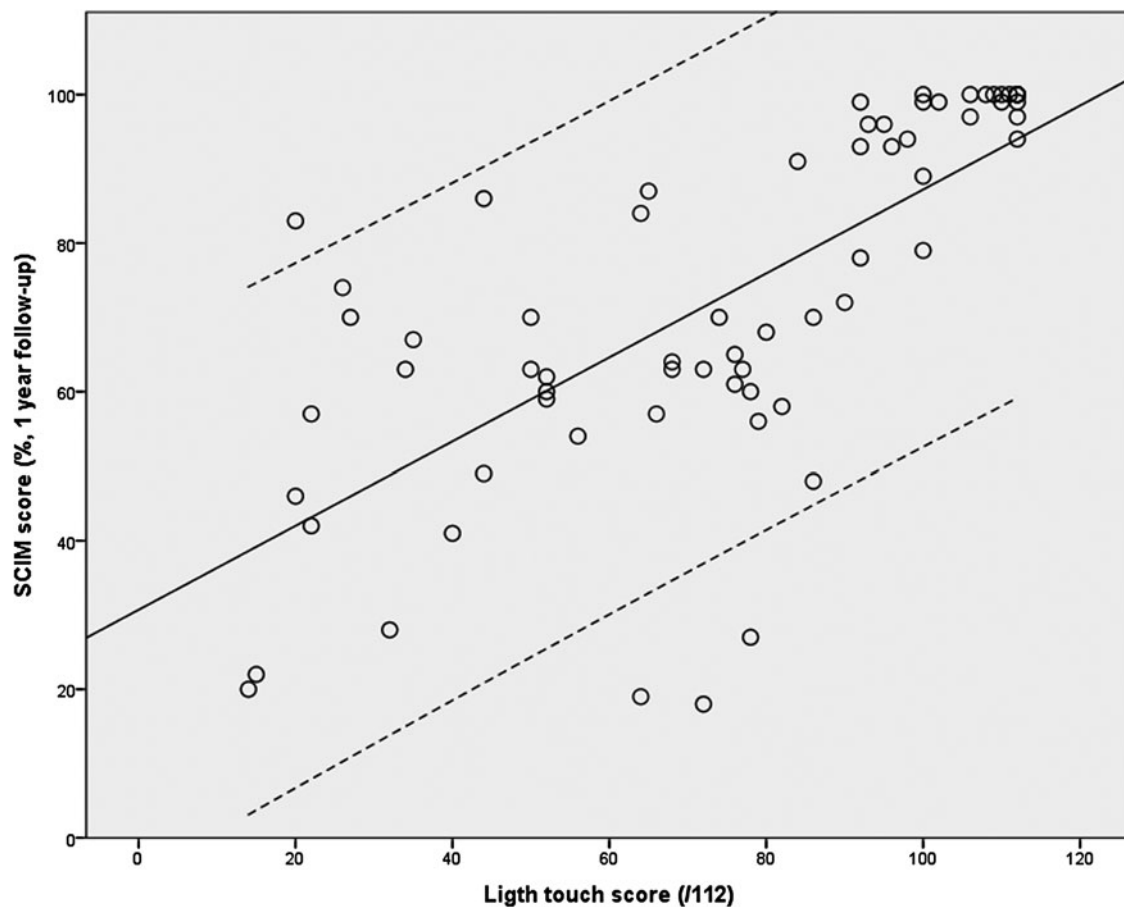


FIG. 2. Correlation between pre-operative American Spinal Injury Association Light Touch score and Spinal Cord Independence Measure (SCIM) at 1 year.

SCI⁹ and the score with the most appropriate performance regarding the instrument's psychometric properties.¹⁰

Interestingly, LT was by far the most powerful predictor for the SCIM at 12 months. Because the LT score uses all the dermatomes unlike the AMS, we believe that it provides a better understanding of the severity of injury. The AMS uses only 10 groups of muscles (C5-T1, L2-S1) and this could explain its lower significance. Other authors, such as Wilson and colleagues,⁸ suggest an important predictive value for the AMS but did not include the LT in their analysis. By including both AMS and LT in our analysis, our data suggest a greater predictive value for the LT score. This might be due to the fact that in the regression model, most of the variance explained by the AMS is already determined by the LT score (i.e., collinearity between the two variables). We find this to be the main reason why, in our study, the LT score has the highest predictive value of SCIM at 1 year post-injury. The same argument prevails regarding the PP score.

According to some authors, the AIS conversion outcome measure is poorly related to the ability to walk in traumatic SCI patients.²⁴ Moreover, unlike the sensory or motor scores, the AIS grade is categorizing the patients in only 5 grades. We consider this to be the main reason for the lower statistical significance when compared with the LT.

The ISS score has a very high predictive value in patients with SCI. This is in correlation with the importance of the clinical management in the acute setting. Indeed, the secondary insults from local ischemia, hypotension, hypoxia, and inflammation needs to be identified, prevented, and treated.²⁵ In consequence, multiple injuries severity can have a large effect on functional recovery. This confirms the findings of Stephan and colleagues.¹⁵

In their prediction model of the FIM 6 to 12 months after the SCI, Wilson and colleagues⁸ included four variables ($R^2=0.52$). Patients' age was a predictor of functional outcome, as well as AMS, AIS grade, and magnetic resonance imaging (MRI) signal. Although we expected the same results, our data showed no correlation between SCIM and patients' age ($p=0.232$). In another study, advanced age (> 65 years) was associated with worse functional outcome after SCI in terms of FIM.²⁶ The same authors noted that this effect was greatest for ASIA B and ASIA C patients and lesser for ASIA A and ASIA D patients. This could explain the absence of a significant relation between age and SCIM, given the fact that there were only eight (10.4%) ASIA B patients and seven (9.1%) ASIA C patients in our study.

There is growing evidence concerning the necessity of early decompression for optimal neurological recovery^{21,27} but in terms of functional recovery, the references are more sparse. Surprisingly, the delay to surgery was not significant in our model for SCIM. This is in conflict with a recent publication of Grassner and colleagues.¹⁹ In their study, where the population was divided into early (< 8 h) and late decompression, the outcome was measured at 1 year. SCIM was significantly higher in the early group. In our data, there was a large range in terms of delay to surgery (Table 3). Moreover, the variable distribution was not Gaussian (mean: 58 h; median: 21 h). This may reflect the difficulty of routing some of the patients in a hospital, even a Level I trauma center in Canada, in such a wide territory. Thus, a median time of 21 h is probably too long for observing significant benefits in terms of functional outcome for patients undergoing early surgery, as opposed to the study of Grassner and colleagues¹⁹ that specifically included a group undergoing early surgery within 8 h of the SCI.

Study limitations

Our series comprises 76 patients, which is a relatively small number. However, the size of our cohort was sufficient for identifying significant predictors of the functional outcome, and for obtaining an adequate performance of our predictive model ($R^2=0.573$). We also recognize that other potential predictors such as abnormal MRI signal was not collected in our data, while some authors took this into account for their prediction model.⁸ It is due to the fact that even if MRI carries great information about the spinal injury, it is not routinely performed in our trauma center when early surgery is required and when it is not likely to influence the surgical planning.

Conclusions

Prediction of functional recovery based on data available during the early acute period after the trauma is of paramount importance for the society, for the patients, and for the caregivers. This study highlights the importance of the initial ASIA evaluation (AIS grade, LT and AMS), as well as the ISS, in predicting patients' functional recovery at 1 year. Our prediction model including only these four predictors is efficient ($R^2=0.57$) and has the potential to guide decision at clinical as well as societal levels.

Acknowledgments

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Author Disclosure Statement

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For the other authors, no competing financial interest exist.

References

- Burke, D.A., Linden, R.D., Zhang, Y.P., Maiste, A.C., and Shields, C.B. (2001). Incidence rates and populations at risk for spinal cord injury: a regional study. *Spinal Cord* 39, 274–278.
- Bernhard, M., Gries, A., Kremer, P., and Böttiger, B.W. (2005). Spinal cord injury (SCI)–prehospital management. *Resuscitation* 66, 127–139.
- Jazayeri, S.B., Beygi, S., Shokrane, F., Hagen, E.M., and Rahimi-Movaghar, V. (2015). Incidence of traumatic spinal cord injury worldwide: a systematic review. *Eur. Spine J.* 4, 905–918.
- National Spinal Cord Injury Statistical Center. (2013). Spinal cord injury facts and figures at a glance. *J. Spinal Cord Med.* 36, 1–2.
- DeVivo, M., Chen, Y., Mennemeyer, S., and Deutsch, A. (2011). Costs of Care Following Spinal Cord Injury. *Top. Spinal Cord Inj. Rehabil.* 16, 1–9.
- Krueger, H., Noonan, V.K., Trenaman, L.M., Joshi, P., and Rivers, C.S. (2013). The economic burden of traumatic spinal cord injury in Canada. *Chronic Dis. Inj. Can.* 33, 113–122.
- van Middendorp, J.J., Hosman, A.J.F., and Doi, S.A.R. (2013). The effects of the timing of spinal surgery after traumatic spinal cord

- injury: a systematic review and meta-analysis. *J. Neurotrauma* 30, 1781–1794.
8. Wilson, J.R., Grossman, R.G., Frankowski, R.F., Kiss, A., Davis, A.M., Kulkarni, A.V., Harrop, J.S., Aarabi, B., Vaccaro, A., Tator, C.H., Dvorak, M., Shaffrey, C.I., Harkema, S., Guest, J.D., and Fehlings, M.G. (2012). A clinical prediction model for long-term functional outcome after traumatic spinal cord injury based on acute clinical and imaging factors. *J. Neurotrauma* 29, 2263–2271.
 9. Anderson, K., Aito, S., Atkins, M., Biering-Sørensen, F., Charlifue, S., Curt, A., Ditunno, J., Glass, C., Marino, R., Marshall, R., Mulcahey, M.J., Post, M., Savic, G., Scivoletto, G., and Catz, A. (2008). Functional recovery measures for spinal cord injury: an evidence-based review for clinical practice and research. *J. Spinal Cord Med.* 31, 133–144.
 10. Furlan, J.C., Noonan, V., Singh, A., and Fehlings, M.G. (2011). Assessment of disability in patients with acute traumatic spinal cord injury: Aa systematic review of the literature. *J. Neurotrauma* 28, 1413–1430.
 11. Anderson, K.D., Acuff, M.E., Arp, B.G., Backus, D., Chun, S., Fisher, K., Fjerstad, J.E., Graves, D.E., Greenwald, K., Groah, S.L., Harkema, S.J., Horton, J.A., Huang, M.N., Jennings, M., Kelley, K.S., Kessler, S.M., Kirshblum, S., Koltenuk, S., Linke, M., Ljungberg, I., Nagy, J., Nicolini, L., Roach, M.J., Salles, S., Scelza, W.M., Read, M.S., Reeves, R.K., Scott, M.D., Tansey, K.E., Theis, J.L., Tolfo, C.Z., Whitney, M., Williams, C.D., Winter, C.M., and Zanca, J.M. (2011). United States (US) multi-center study to assess the validity and reliability of the Spinal Cord Independence Measure (SCIM III). *Spinal Cord* 49, 880–885.
 12. Itzkovich, M., Gelernter, I., Biering-Sørensen, F., Weeks, C., Laramee, M.T., Craven, B.C., Tonack, M., Hitzig, S.L., Glaser, E., Zeilig, G., Aito, S., Scivoletto, G., Mecci, M., Chadwick, R.J., El Masry, W.S., Osman, A., Glass, C.A., Silva, P., Soni, B.M., Gardner, B.P., Savic, G., Bergström, E.M., Bluvstein, V., Ronen, J., and Catz, A. (2007). The Spinal Cord Independence Measure (SCIM) version III: reliability and validity in a multi-center international study. *Disabil. Rehabil.* 29, 1926–1933.
 13. Crozier, K.S., Graziani, V., Ditunno, J.F., and Herbison, G.J. (1991). Spinal cord injury: prognosis for ambulation based on sensory examination in patients who are initially motor complete. *Arch. Phys. Med. Rehabil.* 72, 119–121.
 14. Vazquez, N., Gall, A., Ellaway, P.H., and Craggs, M.D. (2013). Light touch and pin prick disparity in the International Standard for Neurological Classification of Spinal Cord Injury (ISNCSCI). *Spinal Cord* 51, 375–378.
 15. Stephan, K., Huber, S., Häberle, S., Kanz, K.-G., Bühren, V., van Griensven, M., Meyer, B., Biberthaler, P., Lefering, R., Huber-Wagner, S., and TraumaRegister DGU. (2015). Spinal cord injury-incidence, prognosis, and outcome: an analysis of the TraumaRegister DGU. *Spine J.* 15, 1994–2001.
 16. Nott, M.T., Baguley, I.J., Heriseanu, R., Weber, G., Middleton, J.W., Meares, S., Batchelor, J., Jones, A., Boyle, C.L., and Chilko, S. (2014). Effects of concomitant spinal cord injury and brain injury on medical and functional outcomes and community participation. *Top. Spinal Cord Inj. Rehabil.* 20, 225–235.
 17. Sharma, B., Bradbury, C., Mikulis, D., and Green, R. (2014). Missed diagnosis of traumatic brain injury in patients with traumatic spinal cord injury. *J. Rehabil. Med.* 46, 370–373.
 18. Jug, M., Kejžar, N., Vesel, M., Al Mawed, S., Dobravec, M., Herman, S., and Bajrović, F.F. (2015). Neurological recovery after traumatic cervical spinal cord injury is superior if surgical decompression and instrumented fusion are performed within 8 hours versus 8 to 24 hours after injury: a single center experience. *J. Neurotrauma* 32, 1385–1392.
 19. Grassner, L., Wutte, C., Klein, B., Mach, O., Riesner, S., Panzer, S., Vogel, M., Bühren, V., Strowitzki, M., Vastmans, J., and Maier, D. (2016). Early decompression (< 8 h) after traumatic cervical spinal cord injury improves functional outcome as assessed by spinal cord independence measure after one year. *J. Neurotrauma* 33, 1658–1666.
 20. Bourassa-Moreau, É., Mac-Thiong, J.M., Ehrmann Feldman, D., Thompson, C., and Parent, S. (2013). Complications in acute phase hospitalization of traumatic spinal cord injury: does surgical timing matter? *J. Trauma Acute Care Surg.* 74, 849–854.
 21. Bourassa-Moreau, É., Mac-Thiong, J.M., Li, A., Ehrmann Feldman, D., Gagnon, D.H., Thompson, C., and Parent, S. (2016). Do patients with complete spinal cord injury benefit from early surgical decompression? Analysis of neurological improvement in a prospective cohort study. *J. Neurotrauma* 33, 301–306.
 22. Furlan, J.C. and Fehlings, M.G. (2009). The impact of age on mortality, impairment, and disability among adults with acute traumatic spinal cord injury. *J. Neurotrauma* 26, 1707–1717.
 23. Simpson, L.A., Eng, J.J., Hsieh, J.T.C., and Wolfe, D.L. (2012). The health and life priorities of individuals with spinal cord injury: a systematic review. *J. Neurotrauma* 29, 1548–1555.
 24. van Middendorp, J.J., Hosman, A.J.F., Pouw, M.H., EM-SCI Study Group, and Van de Meent, H. (2009). ASIA impairment scale conversion in traumatic SCI: is it related with the ability to walk? A descriptive comparison with functional ambulation outcome measures in 273 patients. *Spinal Cord* 47, 555–560.
 25. Grant, R.A., Quon, J.L., and Abbed, K.M. (2015). Management of acute traumatic spinal cord injury. *Curr. Treat. Options Neurol.* 17, 334.
 26. Wilson, J.R., Davis, A.M., Kulkarni, A.V., Kiss, A., Frankowski, R.F., Grossman, R.G., and Fehlings, M.G. (2014). Defining age-related differences in outcome after traumatic spinal cord injury: analysis of a combined, multicenter dataset. *Spine J.* 14, 1192–1198.
 27. Battistuzzo, C.R., Armstrong, A., Clark, J., Worley, L., Sharwood, L., Lin, P., Rooke, G., Skeers, P., Nolan, S., Geraghty, T., Nunn, A., Brown, D.J., Hill, S., Alexander, J., Millard, M., Cox, S.F., Rao, S., Watts, A., Goods, L., Allison, G.T., Agostinello, J., Cameron, P.A., Mosley, I., Liew, S.M., Geddes, T., Middleton, J., Buchanan, J., Rosenfeld, J.V., Bernard, S., Atresh, S., Patel, A., Schouten, R., Freeman, B.J.C., Dunlop, S.A., and Batchelor, P.E. (2016). Early decompression following cervical spinal cord injury: examining the process of care from accident scene to surgery. *J. Neurotrauma* 33, 1161–1169.

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19 13. Appendix 5: Manuscript published in Journal of Neurotrauma

Journal of Neurotrauma

Journal of Neurotrauma

Journal of Neurotrauma: <http://mc.manuscriptcentral.com/neurotrauma>**The use of regression tree analysis for predicting the functional outcome following traumatic spinal cord injury**

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Manuscript Keywords (Search Terms):	Traumatic spinal cord injury, Prediction of recovery, Machine learning, Regression tree, CART

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Journal of Neurotrauma

October 12, 2017

Dr. John Povlishock, Editor-in-chief

Dear Dr. John Povlishock,

The authors have thoroughly considered the reviewer's comments and would like to express their gratitude for the useful remarks. The answer to each comment and points raised by the reviewer are detailed below. The corrections and modifications made in the manuscript are highlighted.



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Reviewer #1:**Comments to the Author**

This is a very interesting study investigation making use of machine learning algorithms; regression trees to predict the functional outcome following traumatic spinal cord injury.

Abstract: The abstract reflects the content of the paper. Please write in full text all abbreviations.

All abbreviations are now written in full text according to the reviewer's suggestion.

Introduction: is sufficient.

Methods: are sound. The statistical software and algorithms are novel and clearly interesting.

Results: The results are nicely presented.

Discussion: is sound. The use of machine learning algorithms in the form of regression trees is proposed for predicting the functional outcome following traumatic spinal cord injury using a limited number of demographic and clinical predictors collected during the acute care hospitalization.

The authors note the limitations.

Conclusion: The conclusion is sound.

References: The references are relevant and up to date.

Figures and Tables: There are 2 figures and 2 tables which all add to the paper.

The additions made in the manuscript read¹³⁸ as follows:

- *Of particular interest is the work published by Tanadini et al who described the use of recursive partitioning for the prediction of long-term clinical endpoints following a spinal cord injury. This study focused on a specific cohort comprising only patients sustaining a complete cervical spinal cord injury between C4 and C6. Following the recommendations of this work, the current study proposes the use of regression tree algorithms for predicting the functional outcome following complete and incomplete TSCI regardless of the neurological level, using demographic and clinical predictors collected during the acute care hospitalization. Regression trees were also used to evaluate the influence of varying the number of variables considered for predicting the functional outcome. (Introduction, p4)*

Introduction. The introduction provides an adequate frame for the study.

Patients and methods. I don't really know how the regression tree analysis works. I wonder if it works like the recursive partitioning in which the machine chooses the factors that is more closely associated with the outcome and begins the splitting from that factors and then repeats the sequence for other variables until no further splitting is possible. The authors should specified how the system works.

Regression trees are based on the repeated partitioning of a population into subgroups, based on criteria defined by the algorithm, in order to create homogeneous subgroups considering a specific parameter or outcome. This is similar to what recursive partitioning does.

Compared to the work published by Tanadini et al, our study provides two new contributions:

-Evaluation of the capabilities of machine learning algorithms to predict functional recovery of a non-stratified group of patients.

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-Evaluation of the influence of reducing¹³⁹ the number of predictors used for model building.

Details and references were added in the “Methods” section to clarify this point, as follows:

- *Statistical analyses were performed using the classification and regression tree (CART) analysis engine of the Salford Predictive Modeler software (Version 8, Salford Systems, San Diego, CA, USA). Regression trees were first described by Breiman et al.²⁶ and are based on the repeated partitioning of a population into subgroups considering criteria defined by the algorithm. Criteria are chosen depending on their ability to split the population into homogeneous subgroups in terms of functional outcome quantified by the total SCIM score. (Methods, p6)*

Results. I don't really understand the results. Figure 1 presents the simplified tree based on 4 factors, AIS grade, age, neurological level of lesion and energy of the trauma, but the splitting is based only on 2 factors, AIS Grade and lesion level. I wonder how and where age entered the analysis. In the same way, for the analysis based on all 11 factors, the splitting is based only of four of them (AIS grade, level of lesion, ISS and presence of pressure ulcers. And the other factors? Furthermore, in this figure, I don't understand the order in which the factors entered the analysis. According to the figure, ISS is more important than NLI in determining the tree, but the first two splitting are based on AIS grade and NLI and ISS entered the analysis only at the third step and only for patients with high cervical lesions.

The Salford Predictive Modeler builds multiple CART models of varying complexity. All models are then subjected to a cross-validation procedure in order to monitor potential over-fitting. In the end, the algorithm does not always use all predictors to build the best model following cross-validation. Another important aspect of CART modeling is the fact that the user can select the final model, not only based on optimal accuracy – as it was done in the current study – but also on model complexity. For example, from a practical point of view, a model with low complexity and a smaller number of predictors could be more clinically relevant (easier data collection and clinical interpretation,

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decreased risk of missing data, etc.) than ¹⁴⁰ another model with high complexity providing only a marginal increase in accuracy.

The modifications made to the manuscript read as follows:

- *Out of the four predictors used to build the simplified tree, only AIS grade and NLI appeared as primary splitters in the optimized tree following the cross-validation routine. (Results, p9)*
- *Only four out of 11 factors considered for this analysis appeared as primary splitters in the optimized tree following the cross-validation routine. (Results, p10)*
- *Following the cross-validation procedure, not all factors entered for tree building appeared as primary splitters in the optimized tree. The simplified tree was built using four predictors and the optimized tree only considered two of them to build the predictive model. The same observation was made for the complete tree, with the algorithm using only four out of 11 predictors. This observation indicates that the number of predictors could be further reduced from four to two and 11 to four for the simplified and complete tree, respectively, without affecting the prediction performances of the model. However, this should be done knowing that surrogate splitters would not be available to handle missing data if needed, which could have a detrimental effect on the predictive performances of the models. (Discussion, p13)*

Factors with significant importance (greater than zero) do not necessarily appear as primary splitters in the tree. This point can be explained by the concept of surrogate splitters identified by the software. Surrogate splitters are close approximations of the primary splitters presented in the trees and can be used to split a specific subgroup the same way the primary splitter does. Surrogate splitters are needed to handle eventual missing data and are taken into account when computing the variable order of importance. Therefore, a factor appearing only as a surrogate splitter can be associated with a significant importance score without appearing as a primary splitter in the tree, as seen in the results presented in our study. More details on this subject can be found in the Salford Systems website:

<https://www.salford-systems.com/blog/dan-steinberg/what-is-the-variable-importance-measure> Mary Ann Liebert, Inc, 140 Huguenot Street, New Rochelle, NY 10801

Details were added in the methods, results and discussion to clarify this point:

- *The classification and regression tree analysis engine of the Salford Predictive Modeler software identifies surrogate splitters as close approximations of the primary splitters appearing in the trees.²⁶ Surrogate splitters are used by the algorithm to handle eventual missing data and are taken into account when computing the variable importance. (Methods, p7)*
- **Error! Reference source not found.** *also shows the relative importance of variables used during tree building. AIS grade was the most important variable and appeared as the first splitter in the tree, followed by NLI with an importance score of 53.1. Age was considered as a surrogate splitter by the algorithm and was assigned a score of 3.3. Energy of the trauma had no importance in the tree building. (Results, p9)*
- *Once again, the AIS grade was the variable with the most discriminative power followed by ISS (58.7), surgery delay (45.6), NLI (44) and pressure ulcer occurrence (12.9). Age (10.7), trauma mechanism (2.5) and occurrence of UTI (1.5) were considered as surrogate splitters by the algorithm. (Results, p10)*
- *The variables used during tree building were ranked by relative importance. High importance was assigned to the factor appearing at the first split of each trees. Significant importance was also assigned to surrogate factors, not appearing as primary splitters in the tree. (Discussion, p13)*

Discussion. The discussion is adequate, although I would prefer an analysis of the factors determining the outcome and a comparison with previous available articles.

Although this study did not intend to identify predictors of the outcome (see first comment), an analysis of the factors determining the outcome and a comparison with previous studies is provided in the discussion:

- The high importance of the AIS¹⁴² grade, neurological level of injury and age for functional outcome prediction is consistent with other studies.^{8, 34, 35} Other important variables such as occurrence of medical complications (pressure ulcers) or the delay prior to surgery were also mentioned in previous studies.^{36, 37} However, although ISS is not recognized in the literature as a significant factor for functional outcome prediction after TSCI^{6, 8}, it was revealed as an important variable during tree construction in this study. Further work about the use of regression trees in the field of TSCI is needed to confirm this finding, as machine learning algorithms could allow identifying new significant predictors. (Discussion, p13-14)

References. The references are adequate. However, ref 4 and 40 are the same and one should be eliminated (probably ref. 40).

References 4 and 40 are the same. Reference 40 was removed according to the reviewer's suggestion.

The use of regression tree analysis for predicting the functional outcome following traumatic spinal cord injury

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Keywords: Traumatic spinal cord injury, prediction of the recovery, machine learning, regression tree

Abstract

Predicting the long-term functional outcome following traumatic spinal cord injury is needed to adapt medical strategies and to plan an optimized rehabilitation. This study investigates the use of regression tree for the development of predictive models based on acute clinical and demographic predictors.

This prospective study was performed on 172 patients hospitalized following traumatic spinal cord injury. Functional outcome was quantified using the Spinal Cord Independence Measure collected within the first-year post injury. Age, delay prior to surgery and Injury Severity Score were considered as continuous predictors while energy of injury, trauma mechanisms, neurological level of injury, **injury severity**, occurrence of early spasticity, urinary tract infection, pressure ulcer and pneumonia were coded as categorical inputs. A simplified model was built using only AIS grade, **neurological level**, energy and age as predictor and was compared to a more complex model considering all 11 predictors mentioned above.

The models built using 4 and 11 predictors were found to explain 51.4% and 62.3% of the variance of the **Spinal Cord Independence Measure** total score after validation, respectively. The severity of the neurological deficit at admission was found to be the most important predictor. Other important predictors were the Injury Severity Score, age, neurological level and delay prior to surgery.

Regression trees offer promising performances for predicting the functional outcome after a **traumatic spinal cord injury**. It could help to determine the number and type of predictors leading to a prediction model of the functional outcome that can be used clinically in the future.

Introduction

Traumatic spinal cord injury (TSCI) occurs at a rate of about 10 to 60 cases per million individuals depending on the country.¹ Following TSCI, motor and sensory functions can be impaired, leading to a loss of autonomy and a poor quality of life. The functional outcome is typically considered as the most useful primary outcome for patients with chronic TSCI² as patients are mostly concerned with their ability to engage in activities of daily living.³ Predicting the potential of functional recovery is important to guide the treatment, set realistic goals and to plan an optimized rehabilitation as well as to answer questions from the patients and their relatives.^{4,5} There is therefore a need to develop accurate tools able to predict the functional outcome following TSCI, particularly during the early stages after the injury in order to plan subsequent phases of treatment and rehabilitation.

Predictive models of the functional recovery using predictors collected during the acute hospitalization have been proposed previously, mainly using linear⁶⁻⁸ or logistic^{9,10} regressions. Recently, researchers active in various medical fields have described prediction tools based on machine learning algorithms.¹¹⁻¹³ According to those studies, machine learning algorithms exhibit good predictive performances, especially when considering large numbers of variables and non-linear relationships. Among machine learning methods, classification and regression trees (CART) offer promising predictive performances as CART have been found to be consistently as good as, or better than linear and logistic regression models, particularly for datasets with high skew and kurtosis.^{14,15} Specifically, advantages of CART over linear/logistic regression include reporting the actual observed outcomes for real subgroups, the absence of assumptions about the linearity of relationships between independent and dependent variables and the form of underlying distributions, adequate handling of multicollinearity or complex interactions between independent variables, detection of outlier values, ability to handle

missing data, and inclusion of multidimensional data. Predictive models based on regression trees are increasingly popular in the medical field thanks to their good performances, easy implementation and interpretation.¹⁶ However, to date, limited effort was made to use those algorithms in the field of TSCI.^{17, 18} Of particular interest is the work published by Tanadini et al¹⁹ who described the use of recursive partitioning for the prediction of long-term clinical endpoints following a spinal cord injury. This study focused on a specific cohort comprising only patients sustaining a complete cervical spinal cord injury between C4 and C6. Following the recommendations of this work, the current study proposes the use of regression tree algorithms for predicting the functional outcome following complete and incomplete TSCI regardless of the neurological level, using demographic and clinical predictors collected during the acute care hospitalization. Regression trees were also used to evaluate the influence of varying the number of variables considered for predicting the functional outcome.

Methods

Participants

This study was based on a prospective cohort of 172 patients who sustained a TSCI between January 2010 and June 2016. Patients were enrolled prospectively on a voluntary basis during the acute hospitalization at a single Level I trauma center specialized in SCI. This study was approved by the Institutional Review Board of Hopital du Sacré-Coeur de Montréal and all methods were performed in accordance with relevant guidelines and regulations. Patients were included if they sustained a TSCI between C1 and L2 levels, had complete data and were followed for a minimum of 6 months after the trauma.

Variables

Predictors consisted in independent variables that have been proposed in the literature as potential predictors of the functional outcome after a TSCI. All data were collected prospectively by a research nurse during the acute hospitalization.

The injury severity score (ISS) described by Baker et al.²⁰ was used as an indicator of trauma severity. Delay before surgery was defined as the interval of time in hours between the injury and the beginning of surgery, and was considered as a continuous predictor. Mechanism of injury was divided into five categories: sport, blunt assault, fall, motor vehicle accident (MVA) and other (etiologies not easily classified, e.g. falling objects, crush injuries, electrocution, etc.). Energy associated with the injury was classified as low (trivial trauma, fall from standing or walking, assault, etc.) or high (motor-vehicle/motorcycle accident, pedestrian hit by vehicle, fall from more than 10ft, etc.). The occurrence of the three main medical complications occurring following a TSCI²¹, consisting in pneumonia, urinary tract infections or pressure ulcers, was collected during acute care hospitalization and was considered as binary predictors. Occurrence of early spasticity during the acute hospitalization was also assessed and considered as a binary predictor. The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) was used to assess the severity of injury in the form of American Spinal Injury Association Impairment Scale (AIS) grades upon admission for every patient.²² The neurological level of injury (NLI) was defined as the most caudal spinal level with normal sensory and motor functions. NLI was classified into 4 categories comprising high (HC) (C1-C4) and low (LC) (C5-T1) cervical, thoracic (TH) (T2-T10) and thoracolumbar (TL) (T11-L2) injuries as recommended by Dvorak et al.²³

The third version of the Spinal Cord Independence Measure (SCIM-III) was used to quantify the functional outcome. If outcome assessment was not collected at 1-year after the TSCI, the SCIM score at 6 months was considered. SCIM scores were collected by a research nurse within the Level I trauma center. SCIM score at 1-year follow-up was available for 125 patients and the 6-month follow-up was used for the 47 remaining patients. SCIM is a recognized and widely used scale designed to assess functional outcome in individuals with spinal cord lesions²⁴. The total score ranges from 0 to 100 and includes information from self-care, respiration, sphincter management and mobility, with a higher score defining higher functional status.²⁵

Statistical analysis

Statistical analyses were performed using the classification and regression tree (CART) analysis engine of the Salford Predictive Modeler software (Version 8, Salford Systems, San Diego, CA, USA). Regression trees were first described by Breiman et al.²⁶ and are based on the repeated partitioning of a population into subgroups considering criteria defined by the algorithm. Criteria are chosen depending on their ability to split the population into homogeneous subgroups in terms of functional outcome quantified by the total SCIM score.

The regression trees were constructed using the Gini splitting rule and no specific stopping rule was used. For every tree grown, a cross-validation was performed in order to monitor for potential overfitting.²⁷ A 10-fold cross-validation was chosen as it was shown to be adapted for the validation of predictive models built from small populations.²⁸⁻³⁰ During 10-fold cross-validation, the population is divided into 10 sub-populations of equal size, 9 of which are used for model building and the last one is used for model validation. The process is repeated 10 times with different choices of sub-populations for training and testing so that the whole sample is used as training and validation data. K-fold cross-validation is a known method to estimate the error rate of a model. However, it is also known to be a highly variable estimator due to the

randomized partitioning of the population. One way to quantify the variance of the process is to repeat the K-fold cross-validation procedure.³¹ In this study, the cross-validation routine was repeated 100 times for each model. Model performances were then evaluated using R^2 values for the learn and test procedures and were expressed as mean R^2 and standard deviation (SD) computed following the repeated cross validation procedure. The optimal size of the regression tree was selected using the maximum value of R^2 obtained after cross-validation routine.

Two predictive models were built in this study. A complete model included all 11 predictors mentioned above (Table 1). A simplified version of the model was also built using age, AIS grade, energy of injury and neurological level (NLI), as those predictors are often considered to be particularly important according to the literature.^{6, 8, 10, 32} Both models were compared in terms of prediction performances to identify the benefits of considering a large amount of predictive factors.

The relative importance of each predictor was computed for both models. Variable importance reflects the ability of the variable to split a cluster of patients. In other words, it reflects how much influence a predictor has on the long-term SCIM total score according to the model. The most important variable during tree construction was assigned with a score of 100 and the other variables were scaled down proportionally to their importance. The classification and regression tree analysis engine of the Salford Predictive Modeler software identifies surrogate splitters, as close approximations of the primary splitters appearing in the trees.²⁶ Surrogate splitters are used by the algorithm to handle eventual missing data and are taken into account when computing the variable importance.

Results

Table 1 gives an overview of the distribution of each variable across the cohort. Mean age at injury was 48.9 with a standard deviation of 18 years. The most frequent mechanism of injury was fall (45.9%), followed by transport (30.8 %), sport (16.3 %), assault blunt (5.2 %) and other (1.8 %). Energy of injury was considered low in 57 % of the cases and the mean injury severity score was 23.9(10.2). Delay from injury to surgical incision was highly variable with a mean value of 114.9(365.8) hours. Neurological assessment performed during the acute care period showed that AIS A was the most frequent neurological deficit after injury (39.5 %) followed by AIS D (36.1 %), AIS C (14.5%) and AIS B (9.9%). The most frequent neurological level of injury was low cervical (37.8 %) followed high cervical (28.5%), thoracolumbar (20.3%) and thoracic (13.4%). Early spasticity was observed in 54.1 % of the patients. Assessing the occurrence of complications showed that 14.5 % of the patients developed pneumonia, 18.6 % showed signs of pressure ulcer and urinary tract infection was diagnosed in 14.5 % of the cases. The mean SCIM score at follow up was 72.6(27.5).

Table 1 around here

Figure 1 presents the regression tree built considering 4 predictors comprising age, energy of the trauma, ASIA impairment scale grade at admission, neurological level of injury and the SCIM total score as the continuous output. The tree started with a root containing all 172 individuals in the dataset. The first split divided the population based on the AIS grade. The population with grade D formed Group 1, a terminal node with 62 patients and a mean SCIM total score of 95.6(7.8). The remaining group of patients with grades A, B and C was then divided into two

terminal nodes depending of the neurological level of injury. The 30 patients injured at the high cervical level, from C1 to C4, were separated from the rest of the group to form Group 2 with a mean SCIM score of 38.5(27). The remaining 80 patients formed Group 3 with a mean SCIM score of 67.6(20.7). Out of the four predictors used to build the simplified tree, only AIS grade and NLI appeared as primary splitters in the optimized tree following the cross-validation routine.

Figure 1 also shows the relative importance of variables used during tree building. AIS grade was the most important variable and appeared as the first splitter in the tree, followed by NLI with an importance score of 53.1. Age was considered as a surrogate splitter by the algorithm and was assigned a score of 3.3. Energy of the trauma had no importance in the tree building.

Figure 1 around here

Figure 2 shows the regression tree built using all 11 predictors. The first two splits were similar to what was obtained for the simplified tree presented in Figure 1. After the second split, the high cervical NLI group was divided based on the injury severity score (ISS) with a cut-off value of 22 to create Group 2 (15 patients, mean SCIM score of 55.1(26.7)) and Group 3 (15 patients, mean SCIM score of 21.8(13.6)) as terminal nodes. The group of patients with low cervical, thoracic and thoracolumbar NLI was divided based on the occurrence of pressure ulcer (PU). The 17 patients sustaining PU were put into Group 4 with a mean SCIM score of 48.2(18.1). The remaining patients were finally divided into two terminal nodes based on the AIS grade, with grade A (Group 5, 41 patients, mean SCIM score of 66.2(16.1)) separated from the others (Group 6, 22 patients, mean SCIM score of 85(14.7)). Only four out of 11 factors considered for this

analysis appeared as primary splitters in the optimized tree following the cross-validation routine.

Once again, the AIS grade was the variable with the most discriminative power followed by ISS (58.7), surgery delay (45.6), NLI (44) and pressure ulcer occurrence (12.9). Age (10.7), trauma mechanism (2.5) and occurrence of UTI (1.5) were considered as surrogate splitters by the algorithm. Predictors such as spasticity, pneumonia and energy of trauma had no importance during tree construction.

Figure 2 around here

Table 2 reports the performance of both models during the training (Learn) and cross-validation testing (Test) routines. In both cases, a slight overfitting was observed because of R^2 Learn being superior to R^2 Test. The variability of the error estimator computed using the repeated K-fold cross-validation was low with a maximum standard deviation of 0.04 observed for the R^2 test of the larger model after 100 cross-validation routines. The number of predictors considered during model building affected the performance of the models as R^2 reported for both learn and test procedures were higher with 11 predictors considered.

Table 2 around here

of 0.72 was reported by Abdul-Sattar ⁶ for a linear regression between the motor FIM score and 5 predictors collected during the acute phase. Another linear regression considering the FIM score as the continuous output was described by Post et al. ³³ and reported a R^2 value of 0.49 for model building. Unfortunately, these last two models were not validated using a test cohort and their true prediction performances cannot be quantified. These models also used the FIM score, which is not specific to patients with TSCI. On the other hand, the Spinal Cord Independence Measure (SCIM-III) score proved to be a reliable and valid metric to assess the functional outcome specifically for patients with TSCI ²⁴. Accordingly, Richard-Denis et al. ⁸ studied acute predictors of the SCIM within 1-year post-injury. In their linear regression analysis, they obtained a model training R^2 value of 0.67 for tetraplegic patients using the AIS grade, the occurrence of complications, the length of stay and the presence of spasticity collected during the acute hospitalization. As for paraplegic patients, they obtained a model training R^2 value of 0.55 using the AIS grade, the body mass index, the Injury Severity Score and the presence of spasticity collected during the acute hospitalization. However, they did not validate their model in order to provide a R^2 on a test sample. In the light of previous studies predicting the functional outcome in TSCI patients, it appears that regression trees exhibit at least similar predicting performances when compared to linear regression methods, as it was suggested for other patient populations. ^{14, 15}

The number of predictors used for tree building affected the performance of the models during both learning and testing routines as seen in Table 2, with the more complex model exhibiting better performance than the simplified version. In addition, both models still showed acceptable performances following cross-validation as compared to the previously published predictive models. ^{7, 8, 33} Following the cross-validation procedure, not all factors entered for tree building appeared as primary splitters in the optimized tree. The simplified tree was built using four

Discussion

Functional recovery is one of the main concern for patients living with spinal cord injury. An early prediction of the functional outcome can help health professionals to promote efficient care, optimize treatments and set realistic goals. In this study, the use of machine learning algorithms in the form of regression trees is proposed for predicting the functional outcome following complete and incomplete traumatic spinal cord injury using a limited number of demographic and clinical predictors collected during the acute care hospitalization. Machine learning algorithms were also used to assess the effect of the number of predictor considered during tree building on the prediction performances of the models.

The simplified (4 predictors) and complete (11 predictors) models demonstrated good performances during the training routine with mean R^2 learn values of 0.539 and 0.705 respectively. Both models were also subjected to repeated 10-fold cross-validation testing and demonstrated R^2 test values of 0.517 (0.01) and 0.632 (0.03) for the simplified and complete model respectively. The low standard deviations associated with the R^2 test values indicate a good stability of the model after 100 K-fold cross-validation routines. Analysis of the models also showed the importance of each predictor within the prediction algorithm. For the simplified model, AIS grade was the most important predictor followed by NLI and age. AIS grade was also the most significant predictor in the complete model and was followed by ISS, surgery delay, NLI, PU, age, trauma mechanism, and UTI. Spasticity, occurrence of pneumonia or energy of the trauma had no significance in the tree construction.

Several models for predicting the functional outcome following TSCI were previously described in the literature. In 2012, Wilson et al.⁷ reported a linear regression for predicting the FIM score using four predictors at 1 year with a R^2 value of 0.52 observed after bootstrap validation, which is similar to our results using also four predictors in the simplified model. An excellent R^2 value

predictors and the optimized tree only considered two of them to build the predictive model.

The same observation was made for the complete tree, with the algorithm using only four out of 11 predictors. This observation indicates that the number of predictors could be further reduced from four to two and 11 to four for the simplified and complete tree, respectively, without affecting the prediction performances of the model. However, this should be done knowing that surrogate splitters would not be available to handle missing data if needed, which could have a detrimental effect on the predictive performances of the models. These findings confirm the relevance of restricting the number of predictors to the most significant ones to build simplified but accurate predictive models when some predictors are difficult to collect or poorly reliable. Considering fewer predictive variables could lead to an easier and quicker data collection and analysis as well as easier implementation of the predictive models. Although our simplified model was limited to predictors often recognized in the literature as the most important, further work is still required to determine the minimal number and the type of predictors leading to a prediction model that can be used in the clinical setting.

The variables used during tree building were ranked by relative importance. High importance was assigned to the factor appearing at the first split of each trees. Significant importance was also assigned to surrogate factors, not appearing as primary splitters in the tree. The high importance of the AIS grade, neurological level of injury and age for functional outcome prediction is consistent with other studies.^{8, 34, 35} Other important variables such as occurrence of medical complications (pressure ulcers) or the delay prior to surgery were also mentioned in previous studies.^{36, 37} However, although ISS is not recognized in the literature as a significant factor for functional outcome prediction after TSCI^{6, 8}, it was revealed as an important variable during tree construction in this study. Further work about the use of regression trees in the field

of TSCI is needed to confirm this finding, as machine learning algorithms could allow identifying new significant predictors.

Regression trees are increasingly popular in the medical field for predicting binary or continuous output^{16, 38-40} but have not been applied yet to the field of spinal cord injury. This modeling technique is promising considering its simplicity to implement and interpret as it provides a visual representation of important factors influencing the functional outcome of the patients. The predictive models exhibited similar or better performances than what was obtained with linear regression, especially when a large number of variables are included.

Study limitations

SCIM score at 1-year follow-up was available for 125 patients and the 6-month follow-up was used for the 47 remaining patients. Even if most of the recovery happens within the first 6 months following TSCI^{4, 32, 41}, this difference could influence the results presented in this study. Ideally, the same follow-up interval should be used for the whole cohort.

Validation of the models was done using the well-known, K-fold cross-validation routine. If the efficiency of this technique is recognized, it still uses cases from the same dataset for model building and validation. Establishing the precise performance of the models will require an evaluation using a larger dataset, while the use of independent datasets from other centers would be necessary to ensure good external validity of the models.

Conclusion

The use of regression tree algorithm for predicting the long-term functional outcome following traumatic spinal cord injury was investigated in this study. Regression trees exhibit good predictive performance compared to the linear regression models published previously, even with the use of a limited number of predictors. The importance of predictors considered during tree building was mainly consistent with the literature with the initial severity of neurological injury being the most significant factor. Due to their easy implementation and interpretation combined with good predictive performances, regression tree-based models are promising for predicting the functional outcome following traumatic spinal cord injury.

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Author disclosure statement

No competing financial interests exist.

Author Contributions

Y.F. participated in the design of the study, performed the statistical analysis, analyzed the results, wrote the manuscript, reviewed and edited the manuscript. M. B. and A. R.-D. participated in the design of the study, analyzed the results, contributed to the discussion, reviewed and edited the manuscript. C. T. collected the data, analyzed the data, contributed to the discussion, reviewed and edited the manuscript. J.-M. M.-T. was responsible for the design of the study, analyzed the results, contributed to the discussion, reviewed and edited the manuscript. J.-M. M.-T. is the guarantor of this work, had full access to the data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. Singh, A., Tetreault, L., Kalsi-Ryan, S., Nouri, A. and Fehlings, M.G. (2014). Global prevalence and incidence of traumatic spinal cord injury. *Clin Epidemiol* 6, 309-331.
2. Steeves, J.D., Lammertse, D., Curt, A., Fawcett, J.W., Tuszynski, M.H., Ditunno, J.F., Ellaway, P.H., Fehlings, M.G., Guest, J.D., Kleitman, N., Bartlett, P.F., Blight, A.R., Dietz, V., Dobkin, B.H., Grossman, R., Short, D., Nakamura, M., Coleman, W.P., Gaviria, M., Gaviria, M. and Privat, A. (2007). Guidelines for the conduct of clinical trials for spinal cord injury (SCI) as developed by the ICCP panel: clinical trial outcome measures. *Spinal cord* 45(3):206-21.
3. Mittmann, N., Hitzig, S.L. and Catharine Craven, B. (2014). Predicting health preference in chronic spinal cord injury. *J Spinal Cord Med* 37, 548-555.
4. Ditunno, J.F., Jr. (1999). Predicting recovery after spinal cord injury: A rehabilitation imperative. *Arch Phys Med and Rehabil* 80, 361-364.
5. Scivoletto, G., Morganti, B. and Molinari, M. (2004). Neurologic recovery of spinal cord injury patients in Italy. *Arch Phys Med Rehabil* 85, 485-489.
6. Abdul-Sattar, A.B. (2014). Predictors of functional outcome in patients with traumatic spinal cord injury after inpatient rehabilitation: in Saudi Arabia. *NeuroRehabilitation* 35, 341-347.
7. Wilson, J.R., Grossman, R.G., Frankowski, R.F., Kiss, A., Davis, A.M., Kulkarni, A.V., Harrop, J.S., Aarabi, B., Vaccaro, A., Tator, C.H., Dvorak, M., Shaffrey, C.I., Harkema, S., Guest, J.D. and Fehlings, M.G. (2012). A clinical prediction model for long-term functional outcome after traumatic spinal cord injury based on acute clinical and imaging factors. *J. neurotrauma* 29, 2263-2271.
8. Richard-Denis, A., Feldman, D., Thompson, C. and Mac-Thiong, J.M. (2017). Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization. *J Spinal Cord Med*, 1-9.

9. Zörner, B., Blanckenhorn, W.U., Dietz, V. and Curt, A. (2009). Clinical algorithm for improved prediction of ambulation and patient stratification after incomplete spinal cord injury. *J. neurotrauma* 27, 241-252.
10. van Middendorp, J.J., Hosman, A.J., Donders, A.R., Pouw, M.H., Ditunno, J.F., Jr., Curt, A., Geurts, A.C. and Van de Meent, H. (2011). A clinical prediction rule for ambulation outcomes after traumatic spinal cord injury: a longitudinal cohort study. *Lancet* 377, 1004-1010.
11. Cruz, J.A. and Wishart, D.S. (2006). Applications of machine learning in cancer prediction and prognosis. *Cancer Inform* 2, 59-77.
12. Obermeyer, Z. and Emanuel, E.J. (2016). Predicting the future - Big data, machine learning, and clinical medicine. *N. Engl. J. Med.* 375, 1216-1219.
13. Dasgupta, A., Sun, Y.V., Konig, I.R., Bailey-Wilson, J.E. and Malley, J.D. (2011). Brief review of regression-based and machine learning methods in genetic epidemiology: the Genetic Analysis Workshop 17 experience. *Genet. Epidemiol.* 35 Suppl 1, S5-11.
14. Razi, M.A. and Athappilly, K. (2005). A comparative predictive analysis of neural networks (NNs), nonlinear regression and classification and regression tree (CART) models. *Expert Syst Appl* 29, 65-74.
15. Harper, P.R. (2005). A review and comparison of classification algorithms for medical decision making. *Health Policy (New York)* 71, 315-331.
16. Marshall, R.J. (2001). The use of classification and regression trees in clinical epidemiology. *J Clin Epidemiol* 54, 603-609.
17. Hou, Y.F., Lv, Y., Zhou, F., Tian, Y., Ji, H.Q., Zhang, Z.S. and Guo, Y. (2015). Development and validation of a risk prediction model for tracheostomy in acute traumatic cervical spinal cord injury patients. *Eur Spine J* 24, 975-984.
18. Tanadini, L.G., Hothorn, T., Jones, L.A., Lammertse, D.P., Abel, R., Maier, D., Rupp, R., Weidner, N., Curt, A. and Steeves, J.D. (2015). Toward inclusive trial protocols in heterogeneous

neurological disorders: prediction-based stratification of participants with incomplete cervical spinal cord injury. *Neurorehabil Neural Repair* 29, 867-877.

19. Tanadini, L.G., Steeves, J.D., Hothorn, T., Abel, R., Maier, D., Schubert, M., Weidner, N., Rupp, R. and Curt, A. (2014). Identifying Homogeneous Subgroups in Neurological Disorders. *Neurorehabil Neural Repair* 28, 507-515.

20. Baker, S.P., O'Neill, b., Haddon, w.j. and Long, w.b. (1974). The injury severity score: A method for describing patients with multiple injuries and evaluating emergency care. *J Trauma Acute Care Surg* 14, 187-196.

21. Bourassa-Moreau, E., Mac-Thiong, J.M., Ehrmann Feldman, D., Thompson, C. and Parent, S. (2013). Complications in acute phase hospitalization of traumatic spinal cord injury: does surgical timing matter? *J Trauma Acute Care Surg* 74, 849-854.

22. Kirshblum, S.C., Burns, S.P., Biering-Sorensen, F., Donovan, W., Graves, D.E., Jha, A., Johansen, M., Jones, L., Krassioukov, A., Mulcahey, M.J., Schmidt-Read, M. and Waring, W. (2011). International standards for neurological classification of spinal cord injury (Revised 2011). *J Spinal Cord Med* 34, 535-546.

23. Dvorak, M.F., Noonan, V.K., Fallah, N., Fisher, C.G., Rivers, C.S., Ahn, H., Tsai, E.C., Linassi, A.G., Christie, S.D., Attabib, N., Hurlbert, R.J., Fournay, D.R., Johnson, M.G., Fehlings, M.G., Drew, B., Bailey, C.S., Paquet, J., Parent, S., Townson, A., Ho, C., Craven, B.C., Gagnon, D., Tsui, D., Fox, R., Mac-Thiong, J.M. and Kwon, B.K. (2014). Minimizing errors in acute traumatic spinal cord injury trials by acknowledging the heterogeneity of spinal cord anatomy and injury severity: an observational Canadian cohort analysis. *J. Neurotrauma* 31, 1540-1547.

24. Bluvshstein, V., Front, L., Itzkovich, M., Aidinoff, E., Gelernter, I., Hart, J., Biering-Soerensen, F., Weeks, C., Laramie, M.T., Craven, C., Hitzig, S.L., Glaser, E., Zeilig, G., Aito, S., Scivoletto, G., Mecci, M., Chadwick, R.J., Masry, W.S.E., Osman, A., Glass, C.A., Silva, P., Soni, B.M., Gardner,

- B.P., Savic, G., Bergstrom, E.M. and Catz, A. (2011). SCIM III is reliable and valid in a separate analysis for traumatic spinal cord lesions. *Spinal cord* 49, 292-296.
25. Catz, A., Itzkovich, M., Agranov, E., Ring, H. and Tamir, A. (1997). SCIM--spinal cord independence measure: a new disability scale for patients with spinal cord lesions. *Spinal cord* 35, 850-856.
26. Breiman, L., Friedman, J., Stone, C.J. and Olshen, R.A. (1984). *Classification and regression trees*. Taylor and Francis, 368 p.
27. Cawley, G.C. and Talbot, N.L.C. (2010). On Over-fitting in Model Selection and Subsequent Selection Bias in Performance Evaluation. *J Mach Learn Res* 11, 2079-2107.
28. Beleites, C., Baumgartner, R., Bowman, C., Somorjai, R., Steiner, G., Salzer, R. and Sowa, M.G. (2005). Variance reduction in estimating classification error using sparse datasets. *Chemometr Intell Lab Syst* 79, 91-100.
29. Kohavi, R. (1995). A study of cross-validation and bootstrap for accuracy estimation and model selection. In: *Proceedings of the 14th international joint conference on Artificial intelligence - Volume 2*. Morgan Kaufmann Publishers Inc.: Montreal, Quebec, Canada, pps. 1137-1143.
30. Muller, R. and Mockel, M. (2008). Logistic regression and CART in the analysis of multimarker studies. *Clin Chim Acta* 394, 1-6.
31. Kim, J.-H. (2009). Estimating classification error rate: Repeated cross-validation, repeated hold-out and bootstrap. *Comput Stat Data Anal* 53, 3735-3745.
32. Al-Habib, A.F., Attabib, N., Ball, J., Bajammal, S., Casha, S. and Hurlbert, R.J. (2011). Clinical Predictors of Recovery after Blunt Spinal Cord Trauma: Systematic Review. *J Neurotrauma* 28, 1431-1443.

33. Post, M.W., Dallmeijer, A.J., Angenot, E.L., van Asbeck, F.W. and van der Woude, L.H. (2005). Duration and functional outcome of spinal cord injury rehabilitation in the Netherlands. *J Rehabil Res Dev* 42, 75-85.
34. Furlan, J.C. and Fehlings, M.G. (2009). The impact of age on mortality, impairment, and disability among adults with acute traumatic spinal cord injury. *J. neurotrauma* 26, 1707-1717.
35. Ng, Y.S., Jung, H., Tay, S.S., Bok, C.W., Chiong, Y. and Lim, P.A. (2007). Results from a prospective acute inpatient rehabilitation database: clinical characteristics and functional outcomes using the Functional Independence Measure. *Ann Acad Med Singapore* 36, 3-10.
36. Scivoletto, G., Farchi, S., Laurenza, L., Tamburella, F. and Molinari, M. (2013). Impact of multiple injuries on functional and neurological outcomes of patients with spinal cord injury. *Scand J Trauma Resusc Emerg Med* 21, 42.
37. Bourassa-Moreau, É., Mac-Thiong, J.-M., Li, A., Ehrmann Feldman, D., Gagnon, D.H., Thompson, C. and Parent, S. (2015). Do patients with complete spinal cord injury benefit from early surgical decompression? Analysis of neurological improvement in a prospective cohort study. *J. neurotrauma* 33, 301-306.
38. Lemon, S.C., Roy, J., Clark, M.A., Friedmann, P.D. and Rakowski, W. (2003). Classification and regression tree analysis in public health: Methodological review and comparison with logistic regression. *Ann Behav Med* 26, 172-181.
39. Thang, N.D., Erhart, A., Speybroeck, N., Hung, L.X., Thuan, L.K., Hung, C.T., Ky, P.V., Coosemans, M. and D'Alessandro, U. (2008). Malaria in central Vietnam: analysis of risk factors by multivariate analysis and classification tree models. *Malar J* 7, 28.

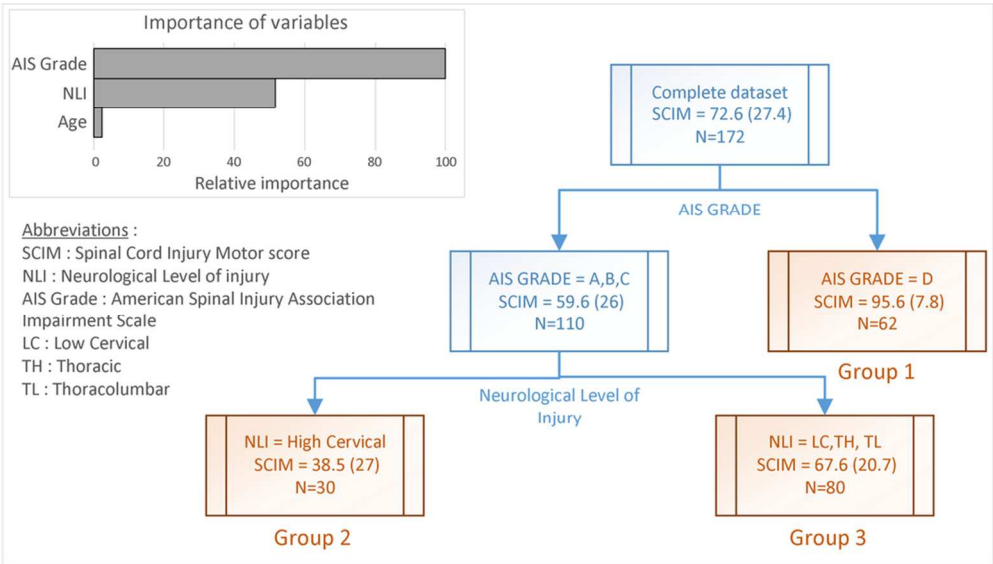


Figure 1 Regression tree built considering 4 predictors and their relative importance
N: Number of patient, SCIM = mean value (standard deviation)

Regression tree built considering 4 predictors and their relative importance
N: Number of patient, SCIM = mean value (standard deviation)

93x57mm (300 x 300 DPI)

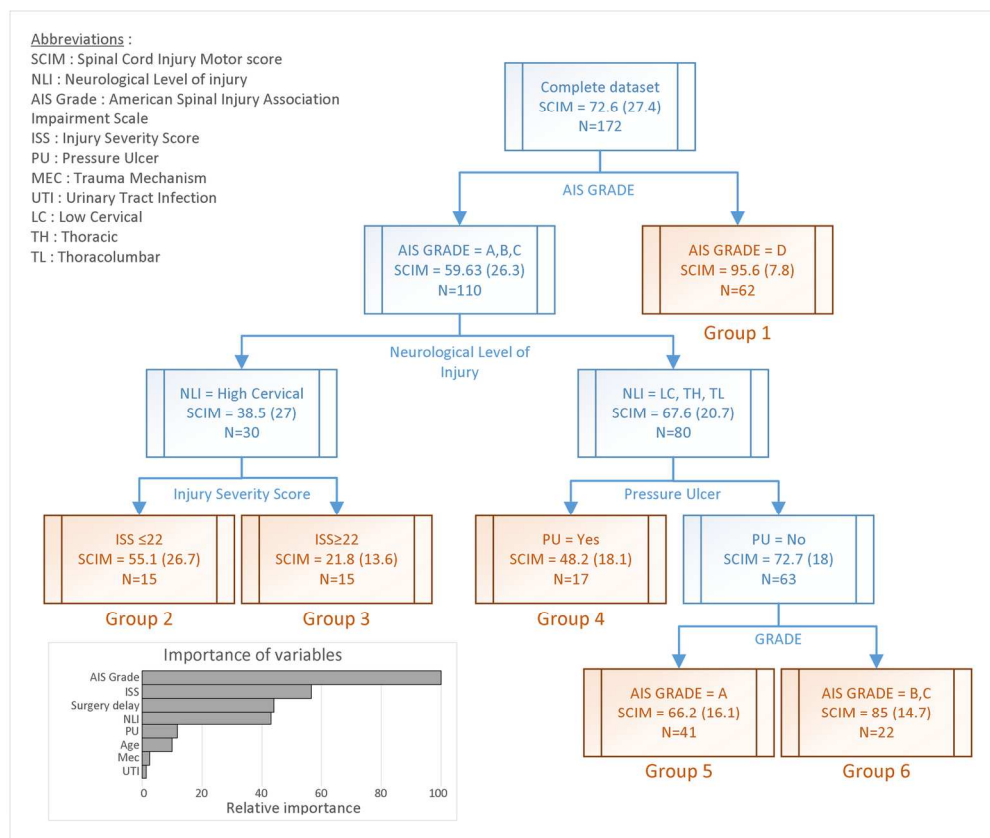


Figure 2 Regression tree built considering 11 predictors and their relative importance
 N: Number of patient, SCIM = mean value (standard deviation)

Regression tree built considering 11 predictors and their relative importance
 N: Number of patient, SCIM = mean value (standard deviation)

154x139mm (300 x 300 DPI)

Table 1 Clinical and demographic characteristics of the 172 patients involved in this study

<u>Output</u>		
Spinal Cord Independence Measure (SCIM) total score	Mean (Standard Deviation)	72.6 (27.5)
<u>Input predictors</u>	-	
Age (years)	Mean (Standard Deviation)	48.9 (18.0)
Injury Severity Score (ISS)	Mean (Standard Deviation)	23.9 (10.2)
Delay from injury to surgical incision (hours)	Mean (Standard Deviation)	114.9 (365.8)
Mechanism of injury	Sport	16.3%
	Assault blunt	5.2%
	Fall	45.9%
	Transport	30.8%
	Other	1.8%
Energy associated with the injury	High	43%
	Low	57%
Pneumonia	Yes	25%
	No	75%
Urinary tract infection	Yes	14.5%
	No	85.5%
Pressure ulcers	Yes	18.6%
	No	81.4%
Early spasticity	Yes	54.1%
	No	45.9%
ASIA Impairment Scale (AIS)	AIS A	39.5%

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	AIS B	9.9%
	AIS C	14.5%
	AIS D	36.1%
Neurological level of injury (NLI)	High Cervical (C1-C4)	28.5%
	Low Cervical (C5-T1)	37.8%
	Thoracic (T2-T10)	13.4%
	Thoracolumbar (T11-L2)	20.3%

Table 2 Performances of both models during training and testing routines

(Mean value (Standard Deviation))

Number of predictors	R ² Learn	R ² Test
4	0,539	0,517 (0,01)
11	0,705	0,632 (0,03)

Figure 1 Regression tree built considering 4 predictors and their relative importance

N: Number of patient, SCIM = mean value (standard deviation)

Figure 2 Regression tree built considering 11 predictors and their relative importance

N: Number of patient, SCIM = mean value (standard deviation)

14. Appendix 6: Manuscript in published in Spinal Cord

Original article

The impact of a specialized spinal cord injury center on the acute respiratory management of patients with complete tetraplegia: comparison with non-specialized centers: an observational study

Running title: respiratory outcome and spinal cord injury center

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Abstract

Study Design: Retrospective cohort study

Objectives: To compare the proportion of tracheostomy placement and duration of mechanical ventilation (MV) in patients with a complete cervical spinal cord injury (SCI) that were managed early or lately in a specialized acute SCI-center. The second objective was to determine the impact of the timing of admission to the SCI-center on the MV support duration.

Setting: A single Level-1 trauma center specialized in SCI care in Quebec (Canada).

Methods: A cohort of 81 individuals with complete tetraplegia over a 6-years period was included. Group 1 (N=57- *early group*-) was admitted prior to surgical management in one specialized acute SCI-center, whereas Group 2 (N=24 -*late group*-) was surgically managed in a non-specialized center and transferred to the SCI-center for post-operative management only. The proportion of tracheostomy placement and MV duration were compared. Multivariate regression analysis was used to assess the impact of the timing of admission to the SCI-center on the MV duration during the SCI-center stay.

Results: Patients in Group 2 had a higher proportion of tracheostomy (70.8% versus 35.1%, $p=0.004$) and a higher mean duration of MV support (68.0 ± 64.2 days versus 21.8 ± 29.7 days, $p=0.006$) despite similar age, trauma severity (ISS), neurological level of injury and proportion of pneumonia. Later transfer to the specialized acute SCI-center was the main predictive factor of longer MV duration, with a strong impact factor ($\beta=946.7$, $p<0.001$).

Conclusions: Early admission to a specialized acute SCI-center for surgical and peri-operative management after a complete tetraplegia is associated with lower occurrence of tracheostomy and shorter mechanical ventilation duration support.

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143 Department of Defense Spinal Cord Injury Research Program.
144 **Keywords:** Spinal cord injury; acute care; mechanical ventilation; tracheostomy; tetraplegia.

Introduction

Acute cervical spinal cord injury (SCI) is a devastating condition for the respiratory system and a leading cause of morbidity and mortality.^{1,2} The proportion of cervical spine trauma has increased in the last years in Canada, reaching 60% of all traumatic SCI.^{3,4} The level and completeness of the SCI are major determinants of the severity of the respiratory condition; the more rostral and complete the injury, the greater the likelihood of respiratory impairment.^{1,2}

Individuals with cervical SCI exhibit reduced lung volumes and flow rates as a result of respiratory muscle dysfunction.^{1,5} They experience decreased lung expansion, highly impaired cough due to weakness of the expiratory muscles, and increased sputum production due to unopposed sympathetic stimulation and decreased surfactant production.² Individuals with acute complete tetraplegia are particularly vulnerable to respiratory failure during the acute phase resulting from the combined effect of spinal shock leading to flaccid chest wall muscles, denervation of the ventilatory muscles, presence of concomitant lung injuries, potential decreased respiratory drive due to concomitant head injuries and narcotic analgesic, and cervical soft tissue edema associated with the surgery.⁵ Between 40 and 80% of subjects with acute complete tetraplegia may therefore require mechanical ventilation (MV) support during the acute care.^{6,7,8} Since prolonged oral/nasal endotracheal tubes is detrimental, tracheostomy placement is required in 10-60% of patients following tetraplegia.^{6,9,10}

Important predictors of MV support requirement following acute SCI include the level and completeness of the SCI, followed by lack of diaphragm function, advanced age and pneumonia.

^{6,7,10} With regards to pulmonary function, spontaneous improvement in the vital capacity (VC) and the first expiratory volume in the first second (FEV1) were also important predictors of MV support.⁷ Not only is requirement for MV support associated with the occurrence of pneumonia (ventilator-associated pneumonia)⁷ and decreased quality of life,¹¹ it is also one of the costliest consequences of tetraplegia, as it is associated with longer intensive care unit (ICU) stay, higher hospital costs, significant infection risks, as well as social isolation and decreased functional outcome.^{8,12} Requirement for MV is also an important risk factor of pneumonia and individuals sustaining complete tetraplegia, even at higher levels of injury, may be successfully weaned from MV during acute care.^{6,8,12} Thus, it is important to attempt weaning in a timely and appropriate fashion to potentially improve respiratory and functional outcome, as well as survival rate.^{7,8}

Individuals sustaining an acute traumatic SCI are generally first transferred to the nearest hospital center for evaluation and medical stabilization. After stabilization, the regional medical team has to decide whether a prompt surgery at the non-specialized regional center or direct transfer to the SCI-center should be prioritized. Specialized acute SCI-centers are familiar with the respiratory management of individuals with cervical SCI (based on the evidence-based),^{2,13-16} resulting in decreased occurrence of respiratory complications and increased rate of successful weaning of MV support.^{2,7,12} A recent systematic review has also suggested that early transfer (within 48 hours) to a specialized acute SCI-center may decrease as much as 50% the total length of stay and decrease the rate and severity of complications, as well as decrease mortality.¹⁴ However, even if early transfer to the specialized acute SCI-center is recommended, it remains a low-level recommendation (level V-expert opinion).¹³ On the other hand, recent studies have suggested that emergent spinal surgery could improve neurological recovery, decrease costs of care and the

191 incidence of complications following traumatic SCI.^{14,17-20} So, optimal timing for transfer to SCI-
192 center should be established with respect to the spinal surgical procedure and the amount of
193 specialized perioperative care provided. This is particularly important for complete cervical SCI,
194 as this condition is associated with limited neurological recovery and a high risk of
195 complications. The impact of transfer delays on relevant respiratory clinical features remains also
196 unknown. Based on the conclusions of important work,^{8,12,14,21} we hypothesized that individuals
197 with complete tetraplegia managed early before surgery in a SCI-center will be less likely to
198 require tracheostomy placement and would be weaned faster from MV support than patients
199 undergoing surgical management in a non-specialized (NS) center with subsequent transfer to a
200 SCI-center. Accordingly, the objectives of this study were to 1) compare the proportion of
201 tracheostomy placement and MV duration in patients with a complete cervical traumatic SCI
202 admitted to a specialized acute SCI-center prior to surgery or only after surgical management in a
203 non-specialized center, and 2) determine the impact of the timing of admission to the SCI-center
204 on MV support duration using a multivariate regression analysis.

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206 **METHODS**207 **Patients**

Individuals sustaining a complete SCI were selected from a prospective database of individuals from the western part of Quebec admitted to a single Level I specialized acute SCI-center between April 2008 and November 2014 after a cervical traumatic SCI from C1 to C8 that was previously used for complementary articles^{21,22}. As we receive around 70 patients with a traumatic SCI per year in our center, the recruitment of patients for this study was relatively stable over the years. Thus, 81 patients (63 males / 18 females; 43.0±18.0 years old) were included in this study. A complete injury consisted in a “grade A” injury on the American Spinal Injury Association (ASIA) impairment scale (AIS), according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI). All patients were treated surgically to decompress and stabilize the spine. Subjects managed non-surgically or with an incomplete cervical SCI were excluded since they exhibit distinct outcomes.

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In line with the objectives of this study, our cohort was subdivided into two groups based on the

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timing of admission to the specialized center. No patients sustaining an acute complete

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tetraplegia were completely managed by a non-specialized center prior to transfer to the intensive

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functional rehabilitation, without prior admission to the specialized acute SCI-center. In other

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words, all patients with a complete traumatic cervical SCI that occurred in the western part of

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Quebec were at some point managed in our specialized acute SCI-center during the period of

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recruitment of this study. Group 1 included 57 individuals transferred “early” to the specialized

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acute SCI-center, where “early” was defined as an admission to a single acute Level-I specialized

216 acute SCI-center *prior to surgical management* to receive complete peri-operative management
 217 by a multidisciplinary team specialized in the acute care and acute rehabilitation of 80 to 100 SCI
 218 patients per year. Group 2 included 24 patients transferred “lately” to the specialized acute SCI-
 219 center *for late postoperative management only* after surgical management in a non-specialized
 220 center. A total of 4 patients (7%) from Group 1 have been transported from the trauma site to a
 221 non-specialized center for initial evaluation, but were transferred to the specialized acute SCI-
 222 center when a SCI was suspected, in order to be surgically managed at the SCI-center.

The organization of SCI care can vary significantly between different regions. In Quebec, Canada, patients sustaining a traumatic SCI should be directed to one of two designated specialized acute SCI-centers according to the geographical region where the trauma occurred (eastern vs. western part of the province). This system was established in the late 1970’s to allow centralization of patients and improve the care of SCI patients, based on the general principles originally devised in the United States.²³

The specialized acute SCI-center involved in the current study offers specialized respiratory management administered by a multidisciplinary team specialized in SCI care. This team is composed of, but not limited to, trauma, intensive care, spine surgery and physical medicine and rehabilitation specialists, as well as many therapists and clinical nurses experienced in SCI care. All patients with complete tetraplegia are admitted to the intensive care unit and transferred to the ward once their condition is considered stable by the intensive care team. All patients, whether admitted prior to (Group 1) or after spinal surgery (Group 2), undergo the same multidisciplinary management. Respiratory care is individualized for each patient and indications for endotracheal

intubation, tracheostomy or MV support follow evidence-based recommendations for the acute care of SCI.^{2,13,15,16} Routine respiratory care for complete cervical SCI involves high frequency percussive ventilation, mechanical and/or manual assisted cough, and non-invasive respiratory assistance or MV support if needed.^{2,13,15,16} Readiness for weaning of MV support is challenged, and managed by the intensive care medical team, when vital capacity reaches at least 15mg/kg along with decreased sputum load, ability to cooperate, patent upper airway, relatively clear chest radiograph with no new changes, and reduction in the requirement for ventilator assistance.⁹ A progressive ventilator-free breathing protocol with high tidal volume is preconized.² Tracheostomy tube is considered in patients that are anticipated to require ventilator support for more than two weeks.²⁴ Specialized rehabilitation therapies are provided continuously throughout hospitalization and include respiratory, physical and speech therapies, and nutrition services. A physical medicine and rehabilitation specialist leads the acute rehabilitation process, applying interventions to promote functional and neurological recovery and prevent medical complications. The physical medicine and rehabilitation specialist also coordinates transfer to a functional rehabilitation facility once the patient's condition does not require additional active medical or surgical intervention.

223 **Data collection**

The local ethics committee board approved this study. Data pertaining to the hospitalization at the SCI-center were prospectively collected by independent research assistants and a medical archivist. For patients in Group 2, chart review was required to collect information pertaining to the presence of complications upon admission to the specialized acute SCI-center.

The following variables were collected in the medical chart: age, gender and history of chronic obstructive pulmonary disease (COPD) (chronic bronchitis, emphysema, asthma and bronchiolitis – confirmed in the chart by a health-care professional-). The weight and height (to determine the presence of obesity (defined with a body mass index of ≥ 30)) and history of smoking (current, former or non-smoker) were asked to the patient on admission. Clinical data, including the trauma severity (as measured by the Injury Severity Score (ISS)), presence of a concomitant traumatic brain injury (TBI) and its severity (mild, moderate or severe), surgical delay, and information regarding the SCI, were also collected. The ISNCSCI were used to assess the severity of neurological injury through the AIS grade within the first 72 hours following the SCI for Group 1, and upon admission for Group 2.²⁵ The neurological level of injury (NLI) was defined as the most caudal segment with normal motor and sensory function bilaterally, as assessed by a trained medical team member within the first 72 hours following the SCI for Group 1, and upon admission for Group 2. The NLI was dichotomized as high tetraplegia (C1-C4), and low tetraplegia (C5-C8). The surgical delay was defined as the number hours between the trauma and the timing of surgical incision and dichotomized with a cut-off of 24 hours based on previous studies.²⁶⁻²⁸ The occurrence of pneumonia during the hospitalization in the SCI-center was collected. Pneumonia was defined as a new progressing lung infiltrate accompanied by at least 2 of the following: 1) body temperature higher than 38° or lower than 36° Celsius; 2) leukocytosis greater than 12,000 or leukopenia below 4,000/ml; 3) purulent pulmonary secretions.¹⁵ The surgical delay was defined as the time (in hours) between the trauma and spinal surgery (time of skin incision), and was dichotomized as <24h or ≥ 24 h post-trauma. The acute care length of stay, both in the intensive care unit (ICU) and the ward, as well as the rate of mortality were noted.

Outcome variables

The main outcome variable was the percentage of individuals who required tracheostomy and MV support as well as the ventilation support duration (in days) at the SCI-center. The proportion of individuals requiring tracheostomy placement, whether the procedure was performed at the specialized acute SCI-center or the non-specialized facility (Group 2) was also calculated, in addition to the proportion of patients requiring MV support. The MV duration was defined as the total number of hours for which patients required MV support during their stay at the specialized acute SCI-center. If intermittent episodes of ventilation were necessary, the number of hours for each of the episodes was added. The MV duration time was then translated into days for both groups.

Statistical analyses

Direct comparison analyses were first performed to assess the first objective of this study. Continuous data were compared between the two groups using Mann-Whitney U tests, while categorical data were compared using chi-square tests. Continuous data were reported as median and interquartile range (IQR), and categorical data were reported as proportions and percentages. Then, the second objective of this study was assessed using a multivariate linear regression analysis based on a general linear model in order to identify predictors of MV support duration and evaluate the impact of timing of admission to the SCI-center (Group 1 or 2). As a first step, multicollinearity between potential factors was tested using Spearman correlations, with a cut-off value of 0.7. Since no collinearity was found between the independent variables, they were all included in the general linear model. The dependent variable was the MV support duration (in

days) during the SCI-center stay, and ten independent variables were included: 1) timing of admission to the SCI-center (main independent variable); 2) age; 3) gender; 4) smoking status (non-smoker vs. former or active smoker); 5) presence of obesity; 6) ISS; 7) occurrence of pneumonia; 8) high (C1-4) or low (C5-8) tetraplegia; 9) presence of concomitant TBI, and 10) surgical delay (<24h vs. $\geq$ 24h). We have also performed the same general linear model with the surgical delay as a continuous variable (instead of dichotomous). We used a backward elimination method, and the magnitude of the impact of each significant factor was reported using the beta coefficient. The R-square refers to the percentage of variance of the dependent variable explained by the final model. The significance level was set at $p < 0.05$ and all statistical analyses were performed using the IBM SPSS Statistics 19 software (Chicago, IL).

RESULTS

A total of 81 subjects with acute traumatic complete tetraplegia were included in this study. Group 1 included 57 patients admitted early to the specialized acute SCI-center (Group 1), while 24 subjects were transferred later to the specialized acute SCI-center (Group 2). No patients sustaining a complete traumatic cervical SCI were treated conservatively (non-surgically) during the period of recruitment. Baseline characteristics, occurrence of pneumonia during acute care and mortality rate exhibit non-significance differences between the two groups (Table 1). The proportion of patients sustaining concomitant mild TBI tended to be greater for Group 1 ($p=0.06$), but the difference was not statistically significant. Patients in Group 1 were more likely to have surgery within 24h ($p=0.051$). Indeed, the mean surgical delay for Group 1 reached 55 days as compared to 80 days for Group 2. However, this difference was not significant. The median surgical delay was similar between the two groups, with 23 days.

Patients from Group 2 spent on average 27.2 ± 28.4 days in the non-specialized hospital prior to their transfer to the SCI-center. While the majority of Group 1 patients (53/57) were initially evaluated in a community hospital prior to their transfer to the SCI-center, the mean delay between trauma and admission at the specialized acute SCI-center was about 7 h (0.3 ± 1.0 day). The total length of stay in the specialized acute SCI-center was significantly increased by 20 days in Group 2 ($p<0.001$). The length of stay in the ICU at the SCI-center was increased by 18 days in Group 2 but this difference did not reach statistical significance ($p=0.13$) (Table 1).

The comparison of respiratory outcomes for Groups 1 and 2 is shown in Table 2. The proportion of patients requiring tracheostomy placement was doubled in Group 2 ($p=0.004$). Although the proportion of patients requiring MV support was similar in both groups, the duration of MV was increased by 46 days for patients in Group 2.

Our results from the multivariate analysis are shown in Table 3. The timing of admission to the specialized acute SCI-center was the most important predictor of the duration of MV, as patients transferred to the specialized acute SCI-center only after surgery (Group 2) required longer MV. Higher NLI (C1-C4) and an increased ISS were significantly associated with increased MV duration. The final model explained almost 34% of the variance in MV support duration ($R^2=0.338$). When the surgical delay was considered as a continuous variable (as opposed to a dichotomous variable), longer surgical delay became a significant variable associated with longer duration of mechanical ventilation, with an impact factor of almost three. The presence of pneumonia during acute care was also added as a significant factor of longer mechanical ventilation duration when the surgical delay is treated as a continuous variable, with an important impact factor of 536.

DISCUSSION

This comparative study suggests that following complete cervical SCI, early admission to a specialized acute SCI-center for surgical and perioperative management (Group 1) decreases the duration of MV support and the rate of tracheostomy placement. The decreased duration in MV support gained with early admission to the specialized acute SCI-center reach numbers previously reported in the SCI literature (for complete tetraplegia)²⁹ and is even underestimated, considering that for patients transferred lately (Group 2) the duration of MV support in the non-specialized center was not included despite a mean of 27.2 days spent in the non-specialized center prior to transfer in the specialized acute SCI-center. The benefits in respiratory care with early admission to a specialized acute SCI-center might be important as they are associated with a shorter length of stay for the acute care, and thereby earlier transfer to intensive functional rehabilitation. Secondly, it is expected that complete surgical and perioperative management in a specialized acute SCI-center will decrease costs and resources use for this patient population for whom the economic burden is already significant.³⁰

Non-specialized centers may argue that performing surgery in their center will decrease the surgical delay, considering that a shorter surgical delay is associated with improved neurological recovery³¹ and decreased incidence of complications,¹⁸ particularly for cervical SCI.¹⁹ However in the current study, the surgical timing was similar when the surgery was performed in the specialized acute SCI-center (Group 1). This observation highlights the fact that transfer to the specialized acute SCI-center do not delay surgical management. It may also underline the ability of a specialized multidisciplinary team to organize prompt evaluation, medical stabilization and

surgical planning, while there are multiple barriers to early surgery.^{26,32} However, the argument for earlier surgery in a non-specialized center could still be considered in certain occasions for geographical reasons, and the influence of geographical distance on the need of early transfer to a SCI center should therefore be explored in a future study. This issue was not a factor in our study since the great majority of individuals from Group 2 had surgery in a non-specialized center located less than 10 km away from our SCI-center.

MV support is generally required during the first days to weeks after the injury.^{2,23,33} But as the chest wall muscle flaccidity transitions to spasticity and accessory muscles strengthen, spontaneous ventilation may be adequate for weaning from MV.^{2,8,33,34} The higher rate of tracheostomy in individuals lately transferred to the specialized acute SCI-center (Group 2) may reflect a false assumption that individuals with complete tetraplegia requiring MV support in the early-acute phase will remain ventilator-dependent. Alternatively, it can also suggest that weaning of MV in patients after a complete cervical SCI remains a difficult task if the treatment team in non-specialized centers only deal with a small number of SCI patients in their usual practice and/or have not gained a wide experience with treating SCI patients during their training. Accordingly, Wong et al. have demonstrated that weaning attempts in individuals with complete tetraplegia acutely hospitalized in non-experienced centers were delayed or not attempted at all.² Yet, up to 60% of individuals with complete tetraplegia can be successfully weaned from MV during acute care.³⁴ Early admission to the specialized acute SCI-center, prior to surgery, may promote faster stabilization of the pulmonary status and more efficient weaning of MV, while decreasing the need for tracheostomy placement. These findings are further reinforced by the fact

that a similar rate of mortality and incidence for MV support was found, suggesting that both groups were similarly vulnerable to respiratory failure.

Since tracheostomy (as opposed to spontaneous ventilation), and MV support are recognized risk factors of pneumonia,^{24,33-35} a higher frequency of pneumonia in patients with later referral (Group 2) was expected. Surprisingly, we found a similar frequency of pneumonia between individuals admitted earlier or later to the specialized acute SCI-center. Because the information pertaining to presence of pneumonia prior to the admission was not unavailable for this study, it is possible that the true incidence of pneumonia in Group 2 patients was underestimated, since these patients were transferred after a mean of 27.2 days after the SCI. Accordingly, it has been shown that pneumonia tends to develop early after a complete cervical SCI.³⁶ One may thus question if this may explain the significant higher rate of tracheostomy found in this group. Although it is not excluded, the fact that the same proportion of individuals required MV support does not support this hypothesis. If the occurrence of pneumonia in the non-specialized center had caused the higher rate of tracheostomy at arrival to the specialized acute SCI-center, we would have expected a higher rate of MV requirement as well, which was not the case in this study. Indeed, it rather suggests that individuals from Group 2 were transferred to the specialized acute SCI-center with a tracheostomy without requirement for MV support. This further supports that both groups were similarly vulnerable in terms of respiratory outcome, which was the main outcome of this study.

Our multivariate regression analysis further reinforces the importance of early transfer for optimizing the respiratory management in complete cervical SCI. Indeed, admission to the

specialized acute SCI-center prior to surgical management was the strongest factor associated with shorter MV duration. It is even more interesting to note that when the surgical delay was considered as a continuous variable, longer surgical delays were also significantly associated with longer duration of MV. Considering that individuals lately transferred to the specialized acute SCI-center tended to be surgically-managed later (with a non-significant mean difference of 25 days), this result may reinforce the importance of early transfer regardless of the location of the injury. The level of injury was associated with MV duration, which is in accordance with the SCI literature.^{6,7} Indeed, complete injuries above C4 produce a significant ventilator muscle paralysis since the phrenic nerve, innervating the diaphragm, arises from the third to the fifth cervical roots.² Important breathing accessory muscles are also denervated, and the loss of expiratory muscle strength results in a severe cough impairment. As a result, these patients exhibit acute respiratory failure and typically do not survive unless MV support is rapidly instituted.^{13,15,16,33} Transition of the flaccid chest wall to spasticity and recruitment of accessory muscles required to initiate MV weaning may take a few weeks after injury.^{2,16} Finally, the burden of associated traumatic injuries – assessed through the ISS in our study – was the last factor associated with MV duration during the SCI-center stay. Not only severe TBI may impair the respiratory drive, but also concomitant chest or lung injuries (such as pneumothorax, hemothorax, pulmonary contusions or flail chest) may further affect the pulmonary physiologic changes.^{6,16,33}

Results of this study may suggest that both groups were similar in terms of severity and vulnerability to respiratory failure. Characteristics related to the patient (age, smoking status, presence of obesity (which may accentuate the restrictive lung syndrome), presence of COPD) and trauma (burden of associated traumatic injuries (as calculated by the ISS score), level of the

SCI) were similar for both groups (Table 1). The severity of the SCI was also similar between the two groups since only individuals with complete SCI were included (AIS-A). There was a strong tendency towards a higher proportion of individuals with a concomitant traumatic brain injury in Group 1 (managed in the acute specialized SCI-center), which reinforces results of this study since an additional neurological injury may worsen outcome following SCI.³⁷ The fact that the proportion of individuals requiring mechanical ventilation support was similar further supports that both groups were similar in terms of severity. We therefore may suggest that difference of severity between the two groups is less likely to have influenced results of this study.

In conclusion, this study is in accordance with previous studies supporting the role of specialized SCI centers in decreasing the mortality and morbidity after a traumatic SCI.^{2,12,15} However, our study is highly relevant because it specifically assesses the importance of a specialized acute SCI-center for improving the respiratory care in patients with a traumatic complete SCI. The healthcare system in Quebec comprises two specialized acute SCI-center in which all traumatic SCI should be transfer during the acute care management. Whether a patient should be transferred prior or after the spinal surgical procedure remains arbitrary, although this information is critical since it may influence the outcome of patients. Based on the results of this study, we may recommend that non-specialized regional centers may emphasize on the importance of rapid transfer to a specialized acute SCI-center prior to spinal surgical management in order to optimize mechanical ventilation support duration.

Limitations

The main limitation of this study is the small number of patients for Group 2. However, we agree that it could be useful, but we were still able to verify our hypothesis and observe a significant influence of the transfer delay on the respiratory management despite the limited number of patients in Group 2. Also, the design of this study may not be the ideal one for answering our important question. Since a randomized-control trial is not possible, a larger cohort of patients with prospectively-collected data in which all potential confounders are identified, would have been beneficial. Indeed, a directed acyclic graph approach³⁸ that aims to yield an unbiased estimate of the effect, and adopt a more conceptual point of view could then be used.

In addition, although our data acquisition in our specialized acute SCI-center was prospective, it was impossible to collect all the data pertaining to the referring non-specialized center, such as the initial rate of pneumonia, the duration of MV and the initial neurological status (ISNCSCI). As mentioned previously, the rate of pneumonia and duration of MV in Group 2 were likely underestimated because they could not be collected prior to admission to our specialized acute SCI-center. Indeed, obtaining these data could only have strengthened the conclusions of this study supporting improved respiratory management for Group 1 patients. The ISNCSCI had to be collected at admission to the specialized acute SCI-center for both groups and was thus compared in the pre- and post-operative period for Group 1 and 2 respectively. Since only individuals with a complete SCI were included in this study, it is less likely to have influenced results of this study. ISNCSCI (AIS scale) is suggested to be collected also in non-specialized centers and transmitted to the specialized acute SCI-center at the time of transfer.

Conclusions

434
435 Individuals sustaining acute traumatic complete tetraplegia may be first transported to local
436 hospital centers from the trauma site to stabilize the medical condition and establish the
437 diagnosis. Subsequent transfer to a specialized acute SCI-center *prior* to spinal surgical
438 management decreased the need for tracheostomy placement and reduced MV duration. Weaning
439 from MV support following complete tetraplegia is complex and is very different from other
440 critically ill patients. A specialized team, experienced with the pulmonary physiologic changes
441 specific to complete cervical SCI, should initiate MV weaning in a timely fashion. Admission to
442 a specialized acute SCI-center prior to surgical management provides a coordinated
443 multidisciplinary approach focusing on the optimization of the respiratory outcomes throughout
444 the different phases of acute care management.

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REFERENCES

1. Zimmer MB, Nantwi K, Goshgarian HG. Effect of spinal cord injury on the respiratory system: basic research and current clinical treatment options. *J spinal Cord Med* 2007;30:319-330.
2. Wong SL, Shem K, Crew J. Specialized respiratory management for acute cervical spinal cord injury: a retrospective analysis. *Top Spinal Cord Inj Rehabil* 2012; 18:282-290.
3. Thompson C, Much J, Parent S, Mac-Thiong JM. Changing demographics of traumatic spinal cord injury: An 11-year study of 831 patients. *J Spinal Cord Med*. 2015; 38(2):214-23.
4. Kattail D, Furlan JC, Fehlings MG. Epidemiology and clinical outcomes of acute spine trauma and spinal cord injury: experience from a specialized spine trauma in Canada in comparison with a large national registry. *J Trauma*. 2009; 67(5):936-43.
5. Kumar N. Respiratory care in traumatic spinal cord injury. *J Spine*. 2016.S7:1-4.
6. Chasha S, Christie S. Systematic review of intensive cardiopulmonary management after spinal cord injury. *J Neurotrauma*. 2011;28:1479-95.
7. Brown R, Di Marco AF, Hoit JD, Garshick E. Respiratory function and management in spinal cord injury. *Respir Care*. 2006;51(8):853-70.
8. Kornblith LZ, Kutcher ME, Callcut RA, Redick BJ, Hu CK, Cogbill TH, *et al*. Mechanical ventilation weaning and extubation after spinal cord injury: a western trauma association multicenter study. *J Trauma Acute Care Surg*. 2013; 75(6):1060-70.
9. Berlowitz DJ, Wadsworth B, Ross J. Respiratory problems and management in people with spinal cord injury. *Breathe* 2016;12:328-40.
10. Ganuza JR, Oliviero A. Tracheostomy in spinal cord injured patients. *Transi med UniSa* 2011;1:151-72.

- 473 11. Charlifue S, Apple D, Burns SP, Chen D, Cuthbert JP, Donovan WH, et al. Mechanical
 474 ventilation, health, and quality of life following spinal cord injury. *Arch Phys Med Rehab*
 475 2011;92(3):457-63.
- 476 12. Zakrasek EC, Neilson JL, Kosarchuk JJ, Crew JD, Ferguson AR, McKenna SL. Pulmonary
 477 outcomes following specialized respiratory management for acute cervical spinal cord injury:
 478 a retrospective analysis. *Spinal Cord*. 2017: 1-7.
- 479 13. Consortium for Spinal Cord Medicine *et al*. Early acute management in adults with spinal
 480 cord injury: a clinical practice guideline for health-care professionals. *J Spinal Cord Med*.
 481 2008;31(4):403-79.
- 482 14. Parent S, Barchi S, LeBreton M, Casha S, Fehlings MG. The impact of specialized centers of
 483 care for spinal cord injury on length of stay, complications and mortality: a systematic review
 484 of the literature. *J Neurotrauma*. 2011; 28(8):1363-70.
- 485 15. Consortium for Spinal Cord Medicine *et al*. Respiratory management following spinal cord
 486 injury: a clinical practice guideline for health-care providers. *J Spinal Cord Med*. 2005;28(5):
 487 259-93.
- 488 16. Stevens RD, Bhardwaj A, Kirsh JR, Mirski MA. Critical care and management in traumatic
 489 spinal cord injury. *J Neurosurg Anesth*. 2003;15(3):215-29.
- 490 17. Mac-thiong JM, Feldman D, Thompson C, Bourassa-Moreau E, Parent S. Does timing of
 491 surgery affect hospitalization costs and length of stay for acute care following a traumatic
 492 spinal cord injury? *J Neurotrauma* 2012; 29:2816-22.
- 493 18. Bourassa-Moreau E, Mac-thiong JM, Feldman DE, Thompson C, Parent S. Non-neurological
 494 outcomes after complete traumatic spinal cord injury: the impact of surgical timing. *J*
 495 *Neurotrauma* 2013.15;30(18):1596-601.

- 496 19. Bourassa-Moreau E, Mac-thiong JM, Li A, Erhmann Feldman D, Gagnon DH, Parent S. Do
497 patients with complete spinal cord injury benefit from early surgical decompression?
498 Analysis of neurological improvement in a prospective cohort study. *J Neurotrauma*.
499 2016;33(3):301-6.
- 500 20. McKinley W, Meade MA, Kirshblum S, Barnard B. Outcomes of early surgical management
501 versus late or no surgical intervention after acute spinal cord injury. *Arch Phys Med Rehab*
502 2004;85 :1818-25.
- 503 21. Richard-Denis A, Ehrmann Feldman D, Thompson C, Bourassa-Moreau E, Mac-Thiong JM.
504 Costs and length of stay for the acute care of patients with motor-complete spinal cord injury
505 following cervical trauma: the impact of early transfer to specialized acute SCI center. *Am J*
506 *Phys Med Rehabil*. 2017;96(7):449-456.
- 507 22. Richard-Denis A, Feldman ED, Thompson C, Mac-Thiong JM. [The impact of acute](#)
508 [management on the occurrence of medical complications during the specialized spinal cord](#)
509 [injury acute hospitalization following motor-complete cervical spinal cord injury](#). *J spinal*
510 *cord med* 2017;19:1-18.
- 511 23. Tuskis DS. The impacts of the model SCI system: historical perspective. *J Spinal Cord Med*.
512 2002;25(4):301-5.
- 513 24. Quershi AZ. Tracheostomy decannulation; A cath-22 for patients with spinal cord injuries. *Int*
514 *J Phys Med Rehabil*. 2013;1(2):1-3.
- 515 25. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Amitabh J, *et al*.
516 International standards for neurological classification of spinal cord injury (Revised 2011).
517 *The Journal of Spinal Cord Medicine*. 2011;34 : 535-546.

- 518 26. Furlan JC, Tung K, Fehlings MG. Process benchmarking appraisal of surgical decompression
 519 of spinal cord following traumatic cervical spinal cord injury : opportunities to reduce delays
 520 in surgical management. *J Neurotrauma* 2013;30 :487-491.
- 521 27. Gupta B, Agrawal P, D'souza N, Dev Soni K. Start time delays in operating room: different
 522 perspectives. *Saudi J Anesth.* 2011;5(3):286-8.
- 523 28. Fehlings MG, Vaccaro A, Wilson JR, Singh A, Cadotte WD, Harrop JS, et al. Early versus
 524 delayed decompression for traumatic cervical spinal cord injury: results of the surgical timing
 525 in acute spinal cord injury study (STASCIS). *PLoS One.* 2012;7(2): e32037.
- 526 29. Roquilly A, Seguin P, Mimos O, Feuillet F, Rosenczweig E Chevalier F *et al.* Risk factors for
 527 prolonged duration of mechanical ventilation in acute traumatic tetraplegic patients—a
 528 restrospective cohort study. *J Crit Care* 2014;29(2):313e7-13.
- 529 30. Krueger H, Noonan VK, Trenaman LM, Joshi P, Rivers CS. The economic burden of
 530 traumatic spinal cord injury in Canada. *Chronic Dis Inj Can.* 2013;33(3):113-22.
- 531 31. Liu J-M, Long X-H, Zhou Y, Peng H-W, Liu Z-L, Huang S-H. Is Urgent Decompression
 532 Superior to Delayed Surgery for Traumatic Spinal Cord Injury? A Meta-Analysis. *World*
 533 *Neurosurg* 2016;87 :124-131
- 534 32. Thompson C, Feldman DE, Mac-Thiong J-M. Surgical management of patients following
 535 traumatic spinal cord injury: identifying barriers to early surgery in a specialized spinal cord
 536 injury center. *J Spinal Cord Med* 2016 [Epub ahead of print].
- 537 33. Berlly M, Kazuko S. Respiratory management during the first five days after spinal cord
 538 injury. *J Spinal Cord Med.* 2007;30:309-18.
- 539 34. Nogueira Nemer S, Valente Barbas CS. Predictive parameters for weaning from mechanical
 540 ventilation. *J Bras Pneumol.* 2011;37(5):669-79.

- 541 35. Como JJ, Sutton ERH, McCunn M, Dutton RP, Johnson SB, Arabi B, *et al*. Characterizing
542 the need for mechanical ventilation following cervical spinal cord injury with neurologic
543 deficits. *J Trauma* 2005;59:912-5.
- 544 36. Fishburn MJ, Marino RJ, Ditunno JF Jr. Atelectasis and pneumonia in acute spinal cord
545 injury. *Arch Phys Med Rehab* 1990;71(3):197-200.
- 546 37. Macciocchi S, Steel RT, Warshowsky A, Thompson N, Barlow K. Co-Occurring Traumatic
547 Brain Injury and Acute Spinal Cord Injury Rehabilitation Outcomes. *Arch Phys Med Rehab*
548 2012 ;93 :1788-94.
- 549 38. Shrier I, Platt RW. Reducing bias through directed acyclic graphs. *BMC Med Res Methodol*
550 2008; 8: 70.
- 551

Table 1: Socio-demographic and clinical characteristics of patients with a complete cervical SCI based on the timing of admission to the SCI-center (n=81)

Characteristics		Admission to the SCI-center		p
		Prior to surgery (Group 1)	After surgery (Group 2)	
	N	57	24	---
Age (years)	Median (IQR)	41.0 (29.3-57.0)	45.5 (22.0-55.0)	0.83
	Mean $\pm$ SD	43.6 $\pm$ 17.8	42.5 $\pm$ 19.0	
Gender	% Male	75.4	83.3	0.56
Smoking status	% Non-smoker	56.1	62.5	0.31
	% Active smoker	22.8	29.2	
	% Former smoker	21.1	8.3	
Obesity	% Body mass index $\geq$ 30	1.8	4.2	0.51
COPD	% COPD	0	0	1.00
ISS	Median (IQR)	29.0 (25.0-42.0)	34.0 (25.0-71.0)	0.31
	Mean $\pm$ SD	35.3 $\pm$ 16.0	42.7 $\pm$ 20.9	
NLI	% C1-C4	56.1	66.7	0.46
	% None	49.1	75.0	
TBI	% Mild	43.9	20.8	0.06
	% Moderate	3.5	4.2	
	% Severe	3.5	0.0	
Pneumonia	% Pneumonia	50.9	41.7	0.48
Surgical delay (h)	% $\leq$ 24h post-trauma	54.4	29.2	0.051
	Median (IQR)	23.0 (14.9-37.3)	23.0 (14.9-36.2)	
	Mean $\pm$ SD	54.9 $\pm$ 129.6	80.3 $\pm$ 197.1	
In-hospital death	% Deceased	8.8	8.3	1.00
Length of stay (days)		17.0 (8.5-41.5)	35.5 (8.0-91.5)	0.13
	SCI-center (Median (IQR))	28.1 $\pm$ 28.0	49.2 $\pm$ 44.8	
	ICU			
	Total	48.0 (24.0-72.5)	68.5 (32.5-120.0)	
	Mean $\pm$ SD)	57.0 $\pm$ 43.3	78.0 $\pm$ 45.9	
Length of stay (days)	Total acute care: non-specialized center + SCI-center (Median (IQR))	49.0 (24.5-72.5)	95.5 (57.8-146.8)	<0.001
	Mean $\pm$ SD)	57.0 $\pm$ 43.3	105.3 $\pm$ 56.5	

SCI: Spinal Cord injury; COPD: chronic obstructive pulmonary disease; ISS: Injury Severity

Score; NLI: neurological level of injury; TBI: traumatic brain injury; ICU: intensive care unit;

NS-center: non-specialized; IQR: Interquartile range

Table 2: Respiratory outcomes in patients with a complete cervical SCI early and lately admitted to the SCI-center (n=81)

Respiratory outcome		Admission to the SCI-center		p
		Prior to surgery (Group 1)	After surgery (Group 2)	
N		57	24	---
Tracheostomy	% with tracheostomy	35.1	70.8	0.004
MV support	% with MV support	86.0	79.2	0.51
	Duration (days) MV support	6.8 (1.1-35.7)	57.2 (6.3-119.8)	0.006
	(Median (IQR))	21.8 (29.7)	68.0 (64.2)	
	Mean $\pm$ SD)			

SD: standard deviation; MV: mechanical ventilation

Table 3: Predictors of duration of mechanical ventilation (in days) for subjects with a complete cervical SCI: results of the multivariate analysis (n=81)

Predictors		Beta coefficient (95% CI)	p
Timing of admission at SCI-center	Prior to surgery (Group 1)	-946.7 (-1413.6, -479.7)	<0.001
	After surgery (Group 2)	Reference category	
NLI	C1-C4	588.7 (142.2,1035.2)	0.010
	C5-C8	Reference category	
	ISS	13.5 (0.9, 26.1)	0.036

NLI: Neurological level of injury; CI: confidence interval; ISS: injury severity score

15. Appendix 7: Manuscript published to Journal of Neurotrauma

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Early predictors of global functional outcome after traumatic spinal cord injury: a systematic review

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Early predictors of global functional outcome after traumatic spinal cord injury: a systematic review

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Running head: functional outcome and spinal cord injury

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Abstract

Accurately predicting functional recovery in an asset for all clinicians and decision makers involved in the care of patients with acute traumatic spinal cord injury (TSCI). Unfortunately, there is a lack of information on the relative importance of significant predictors of global functional outcome. There is also a need for identifying functional predictors that can be timely optimized by the medical and rehabilitation teams throughout the hospitalizations phases. The main objective of this work was to systematically review and rate factors that are consistently and independently associated with global functional outcome in individuals with TSCI. This review also proposes a new conceptual framework that illustrates the impact of specific categories of factors and their interaction with each other. The grade of severity of the SCI is the main predictor of global functional outcome following TSCI. Other factors may modulate this interaction according to their respective strength of impact. Younger age, lower neurologic level of injury and higher initial motor score were the main socio-demographic and trauma-related factors. Surgical management, higher functional status at discharge from acute care, shorter acute care length of stay, and access to specialized multidisciplinary functional rehabilitation were main modifiable factors. Prevention of medical complications, higher intensity and patient participation level in functional rehabilitation therapies were also contributing factors associated with improved global functional outcome.

Keywords: function, spinal cord injury, prediction, acute care, rehabilitation

Introduction

Traumatic spinal cord injury (TSCI) is associated with serious permanent functional limitations requiring assistance in daily living and instrumental activities, as well as social isolation and decreased quality of life in these individuals.^{1,2} Functional limitations related to SCI therefore represent an important social and economic issue.³ In fact, enhancing functional status following SCI remains one of the main goals of the medical and rehabilitation team, and a major concern for patients.⁴ The benefits of early prediction of chronic functional status are well recognized: improved medical and rehabilitation plans, enhanced collaboration with patients and their relatives, better management of hospital resources and directing future research.⁵ Moreover, a sound scientific knowledge of early predictors is certainly essential in order to assess the efficacy of interventions during rehabilitation that may alter one's functional status.

Previous systematic reviews (Al-Habib et al. 2011; Wilson et al. 2012) on this topic have been proposed in the literature. However, no synthesis of the relative importance of predictive factors of functional recovery has been provided since previous systematic reviews did not review the strength of association between each predictive factor and functional outcome. Moreover, several studies pertaining to the early predictors of functional outcome have been performed recently and therefore were not considered in previous systematic reviews. In addition, there is still an information gap regarding which factors found during acute care hospitalization and inpatient functional rehabilitation can be modified by the medical and rehabilitation team to improve the outcome.

Accordingly, the main objective of this work was to systematically review factors that are consistently and independently associated with global functional outcome in individuals with TSCI. Another objective of this systematic review was to determine the level of evidence of each “modifiable” early predictor of functional outcome following a SCI. This review also proposes a conceptual framework to identify the most important predictors and better understand their interactions. This information may help health professionals to guide their decisions and plan efficient resource use based on the factors most relevant to the functional recovery.

Materials and methods

Information sources and search strategy

We performed a computerized literature review using MEDLINE, EMBASE and Cochrane databases. The following terms were searched: “Spinal cord injury” AND “function” or “outcome” AND “predict*” OR “prognos*”. The literature search was limited to human and English-language studies published between January 1st 1970 and April 1st 2017.

Eligibility criteria

This work aim to review studies assessing the functional outcome following an acute SCI in patients over 12 years of age, using a global and validated functional outcome measure. The inclusion and exclusion criteria are listed in Table 1. All included studies were required to identify clinical predictors of functional outcome using multiple regression analyses in order to weigh their importance, using an odds ratio for logistic regression or beta coefficient for linear regression.

Selection and data collection process

Each abstract was reviewed by two of the authors (ARD and CT) in order to remove duplicates and non-relevant studies based on our eligibility criteria and objectives of this review. The complete article was also reviewed for identification of relevant abstracts in the bibliography for inclusion in the systematic review. Data extraction was then performed by three independent reviewers (ARD, CT, JMMT). All factors included in the analyses as potential predictive factors were extracted, as well as the study design, primary outcome and timing of follow-up. The quality of evidence of the individual studies was assessed based on the Oxford Centre for Evidence-Based Medicine modified by Wright et al. (2000) and is referred as the level of

evidence (LoE).⁶ The strength of association with the functional outcome measure was reported using the multivariate regression analysis coefficient. Beta coefficient was thus used for continuous dependant variables (linear regression), while adjusted odd ratio was used for dichotomized dependent variables (logistic regression). However, the latter was not used in any study included in this review because all functional outcome measures were continuous. All multivariate models using a global and validated functional outcome measure were included in this review regardless of the potential confounding and interaction variables considered. The R-square value (preferably the adjusted-R² value) was extracted in cases of continuous outcomes, to quantify the proportion of variation that is explained by the final model and assess the goodness-of-fit.

Any unclear or missing information among individual studies was addressed to the corresponding author. Disagreement in the selection or collection process was first discussed between the reviewers (ARD, CT, JMMT) to reach consensus, but another author (BHN) made the final decision if disagreement still persisted.

Results

The MEDLINE database generated 921 references, while the EMBASE and Cochrane databases provided 940 and 53 references respectively, totalling in 1,914 potential studies. After eliminating duplicates and applying eligibility criteria, 77 articles remained. After reviewing all 77 articles, the first reviewer (ARD) selected fifteen studies, while 16 were selected by the second reviewer (CT). After discussion between the reviewers, consensus was reached and 15 studies were finally included in this systematic review (Figure 1).

Table 2 presents studies that have assessed potential predictors of global functional recovery classified into six sub-categories: 1) socio-demographic factors; 2) characteristics of the SCI; 3) trauma-related factors; 4) treatment-related factors; 5) factors related to acute care hospitalization; and 6) factors related to inpatient functional rehabilitation. Studies that have identified significant predictive factors of global functional recovery adjusted for their respective covariates are also showed in Table 2.

Table 3 presents the studies included in this systematic review. Five prospective and ten retrospective cohort studies were included. Eight of the 10 retrospective cohort studies were performed on a prospective database. The study by Li et al. (2012)⁷ included the lowest number of individuals (51 patients), while the study by Whiteneck et al. (2012)⁸ included the largest number of subjects (1376 patients). Five studies were graded as LoE-I^{7, 9-12} and ten were designated as LoE-II.^{8, 13-21} Three studies have used functional gain as primary outcome,^{7, 9, 18} while the remaining studies have used a final functional score while generally accounting for the initial functional score. The most studied measure of functional outcome was the FIM motor

score (9 studies).^{8-11, 13, 15-17, 21} The SCIM was used in four studies,^{14, 18-20} while the FIM total score¹² and the Modified Barthel Index⁷ were collected in one study each. Functional outcome assessment was performed at discharge from inpatient rehabilitation (4 studies),^{7, 9, 10, 21} six months post injury (one study)¹⁹, one year post-injury (7 studies)^{8, 11, 14, 16-18, 20}, two years or more post-injury (2 studies)^{12, 13} and either 6 months or 12 months post-SCI (one study)¹⁵. The percentage of variance explained by the different models, as reported by the R-square value, ranged between 31%¹⁴ and 75%.¹² Two studies did not report this value.^{7, 13}

Global rating of the relative importance of predictive factors of chronic functional outcome assessed in this study is presented in Table 4.

Socio-demographic factors

Age

Younger age was an important socio-demographic factor significantly associated with improved functional outcome, as identified in 10 studies.^{7, 8, 11-18} One study considered age as a dichotomized variable ($\leq$ vs. $>$ 50 years old)¹¹, while others considered age as a continuous variable. Younger age was generally identified as a main predictor of higher functional outcome.

Comorbidities

Less comorbidities, as quantified by the Charlson Comorbidity Index²² or the Maximum Comprehensive Severity Index,²³ were also associated to greater functional improvement in 3 studies,^{11, 13, 16} while four other studies failed to demonstrate a relationship between functional outcome and the burden of comorbidities.^{8, 12, 17, 20} Therefore, presence of comorbidities remains a controversial factor of functional outcome.

Sex, gender and primary payer

While the majority of studies included sex as an independent variable, only Li et al. (2012)⁷ and Pouw et al. (2011)¹⁴ suggested that male sex was moderately associated with greater gain in the MBI or SCIM score, respectively.

Four studies using the same prospective database (SCIREhab)^{8, 11, 16, 17} considered the type of primary payer as a potential predictive factor of functional outcome. In these studies, patients with a private health insurance plan exhibited higher functional scores as compared to patients with a public health insurance plan. The type of primary payer was revealed as a main factor along with younger age, although less significant than SCI characteristics (severity and neurologic level of injury).¹⁷

Body mass index and other factors

The influence of the body mass index (BMI) was evaluated in five studies.^{8, 11, 16, 17, 19} When obesity was identified with a BMI of ≥ 30 , it was not significantly associated with functional outcome. However, when obesity was defined as a BMI of ≥ 40 , or when BMI was considered as a continuous variable (for paraplegia), it was significantly associated with decreased functional outcome.^{11, 19} The level of education, employment status, primary language, smoking status, marital status and ethnicity were generally not revealed as significant factors of functional outcome.

Characteristics of the SCI

The severity of the SCI was the main predictive factor associated with chronic functional outcome identified in this systematic review. All studies that have assessed the severity of the

SCI have identified that less severe neurological deficit in terms of AIS grade was strongly associated with improved functional outcome.^{8-12, 14-20} Two studies included in this systematic review did not assess the severity of the SCI as a predictive factor. First, Dvorak et al.(2005) only included patients sustaining a central cord syndrome (therefore motor-incomplete SCI), which may explain the exclusion of AIS grade as a potential predictive, factor in this study. Then, Li et al. (2012) failed to include the severity of the SCI as a predictive factor, without obvious reason. Four studies based on the same database (SCIREhab)^{8, 11, 16, 17} categorized patients into four typical groups according to the NLI and AIS grade: 1) C1-C4 with AIS grades A to C, 2) C5-C8 with AIS grades A to C, 3) paraplegia with AIS grades A to C, and 4) AIS grade D injuries irrespective of the NLI. These studies showed similar result with less severe SCI associated with higher FIM motor scores. They also suggested that for specific AIS grades, lower neurological levels of injury might be significantly associated with improved chronic functional outcome. However, when the NLI was considered as an independent factor in the statistical analyses, results were conflicting. Four studies^{9,10,7,21} observed that NLI was associated with the functional outcome, while two others^{19,20} did not find a significant association between NLI and functional outcome. Light touch sensory score was revealed as significant in the two studies that have considered this factor, while the pinprick sensory score was not.^{12, 20} The ASIA motor score was also revealed as an important factor,^{12, 20, 24} but less consistently than the AIS grade. The computed vibration score was only assess in one study.¹²

Trauma-related factors

Presence of intramedullary MRI signal abnormality was only assessed in only study included in this systematic review.¹⁵ In this study, the absence of MRI signal abnormalities was related to increased FIM motor score when adjusted with the severity, the ASIA motor score and age. The

mechanism of traumatic injury was assessed in eight studies,^{8, 9, 11, 13, 16, 17, 19, 20} but only one identified this factor as predictive of functional recovery.¹¹ The severity of the trauma (or the burden of associated traumatic injuries) was only assessed in three studies,^{12, 19, 20} and was identified as predictive of chronic functional outcome in the two most recent studies.^{19, 20} However, the specific presence of a concomitant traumatic brain injury was not identified as a significant factor,^{19, 20} such as the presence of spinal fracture (in a central cord syndrome cohort),¹³ level of bony injury¹² or work-related injury.^{8, 11, 16, 17}

Treatment-related factors

Two studies examined the relationship between chronic functional outcome and the type of spinal management (medical vs. surgical).^{12, 13, 18} Dvorak et al.¹³ and Saboe et al.¹² showed a positive association between spine surgery (as opposed to conservative treatment) and FIM motor (Dvorak et al.)¹³ or total score (Saboe et al.)¹² two years post-SCI. Timing of surgery was assessed in three studies,¹⁸⁻²⁰ but only Grassner et al.¹⁸ showed that surgery performed within 8h after SCI was significantly associated with greater improvement in SCIM scores 12 months post-injury. The administration of corticosteroids was only shown to be weakly associated with functional outcome in one of two studies.^{12, 18}

Factors related to acute care hospitalization

Shorter length of stay in acute care, also defined as the time period between the SCI and the admission in inpatient rehabilitation, was assessed in eight studies^{7-11, 16, 17, 19, 21} and was not identified as a significant predictive factor of functional outcome in only one of them.⁷ Saboe et al. (1997)¹² showed that shorter length of stay in the intensive care unit was significantly associated with higher FIM total scores 2 years after a SCI. Li et al.⁷ also considered the rescue

time (in the context of an earthquake), which was predictive of functional outcome only when combined with the access to specialized rehabilitation facility.

The occurrence of medical complications during acute care hospitalization following TSCI was assessed in two studies, where both identified this factor as predictive of chronic functional outcome.^{12, 19} One study evaluated the impact of developing spasticity during acute care on the functional outcome, and observed that it was an important predictive factor of higher functional scores, regardless of the type and level of the injury.¹⁹

Functional status at discharge from acute care (which also refers to functional status at admission to the functional rehabilitation facility), was a important factor identified as predictive of chronic functional outcome in the seven studies that have assessed this factor, adjusting for important covariates.^{8, 9, 11, 16-18, 21} When the outcome consisted in a global functional score, higher functional score at discharge from acute care was identified as predictive (with a moderate strength of association).^{8, 11, 16, 17} On the opposite, when functional gain consisted in the outcome measure, lower functional status was identified as predictive factor.^{9, 18}

Factors related to inpatient functional rehabilitation

One prospective cohort study (Li et al. 2012)⁷ showed a strong impact of specialized multidisciplinary inpatient rehabilitation on functional outcome in comparison with standard rehabilitation. The impact of inpatient rehabilitation length of stay on chronic functional outcome was assessed in five studies,^{8, 9, 16, 17, 21} but was revealed as significantly associated with functional outcome in the Abdul-Sattar et al.(2014) study.⁹ The occurrence of medical complications during the functional rehabilitation process was only assessed in two studies,^{9, 12}

where Saboe et al.¹² identified this factor as predictive of higher FIM total score two years post injury. Post et al. (2005)¹⁰ also examined bedrest days needed as a consequence of medical complications (namely pressure ulcers), noting a weak association between higher FIM motor scores and fewer days of bedrest due to pressure ulcers. However, chronic functional outcome was not related to the total days of rehabilitation interruption.¹²

Intensity of rehabilitation therapies on chronic functional outcome was explored by Whiteneck et al. (2012)⁸ who found that increased time spent for physical therapy and decreased time spent in social work were weakly associated with higher FIM motor scores. However, the time spent for nursing care, speech therapy, psychological management and occupational therapy was not associated with functional outcome. On the other hand, Ozelie et al. (2012)¹⁶ reported that increased time spent for certain specific interventions during occupational therapy (i.e. assessment, home management skills, strengthening / endurance) was associated with better functional outcome, whereas other interventions such as assistive technology, bed mobility, communication and self-feeding were not. Teeter et al. (2012)¹⁷ also reported improved functional outcome for increased time spent for certain specific physical therapy interventions (i.e. assessment, gait, pre-gait, airway/respiratory management). Patient participation level was found to be a predictive of higher functional outcome in the two studies that have assessed this factor.^{16, 17} Clinician experience in physical or occupational therapy,^{8, 16, 17} location of the specialized rehabilitation center,^{8, 16, 17} discharge destination,⁹ nor ventilator use at admission¹¹ were associated with chronic functional outcome.^{16, 17}

Lower anxiety and depression scores on the HADS questionnaire⁹ at admission to inpatient rehabilitation were also weakly predictive of improved functional outcome. Dvorak et al. 2005¹³

assessed the presence of spasticity at follow-up of individuals with central cord syndrome minimally two years post injury and functional outcome. Finally, the neurological evaluation at discharge from functional rehabilitation was only assessed in one study by Saboe et al. (1997).¹² Increased ASIA motor score was the only neurological assessment (as opposed to light touch, pinprick and computed vibration sensory scores and the AIS grade) significantly associated with higher total FIM score two years post-SCI.¹²

Discussion

This work systematically reviewed acute predictors of global functional outcome from discharge from inpatient rehabilitation up to two years after the injury. As opposed to previous systematic reviews,^{24, 25} the current work considered the relevance of each predictive factors by considering the influence of covariates that were included in multiple regression models. This systematic review is therefore the first to provide a global rating of predictive factors of chronic functional outcome following TSCI (Table 4). This work also proposes a new conceptual framework (Figure 2) describing the relative importance of these predictors and their interaction with each other. In addition, this systematic review is also invaluable, considering the growing body of evidence published in the latest years, with 10 of the 15 included articles published after the systematic review from Wilson et al. (2012).^{7-9, 11, 16-21}

Factors of functional recovery will be discussed based on the importance proposed by authors of this systematic review (Table 4). For each of the categories, modifiable factors (on which the medical and rehabilitation team can intervene) will be discussed first, from acute care to functional rehabilitation factors. Discussion about the conceptual framework of predictive factors (Figure 2) will follow.

Main predictive factor of functional outcome

This work is in agreement with previous work suggesting that the severity of the SCI, evaluated by the ASIA (American Spinal Injury Association) Impairment Scale (AIS) is the strongest predictive factor of functional outcome when adjusting for relevant covariates (socio-demographic, related to the injury, to the treatment and related to the acute and rehabilitation

hospitalizations). Incomplete SCI (sensory and/or motor sparing in the sacral examination) was more likely to be associated with increased functional outcome. Individual with sacral sparing following acute spinal cord injury report greater functional independence (self-care, sphincter control, mobility and locomotion) and exhibit improved neurologic recovery one-year postinjury compared to individuals with complete (AIS-A) individuals.²⁶ The combination of voluntary anal contraction and preserved S4-S5 light touch and pinprick sensation during acute care was shown predictive of chronic-phase independent ambulation outcome.²⁷ The severity of the SCI is the most important predictor from which the neuro-functional prognosis is determined. Several factors (intrinsic and/or modifiable) will also intervene and modulate the functional recovery according to their impact and their timing, but to a lesser extent (Figure 2).

Strongly predictive factors of global functional outcome after TSCI

Surgical management

Surgical management following TSCI is a standard of care for the great majority of patients.²⁸⁻³¹ Indications for surgery following spinal trauma include a progressive or severe neurologic deficit, presence of residual spinal cord compression, instability of the spine not allowing for early mobilization, correction of a deformity, and prevention of subsequent neurologic deterioration or deformation.²⁹ However, there is no conclusive Class I clinical data supporting surgical management over conservative management with regards to clinical and functional outcome following acute TSCI.³² Since surgical management aim to decompress and stabilize the spine in order to minimize secondary injury to the spinal cord, it is classified as an important factor associated with improved outcome following acute TSCI.^{29, 31}

However, controversy surrounds the treatment of traumatic central cord syndrome, as there are some strong advocates of nonsurgical management for this clientele. However, as found in the Dvorak' study included in this systematic review, surgical treatment was showed in many studies to improve neurological and functional outcome.^{13, 33, 34}

Functional status at discharge from acute care and acute care length of stay

Functional improvement and final functional score both relate with the baseline functional status at discharge from acute care (or admission to inpatient rehabilitation), but in opposite direction. A lower functional score was associated to a larger functional gain but lower final functional score, while a higher baseline function was associated to a smaller functional gain but higher final functional score. Individuals starting inpatient rehabilitation with a lower baseline score are less limited by a ceiling effect and therefore have more potential for improvement.^{18, 35} Individuals with a higher baseline function at admission to inpatient rehabilitation ultimately reach higher final functional scores, highlighting the importance of optimizing the functional status early during the acute hospitalization. The extent to which the acute rehabilitation team should concentrate on functional skills during acute care remains to be determined. However, any efforts in optimizing the early functional status during acute care should not increase the length of stay, since shorter duration of acute care hospitalization was also associated to improved functional recovery after inpatient rehabilitation (adjusting for the level and severity of the SCI).^{9, 19} Shorter length of stay can also be associated with underlying factors (such as decreased complications, comorbidities or associated injuries) that independently promote functional recovery.

Specialized functional rehabilitation process

When functional gain during inpatient rehabilitation was considered, factors related to the rehabilitation process (rehabilitation length of stay, specialized multidisciplinary rehabilitation) showed a strong influence.^{7,9} Specialized multidisciplinary rehabilitation programs have showed their superiority in terms of functional outcome compared to healthcare system without such program.³⁶ In this regard, benefit from a specialized multidisciplinary rehabilitation program after acute care hospitalization is potentially a critical predictive factor of functional improvement following TSCI. However, there is limited evidence to support this since specialized multidisciplinary rehabilitation is considered as a standard of care for the great majority of SCI patients. It is therefore difficult to fully quantify the influence of specialized multidisciplinary rehabilitation on the functional outcome, since almost all patients included in this systematic review have undergone inpatient functional rehabilitation (which is why this factor is classified as strongly predictive in italic in Table 4).

Non-modifiable factors: age, neurologic level of injury and ASIA motor score

Younger age was the main socio-demographic factor associated with increased functional outcome, which is in accordance with the SCI literature.^{7, 8, 11, 12, 14-16, 18} Although, age was not shown to significantly influence the AIS conversion rate nor the ASIA motor score, older age has an important negative moderating effect on the relation between the AIS grade and functional recovery.³⁷ More specific rehabilitation protocols more oriented towards the geriatric population may help in improving functional recovery as younger individuals.³⁸

The AIS motor score was an important predictive factor of functional outcome, since it is directly related to the AIS grade.^{39,40} However, the ASIA motor score does not consider the neurologic sacral evaluation (as opposed to the AIS grade), which is a critical factor of neurological and functional recovery.^{26,27}

The neurological level of injury (NLI) is also an important predictive factor of functional recovery, particularly when it is dichotomized into tetraplegia and paraplegia,^{7, 9, 10} or considered for a specific severity of the injury (AIS grade), as shown by Ozelie et al (2012),¹⁶ Teeter et al. (2012)¹⁷ and Horn et al. (2013).¹¹

Moderately predictive factors contributing to functional outcome following TSCI

The occurrence of medical complications

The impairment of sensory, motor and autonomic systems makes subjects with SCI very vulnerable to medical complications, particularly during the acute care phase.⁴¹ The occurrence of medical complication may delay the rehabilitation process and community reintegration,⁴² particularly given that it also predisposes individuals with SCI at higher risk of chronic recurrences.^{19, 43} One may also question if systemic inflammation related to the occurrence of severe medical complications may also alter the inflammation response following acute TSCI.⁴⁴ In this review, one study has identified the occurrence of complications during acute care as a predictive factor of functional recovery,¹⁹ while another study assessing the occurrence of complications during functional rehabilitation did not.¹³ However, the latter focussed solely on subjects with central cord syndrome, which exhibit distinct outcomes.⁴⁵ Saboe et al (1997) has also identified the occurrence of complications as a predictor of worst functional outcome, but unfortunately did not differentiate between the occurrence during acute care and functional rehabilitation. Thus, prevention of medical complications remains an important goal of the management of patients with TSCI during the acute care and functional rehabilitation phases, which

benefit from a proactive and an integrated approach ideally provided by a multidisciplinary team experienced in SCI care.^{41, 46} However, continued work is needed to better evaluate its impact on the functional outcome.

Intensity of rehabilitation therapies and patient participation level during functional rehabilitation

The type and quantity of therapies during functional rehabilitation was assessed in the four studies included in this systematic review.^{8, 11, 16, 17} Conclusions on the impact of the amount of time devoted to specific therapies are however difficult to draw since it may simply reflect the severity of the SCI. Indeed, it is expected that increased time devoted to respiratory management, power wheelchair assessment or self-feeding equipment is associated with worst functional outcome since it mainly involves more severely affected individuals (in terms of AIS grade and NLI). However, results may also suggest that longer duration of rehabilitation therapies specific to the patient's needs may enhance functional gain. Some important factors (such as the rehabilitation resources availability and the healthcare system organization) should be considered in this context.

Increased patient's participation level in physical and occupational therapies during functional rehabilitation^{16, 17} may optimize the acquisition of functional skills and accelerate the rehabilitation process. It is therefore suggested that the rehabilitation team quickly assess the patient's level of motivation and quickly incorporate ways to improve it. Teaching activities, early psychological support and screening of mood disorders may be relevant examples that could be integrated early during the acute rehabilitation phase.

Non-modifiable factors: Intramedullary MRI signal abnormality, initial ASIA light touch score and type of primary payer

Specific abnormal MRI signals (presence of intramedullary hematoma, spinal cord contusion encompassing more than one spinal segment, and high cervical locations) were showed to be associated with severe neurologic deficits and poorer neurological and functional recovery.^{47, 48}

Its independent effect on the functional recovery considering covariates was only assessed in the Wilson et al. (2012) study, which is why it was designated as a contributing factor of functional recovery. Future studies should evaluate the independent effect of MRI abnormalities considering important factors, such as the NLI, the baseline functional status and the acute care length of stay (Table 4).

The ASIA light touch and pinprick sensory scores are an integral part of the basic neurological examination of individuals with SCI.³⁹ Although the preservation of pinprick sensation below the level of injury was showed to be associated with excellent prognosis for regaining functional ambulation,²⁰ this systematic review failed to identify this factor, and thus is classified in this work as weakly predictive. On the other hand, light touch sensation has a tendency to score higher than pinprick in SCI subjects, and may explain results obtained in the studies that have assessed both sensations. Discrepancy between the light touch and pinprick sensations could related to the higher complexity of the pinprick testing and the difference in the extent of the injury in the posterior and the spinothalamic tracts.^{20, 49}

The type of primary payer (insurance coverage) was also a predictor of functional outcome in four studies,^{8, 11, 16, 17} with the presence of private insurances being associated with better functional outcome in comparison with public primary payer (Medicaid) and worker's compensation. In the context where patients sustaining a SCI generally require a significant

amount of home adaptations, assistive devices and external human assistance, it is possible that patients with private insurances may better be financially supported. However, conclusions regarding the type of primary payer may not apply everywhere, since the financial care health system generally differs from one country to another.

Weakly predictive factors

Timing of spinal surgery

While the recommendations towards surgical management for TSCI are well recognized, there is considerable uncertainty regarding the role of the timing of surgical decompression following TSCI. Three studies have assessed this factor in this systematic review,¹⁸⁻²⁰ but only Grassner (who has treated the surgical delay as a dichotomized variable (≤ 8 h vs > 8 h) as compared to the surgical delay as a continuous variable)¹⁸ has identified it as a predictive factor of chronic functional recovery. Previous studies have suggested that patients who undergo early surgical decompression may exhibit similar outcome to patients who received a delayed surgical decompression.⁵⁰ However, there is evidence to suggest that early surgical management is safe and may improve clinical and neurological outcomes following TSCI.⁵⁰⁻⁵² Based on the surgical SCI literature, early surgical intervention should be considered in all patients from 8 to 24 h following acute traumatic SCI.⁵⁰

Non-modifiable factors: trauma severity, comorbidities and body mass index

Trauma severity refers to the burden of associated traumatic injuries, and was showed to have a detrimental effect on the functional outcome in two studies of the three studies that have assessed this factor.^{12, 19, 20} Although a high percentage of individuals with TSCI presents with multiples

associated injuries, its effect on the functional recovery is still debated.⁵³ Future studies should clarify this issue.

Traumatic SCI usually occurs in more active and younger individuals, which may explain why comorbidities were significantly associated with functional outcome in only three of the seven studies that have considered this factor. In these studies, the burden of comorbidities was not revealed as a strong factor associated with functional outcome. However, considering that there is an increasing incidence of SCI in the elderly,⁵⁴ comorbidities should be examined when assessing potential for functional recovery.⁵⁵ Although the influence of comorbidities on the outcome following SCI remain unclear,⁵⁶ it is reasonable to believe that a higher burden of comorbidities may prolong the length of stay, promote the occurrence of medical complications and delay the rehabilitation process, hence the importance of ensuring that confounders are considered when evaluating these factors.⁵⁷

Increased body mass index was identified as a predictive factor of decreased functional recovery in two^{11, 19} of the five studies that have assessed this factor. However, the body mass index was treated differently in these studies (dichotomized with different cut-off values or treated as a continuous variable), which may explain the variation between results of these studies.

Overweight or obesity may represent an additional challenge for mobility and accomplishing activities of daily living, such as transfers, sphincter management, wheelchair propulsion or the use of technical aids for ambulation. Moreover, obesity may increase respiratory dysfunction associated with SCI by aggravating restrictive pulmonary syndrome,⁵⁸ which in turn can alter general function.¹⁹ Therefore, the impact of obesity may deserve more attention as it may potentially impact functional recovery following TSCI and its prevalence has continuously increased during the last decades in the American population.⁵⁹

Factors of low or no impact on functional recovery

Administration of corticosteroids

Many studies have debated recommendations towards the use of corticosteroids as a neuroprotective agent following acute TSCI. Although one study by Saboe et al. (1997) has identified this factor as predictive of improve chronic functional recovery,¹² current recommendations are now clear. There is no clinical evidence to definitively recommend the use of any neuroprotective pharmacologic agent, including steroids, in the treatment of acute spinal cord injury, as it has been associated to important side effects and secondary conditions.²⁸ □

Functional rehabilitation length of stay

Functional rehabilitation length of stay was not revealed as a significant predictor of functional recovery in four of the five studies that have assessed this factor (Table 2). Although the importance of specialized inpatient functional rehabilitation following TSCI is recognized, there is no consensus regarding the optimal intensity or length of stay of functional rehabilitation services.⁶⁰ As a consequence, there is a great variability in terms of length of stay and intensity of rehabilitation services between the different centers and institutions.⁶¹ This may explain why this factor was not revealed as considerable in this systematic review. As discussed by Lamontagne et al. (2013), clinicians in functional rehabilitation facilities are left with this important decision (rehabilitation length of stay) on which many factors interfere. In one hand, less than optimal inpatient rehabilitation services could limit patient' abilities and therefore lead to increased social cost. On the other hand, services that exceed an optimal breakpoint would have a reduced impact on one's function and limit the access to other patients. The key is likely to be in improving the effectiveness of the existing rehabilitation resources, which may be optimized using an integrated approach in an organized healthcare system dedicated to this clientele (specialized SCI-centers).⁶²

One reason why Abdul-Sattar et al. (2014)⁹ has identified functional rehabilitation as their main factor of functional outcome is that functional gain (FIM motor score improvement from admission to discharge of functional rehabilitation) consisted in the outcome measure. As suggested previously, the use of functional gain as the outcome measure may highlight the impact of rehabilitation/ treatment measure.

Many factors needs further assessment in order to better evaluate their impact on functional recovery, such as the days of functional rehabilitation interruption, presence of spasticity, presence of depression or anxiety and intensive care length of stay (Table 4).

Conceptual framework

Figure 2 illustrates the relationship between the various factors involved in the functional recovery following an acute SCI. The main categories of predictors of functional outcome are showed: 1) severity of the SCI 2) socio-demographic factors; 3) trauma-related factors; 4) other characteristics of the SCI and 4) modifiable factors (treatment-related, acute care and inpatient rehabilitation factors). As shown in Figure 2, the severity of the SCI is directly related to the functional outcome following TSCI. The other factors modulate this interaction according to the strength of their impact as discussed previously (Table 4). Intrinsic factors also impact on the modifiable factors (related to the acute care and functional rehabilitations phases). The latter have a critical place in the process of functional recovery following TSCI since they represent our main opportunities to improve functional recovery. The baseline functional status may be a cornerstone in the functional rehabilitation process since it is the starting point of the functional work that is still largely unexplored.

Factors to consider in the future

Other factors may have not been evaluated in this systematic review, since studies pertaining to identify predictors of functional outcome may have not fulfilled our inclusion criteria. For instance, management by a specialized multidisciplinary team during acute care (acute SCI-center), the specific intensity and patient participation level to rehabilitation therapies during acute care, as well as the intensity of nursing care during acute care.^{19, 41, 62, 63} The presence of cognitive deficits (premorbid or associated to the trauma), presence of mood disorders and the functional/ physical status prior to the injury, are clinical factors that may influence the ability of the patient to fully participate to the rehabilitation process and consequently affect the long-term functional recovery. Future studies should assess these issues since the population of individuals with traumatic SCI is aging⁵⁴ and these factors may help in predicting the functional outcome.

Study limitations

The authors acknowledge that the ranking of functional outcome predictors proposed in this review rely on the studies that were included in this review, relevant additional studies in the SCI literature and clinical experience of the multidisciplinary authors involved in this work. Therefore, this should guide knowledge users and decision makers in their own medical context. The authors also recognized that some studies assessing functional outcome were not included in this work because they have not fulfilled the inclusion criteria of this review, notably the presence of a multivariate regression model. However, the exclusive inclusion of studies that have proposed multivariate regression models to identify significant predictors of functional outcome allow a better assessment of the relative importance of each factor with regards to their

respective covariates. Important factors may also be related to more specific functional outcome, such as ambulation, sphincter management or hand function. Authors believe that these outcome measures deserve their own systematic review.

It would also been interesting to identify predictors of functional *independence* (as opposed to predictors of higher functional score) since a continuous functional score is less meaningful in terms of functional achievements. Unfortunately, there was no study that has fulfilled criteria of this systematic review that have used such as outcome measure or have dichotomized the functional outcome score for that purpose. Continuous functional score may propose a global picture of the functional status of an individual. Future studies may assess the comparison between factors of global functional outcome and factors of functional independence.

Conclusions

This systematic review of the literature is the first to propose a ranking of early predictive factors of chronic functional outcome following traumatic spinal cord injury (TSCI). This work also discussed of the relationship between factors of functional recovery while highlighting the ones that may be optimized, throughout the hospitalization phases, in order to optimize chronic functional outcome.

The main socio-demographic and trauma-related factors associated with higher functional outcome identified in this review are: **decreased severity of the SCI, younger age, lower neurologic level of injury, and the higher initial ASIA motor score.**

The main modifiable factors are: **presence of surgical management, higher functional status at discharge from acute care, shorter acute care length of stay, presence of a specialized multidisciplinary functional rehabilitation process.**

Modifiable factors also contributing (maybe to a lesser extent) to higher functional outcome following TSCI are: **prevention of medical complications, higher intensity and patient participation level in functional rehabilitation therapy**

References

1. Dijkers M. Quality of life after spinal cord injury: a meta analysis of the effects of disablement components. *Spinal cord*. 1997 Dec;35(12):829-40. PubMed PMID: 9429262.
2. Kennedy P, Lude P, Taylor N. Quality of life, social participation, appraisals and coping post spinal cord injury: a review of four community samples. *Spinal cord*. 2006 Feb;44(2):95-105. PubMed PMID: 16130026.
3. Krueger H, Noonan VK, Trenaman LM, Joshi P, Rivers CS. The economic burden of traumatic spinal cord injury in Canada. *Chronic Dis Inj Can*. 2013 Jun;33(3):113-22. PubMed PMID: 23735450.
4. Anderson KD. Targeting recovery: priorities of the spinal cord-injured population. *Journal of neurotrauma*. 2004 Oct;21(10):1371-83. PubMed PMID: 15672628.
5. Burns AS, Ditunno JF. Establishing prognosis and maximizing functional outcomes after spinal cord injury: a review of current and future directions in rehabilitation management. *Spine (Phila Pa 1976)*. 2001 Dec 15;26(24 Suppl):S137-45. PubMed PMID: 11805621.
6. Wright JG SM. Introducing a new Journal section: Evidence-Based Orthopaedics. *J Bone Joint Surg Am*. 2000;82:759-60.
7. Li Y, Reinhardt JD, Gosney JE, Zhang X, Hu X, Chen S, et al. Evaluation of functional outcomes of physical rehabilitation and medical complications in spinal cord injury victims of the Sichuan earthquake. *J Rehabil Med*. 2012 Jun;44(7):534-40. PubMed PMID: 22674233.
8. Whiteneck G, Gassaway J, Dijkers MP, Heinemann AW, Kreider SE. Relationship of patient characteristics and rehabilitation services to outcomes following spinal cord injury: the SCIREhab project. *The journal of spinal cord medicine*. 2012 Nov;35(6):484-502. PubMed PMID: 23318033. Pubmed Central PMCID: 3522893.
9. Abdul-Sattar AB. Predictors of functional outcome in patients with traumatic spinal cord injury after inpatient rehabilitation: in Saudi Arabia. *NeuroRehabilitation*. 2014 Jan 01;35(2):341-7. PubMed PMID: 24990019.
10. Post MW, Dallmeijer AJ, Angenot EL, van Asbeck FW, van der Woude LH. Duration and functional outcome of spinal cord injury rehabilitation in the Netherlands. *J Rehabil Res Dev*. 2005 May-Jun;42(3 Suppl 1):75-85. PubMed PMID: 16195965.
11. Horn SD, Smout RJ, DeJong G, Dijkers MP, Hsieh CH, Lammertse D, et al. Association of various comorbidity measures with spinal cord injury rehabilitation outcomes. *Archives of physical medicine and rehabilitation*. 2013 Apr;94(4 Suppl):S75-86. PubMed PMID: 23527775.
12. Saboe LA, Darrah JM, Pain KS, Guthrie J. Early predictors of functional independence 2 years after spinal cord injury. *Archives of physical medicine and rehabilitation*. 1997 Jun;78(6):644-50. PubMed PMID: 9196473.
13. Dvorak MF, Fisher CG, Hoekema J, Boyd M, Noonan V, Wing PC, et al. Factors predicting motor recovery and functional outcome after traumatic central cord syndrome: a long-term follow-up. *Spine (Phila Pa 1976)*. 2005 Oct 15;30(20):2303-11. PubMed PMID: 16227894.
14. Pouw MH, Hosman AJ, van Kampen A, Hirschfeld S, Thietje R, van de Meent H. Is the outcome in acute spinal cord ischaemia different from that in traumatic spinal cord injury? A cross-sectional analysis of the neurological and functional outcome in a cohort of 93 paraplegics. *Spinal cord*. 2011 Feb;49(2):307-12. PubMed PMID: 20805834.
15. Wilson JR, Grossman RG, Frankowski RF, Kiss A, Davis AM, Kulkarni AV, et al. A clinical prediction model for long-term functional outcome after traumatic spinal cord injury based on acute clinical and imaging factors. *Journal of neurotrauma*. 2012 Sep;29(13):2263-71. PubMed PMID: 22709268. Pubmed Central PMCID: 3430477.

16. Ozelie R, Gassaway J, Buchman E, Thimmaiah D, Heisler L, Cantoni K, et al. Relationship of occupational therapy inpatient rehabilitation interventions and patient characteristics to outcomes following spinal cord injury: the SCIR rehab project. *The journal of spinal cord medicine*. 2012 Nov;35(6):527-46. PubMed PMID: 23318035. Pubmed Central PMCID: 3522895.
17. Teeter L, Gassaway J, Taylor S, LaBarbera J, McDowell S, Backus D, et al. Relationship of physical therapy inpatient rehabilitation interventions and patient characteristics to outcomes following spinal cord injury: the SCIR rehab project. *The journal of spinal cord medicine*. 2012 Nov;35(6):503-26. PubMed PMID: 23318034. Pubmed Central PMCID: 3522894.
18. Grassner L, Wutte C, Klein B, Mach O, Riesner S, Panzer S, et al. Early Decompression (< 8 h) after Traumatic Cervical Spinal Cord Injury Improves Functional Outcome as Assessed by Spinal Cord Independence Measure after One Year. *Journal of neurotrauma*. 2016 Sep 15;33(18):1658-66. PubMed PMID: 27050499.
19. Richard-Denis A, Feldman D, Thompson C, Mac-Thiong JM. Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization. *The journal of spinal cord medicine*. 2017 Feb 15;1-9. PubMed PMID: 28198660.
20. Kaminski L, Cordemans V, Cernat E, M'Bra KI, Mac-Thiong JM. Functional Outcome Prediction after Traumatic Spinal Cord Injury Based on Acute Clinical Factors. *Journal of neurotrauma*. 2017 Jun 15;34(12):2027-33. PubMed PMID: 28129730.
21. Mahmoud H, Qannam H, Zbogor D, Mortenson B. Spinal cord injury rehabilitation in Riyadh, Saudi Arabia: time to rehabilitation admission, length of stay and functional independence. *Spinal cord*. 2017 May;55(5):509-14. PubMed PMID: 28139661.
22. Charlson ME, Charlson RE, Peterson JC, Marinopoulos SS, Briggs WM, Hollenberg JP. The Charlson comorbidity index is adapted to predict costs of chronic disease in primary care patients. *J Clin Epidemiol*. 2008 Dec;61(12):1234-40. PubMed PMID: 18619805.
23. Willson DF, Horn SD, Smout R, Gassaway J, Torres A. Severity assessment in children hospitalized with bronchiolitis using the pediatric component of the Comprehensive Severity Index. *Pediatr Crit Care Med*. 2000 Oct;1(2):127-32. PubMed PMID: 12813263.
24. Wilson JR, Cadotte DW, Fehlings MG. Clinical predictors of neurological outcome, functional status, and survival after traumatic spinal cord injury: a systematic review. *Journal of neurosurgery Spine*. 2012 Sep;17(1 Suppl):11-26. PubMed PMID: 22985366.
25. Al-Habib AF, Attabib N, Ball J, Bajammal S, Casha S, Hurlbert RJ. Clinical predictors of recovery after blunt spinal cord trauma: systematic review. *Journal of neurotrauma*. 2011 Aug;28(8):1431-43. PubMed PMID: 19831845. Pubmed Central PMCID: 3143416.
26. Kirshblum S, Botticello A, Lammertse DP, Marino RJ, Chiodo AE, Jha A. The impact of sacral sensory sparing in motor complete spinal cord injury. *Archives of physical medicine and rehabilitation*. 2011 Mar;92(3):376-83. PubMed PMID: 21353822. Pubmed Central PMCID: 3698852.
27. van Middendorp JJ, Hosman AJ, Pouw MH, Group E-SS, Van de Meent H. Is determination between complete and incomplete traumatic spinal cord injury clinically relevant? Validation of the ASIA sacral sparing criteria in a prospective cohort of 432 patients. *Spinal cord*. 2009 Nov;47(11):809-16. PubMed PMID: 19468282.
28. Consortium for Spinal Cord M. Early acute management in adults with spinal cord injury: a clinical practice guideline for health-care professionals. *The journal of spinal cord medicine*. 2008;31(4):403-79. PubMed PMID: 18959359. Pubmed Central PMCID: 2582434.
29. Grant RA, Quon JL, Abbed KM. Management of acute traumatic spinal cord injury. Current treatment options in neurology. 2015 Feb;17(2):334. PubMed PMID: 25630995.

30. Markandaya M, Stein DM, Menaker J. Acute Treatment Options for Spinal Cord Injury. Current treatment options in neurology. 2012 Feb 03. PubMed PMID: 22302639.
31. Wilson JR, Fehlings MG. Emerging approaches to the surgical management of acute traumatic spinal cord injury. Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics. 2011 Apr;8(2):187-94. PubMed PMID: 21373951. Pubmed Central PMCID: 3101827.
32. Li Y, Walker CL, Zhang YP, Shields CB, Xu XM. Surgical decompression in acute spinal cord injury: A review of clinical evidence, animal model studies, and potential future directions of investigation. Frontiers in biology. 2014 Feb 01;9(2):127-36. PubMed PMID: 24899887. Pubmed Central PMCID: 4041293.
33. Yamazaki T, Yanaka K, Fujita K, Kamezaki T, Uemura K, Nose T. Traumatic central cord syndrome: analysis of factors affecting the outcome. Surgical neurology. 2005 Feb;63(2):95-9; discussion 9-100. PubMed PMID: 15680638.
34. Chen L, Yang H, Yang T, Xu Y, Bao Z, Tang T. Effectiveness of surgical treatment for traumatic central cord syndrome. Journal of neurosurgery Spine. 2009 Jan;10(1):3-8. PubMed PMID: 19119925.
35. Harlan WR, 3rd, Sandler SA, Lee KL, Lam LC, Mark DB. Importance of baseline functional and socioeconomic factors for participation in cardiac rehabilitation. Am J Cardiol. 1995 Jul 01;76(1):36-9. PubMed PMID: 7793400.
36. Divanoglou A, Westgren N, Bjelak S, Levi R. Medical conditions and outcomes at 1 year after acute traumatic spinal cord injury in a Greek and a Swedish region: a prospective, population-based study. Spinal cord. 2010 Jun;48(6):470-6. PubMed PMID: 20029392.
37. Wilson JR, Davis AM, Kulkarni AV, Kiss A, Frankowski RF, Grossman RG, et al. Defining age-related differences in outcome after traumatic spinal cord injury: analysis of a combined, multicenter dataset. The spine journal : official journal of the North American Spine Society. 2014 Jul 01;24(7):1192-8. PubMed PMID: 24210580.
38. Furlan JC, Fehlings MG. The impact of age on mortality, impairment, and disability among adults with acute traumatic spinal cord injury. Journal of neurotrauma. 2009 Oct;26(10):1707-17. PubMed PMID: 19413491. Pubmed Central PMCID: 2822797.
39. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, et al. International standards for neurological classification of spinal cord injury (revised 2011). The journal of spinal cord medicine. 2011 Nov;34(6):535-46. PubMed PMID: 22330108. Pubmed Central PMCID: 3232636.
40. Kirshblum SC, Waring W, Biering-Sorensen F, Burns SP, Johansen M, Schmidt-Read M, et al. Reference for the 2011 revision of the International Standards for Neurological Classification of Spinal Cord Injury. The journal of spinal cord medicine. 2011 Nov;34(6):547-54. PubMed PMID: 22330109. Pubmed Central PMCID: 3232637.
41. Richard-Denis A, Erhmann Feldman D, Thompson C, Mac-Thiong JM. The impact of acute management on the occurrence of medical complications during the specialized spinal cord injury acute hospitalization following motor-complete cervical spinal cord injury. The journal of spinal cord medicine. 2017 Jul 19:1-18. PubMed PMID: 28724333.
42. Consortium for Spinal Cord Medicine Clinical Practice G. Pressure ulcer prevention and treatment following spinal cord injury: a clinical practice guideline for health-care professionals. The journal of spinal cord medicine. 2001 Spring;24 Suppl 1:S40-101. PubMed PMID: 11958176.

43. Salzberg CA, Byrne DW, Cayten CG, van Niewerburgh P, Murphy JG, Viehbeck M. A new pressure ulcer risk assessment scale for individuals with spinal cord injury. *American journal of physical medicine & rehabilitation*. 1996 Mar-Apr;75(2):96-104. PubMed PMID: 8630201.
44. Bethea JR, Dietrich WD. Targeting the host inflammatory response in traumatic spinal cord injury. *Current opinion in neurology*. 2002 Jun;15(3):355-60. PubMed PMID: 12045737.
45. Aito S, D'Andrea M, Werhagen L, Farsetti L, Cappelli S, Bandini B, et al. Neurological and functional outcome in traumatic central cord syndrome. *Spinal cord*. 2007 Apr;45(4):292-7. PubMed PMID: 16773038.
46. Parent S, Barchi S, LeBreton M, Casha S, Fehlings MG. The impact of specialized centers of care for spinal cord injury on length of stay, complications, and mortality: a systematic review of the literature. *Journal of neurotrauma*. 2011 Aug;28(8):1363-70. PubMed PMID: 21410318. Pubmed Central PMCID: 3143414.
47. Miyanji F, Furlan JC, Aarabi B, Arnold PM, Fehlings MG. Acute cervical traumatic spinal cord injury: MR imaging findings correlated with neurologic outcome--prospective study with 100 consecutive patients. *Radiology*. 2007 Jun;243(3):820-7. PubMed PMID: 17431129.
48. Flanders AE, Spettell CM, Friedman DP, Marino RJ, Herbison GJ. The relationship between the functional abilities of patients with cervical spinal cord injury and the severity of damage revealed by MR imaging. *AJNR American journal of neuroradiology*. 1999 May;20(5):926-34. PubMed PMID: 10369368.
49. Vasquez N, Gall A, Ellaway PH, Craggs MD. Light touch and pin prick disparity in the International Standard for Neurological Classification of Spinal Cord Injury (ISNCSCI). *Spinal cord*. 2013 May;51(5):375-8. PubMed PMID: 23318558.
50. Furlan JC, Noonan V, Cadotte DW, Fehlings MG. Timing of decompressive surgery of spinal cord after traumatic spinal cord injury: an evidence-based examination of pre-clinical and clinical studies. *Journal of neurotrauma*. 2011 Aug;28(8):1371-99. PubMed PMID: 20001726. Pubmed Central PMCID: 3143409.
51. Mac-Thiong JM, Feldman DE, Thompson C, Bourassa-Moreau E, Parent S. Does timing of surgery affect hospitalization costs and length of stay for acute care following a traumatic spinal cord injury? *Journal of neurotrauma*. 2012 Dec 10;29(18):2816-22. PubMed PMID: 22920942.
52. Bourassa-Moreau E, Mac-Thiong JM, Ehrmann Feldman D, Thompson C, Parent S. Complications in acute phase hospitalization of traumatic spinal cord injury: does surgical timing matter? *The journal of trauma and acute care surgery*. 2013 Mar;74(3):849-54. PubMed PMID: 23425747.
53. Scivoletto G, Farchi S, Laurenza L, Tamburella F, Molinari M. Impact of multiple injuries on functional and neurological outcomes of patients with spinal cord injury. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2013 May 30;21:42. PubMed PMID: 23718823. Pubmed Central PMCID: 3669625.
54. Thompson C, Mutch J, Parent S, Mac-Thiong JM. The changing demographics of traumatic spinal cord injury: An 11-year study of 831 patients. *The journal of spinal cord medicine*. 2015 Mar;38(2):214-23. PubMed PMID: 25096709. Pubmed Central PMCID: 4397204.
55. Krassioukov AV, Furlan JC, Fehlings MG. Medical co-morbidities, secondary complications, and mortality in elderly with acute spinal cord injury. *Journal of neurotrauma*. 2003 Apr;20(4):391-9. PubMed PMID: 12866818.
56. Kreinest M, Ludes L, Biglari B, Kuffer M, Turk A, Grutzner PA, et al. Influence of Previous Comorbidities and Common Complications on Motor Function after Early Surgical

Treatment of Patients with Traumatic Spinal Cord Injury. *Journal of neurotrauma*. 2016 Dec 15;33(24):2175-80. PubMed PMID: 27153735.

57. Berlowitz DR, Hoenig H, Cowper DC, Duncan PW, Vogel WB. Impact of comorbidities on stroke rehabilitation outcomes: does the method matter? *Archives of physical medicine and rehabilitation*. 2008 Oct;89(10):1903-6. PubMed PMID: 18929019.

58. Gater DR, Jr. Obesity after spinal cord injury. *Physical medicine and rehabilitation clinics of North America*. 2007 May;18(2):333-51, vii. PubMed PMID: 17543776.

59. Sturm R. Increases in morbid obesity in the USA: 2000-2005. *Public health*. 2007 Jul;121(7):492-6. PubMed PMID: 17399752. Pubmed Central PMCID: 2864630.

60. Lamontagne ME, Gagnon C, Allaire AS, Noreau L. Effect of rehabilitation length of stay on outcomes in individuals with traumatic brain injury or spinal cord injury: a systematic review protocol. *Systematic reviews*. 2013 Jul 20;2:59. PubMed PMID: 23870623. Pubmed Central PMCID: 3733646.

61. Noonan VK, Chan E, Santos A, Soril L, Lewis R, Singh A, et al. Traumatic Spinal Cord Injury Care in Canada: A Survey of Canadian Centres. *Journal of neurotrauma*. 2017 Apr 01. PubMed PMID: 28367684.

62. Richard-Denis A, Ehrmann Feldman D, Thompson C, Bourassa-Moreau E, Mac-Thiong JM. Costs and Length of Stay for the Acute Care of Patients with Motor-Complete Spinal Cord Injury Following Cervical Trauma: The Impact of Early Transfer to Specialized Acute SCI Center. *American journal of physical medicine & rehabilitation*. 2017 Jul;96(7):449-56. PubMed PMID: 28628531.

63. Richard-Denis A, Thompson C, Bourassa-Moreau E, Parent S, Mac-Thiong JM. Does the Acute Care Spinal Cord Injury Setting Predict the Occurrence of Pressure Ulcers at Arrival to Intensive Rehabilitation Centers? *American journal of physical medicine & rehabilitation*. 2016 Apr;95(4):300-8. PubMed PMID: 26418488.

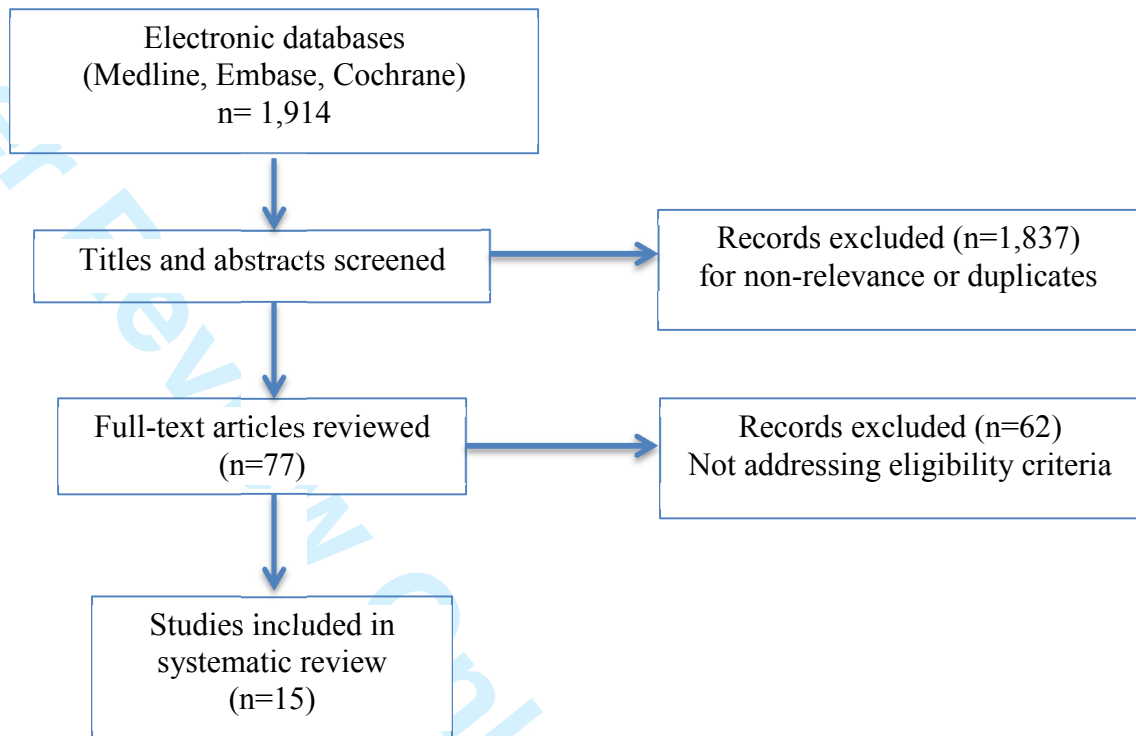
64. Cohen JT, Marino RJ, Sacco P, Terrin N. Association between the functional independence measure following spinal cord injury and long-term outcomes. *Spinal cord*. 2012 Oct;50(10):728-33. PubMed PMID: 22641254.

65. Itzkovich M, Gelernter I, Biering-Sorensen F, Weeks C, Laramee MT, Craven BC, et al. The Spinal Cord Independence Measure (SCIM) version III: reliability and validity in a multi-center international study. *Disability and rehabilitation*. 2007 Dec 30;29(24):1926-33. PubMed PMID: 17852230.

66. Furlan JC, Noonan V, Singh A, Fehlings MG. Assessment of disability in patients with acute traumatic spinal cord injury: a systematic review of the literature. *Journal of neurotrauma*. 2011 Aug;28(8):1413-30. PubMed PMID: 20367251. Pubmed Central PMCID: 3143412.

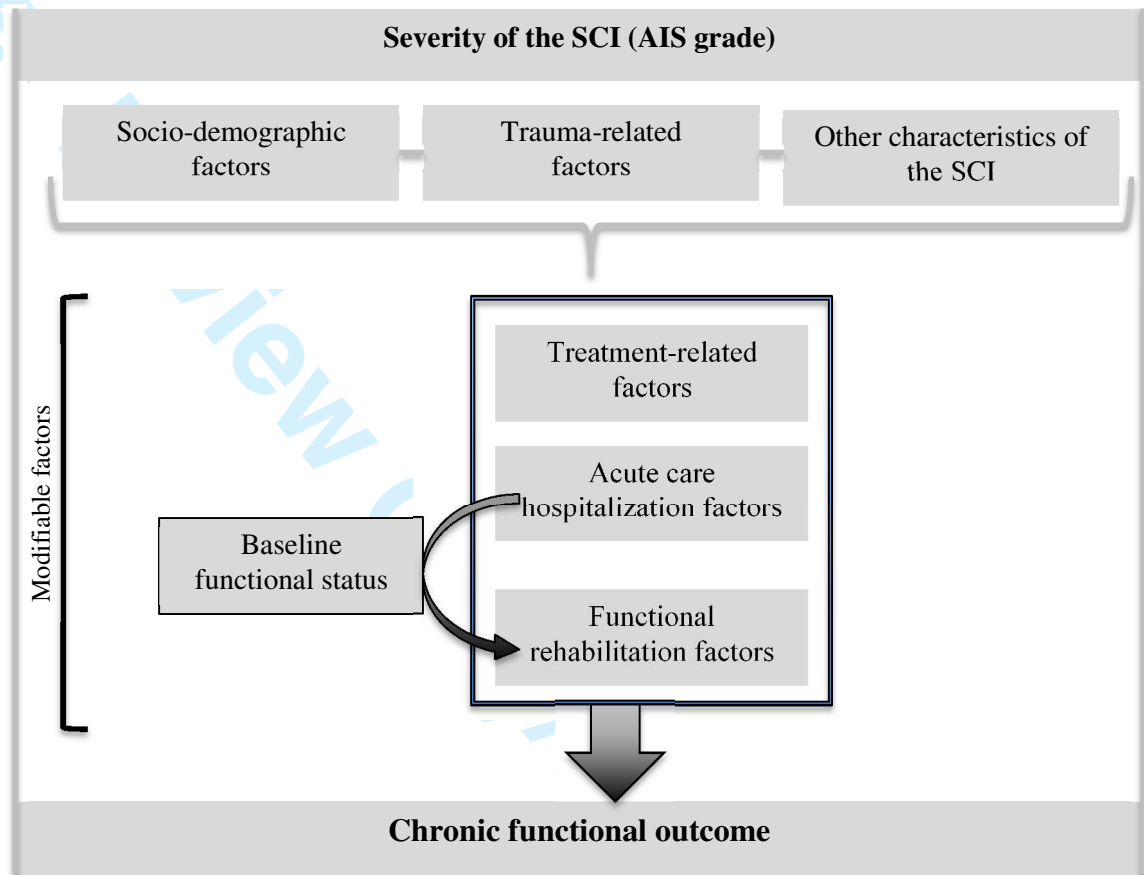
67. McMillan TM, Weir CJ, Ireland A, Stewart E. The Glasgow Outcome at Discharge Scale: an inpatient assessment of disability after brain injury. *Journal of neurotrauma*. 2013 Jun 01;30(11):970-4. PubMed PMID: 23230909.

Figure 1: Search strategy diagram for this systematic review



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Figure 2: Conceptual framework illustrating the interaction between factors influencing functional recovery following traumatic spinal cord injury



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Table 1: Inclusion and exclusion criteria

	Inclusion	Exclusion
Publication type	- Studies published after January 1st 1970 - Language: English	- Editorials, letters, systematic reviews, meta-analyses, preliminary reports with results published in later versions, expert opinions, conferences and textbooks
Population	- Individuals with acute SCI - Age ≥ 12 years old - Injury severity AIS A-D - Blunt and penetrating trauma included - All neurological levels included	- Age < 12 - Animal studies - Studies specific to SCIWORA syndrome and non-traumatic SCI
Outcome	- Studies including: 1) Clinical information available during acute care (or at inpatient rehabilitation admission) 2) Outcome measure available after discharge from acute care 3) Functional outcome measured by a global functional validated? outcome scale (FIM^a, MBI^b, SCIM^c, GOS^d.)	- Studies focusing on specific domains of functional outcome (ambulation, etc.) or not reporting functional outcome.
Study design	- Studies controlling for potential confounders through multiple regression analyses - Studies providing an effect measure (odds ratios, beta coefficients)	- Studies not intending to identify predictors of functional outcome. - Case series or cohort studies with < 10 patients

SCI: Spinal Cord Injury; NLI: Neurological Level of Injury; ISNCSCI: International Standards for Neurological Classification of Spinal Cord Injury; SCIWORA: Spinal Cord Injury without Radiologic Abnormality; FIM: Functional Independence Measure; MBI: Modified Barthel Index; SCIM: Spinal Cord Independence Measure; GOS: Glasgow Outcome Scale.

^a Cohen et al. Spinal Cord 2012⁶⁴

^b Itzkovich et al. Disabil Rehabil 2007⁶⁵

^c Furlan et al. J Neurotrauma 2011⁶⁶

^d McMillan et al. J Neurotrauma 2013⁶⁷

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Table 2: Classification of significant (S) and non-significant (NS) factors in relationship with chronic functional outcome.

	A.-Sattar 2014	Dvorak 2005	Post 2005	Pouw 2011	Whiteneck 2012	Wilson 2012	Horn 2013	Ozelle 2012	Teeter 2012	Grassner 2016	Saboe 1997	Li 2012	R.-Denis 2017	Kaminski 2017	Mahmoud 2017
Socio-demographic															
Age	NS	S		S	S	S	S	S	S	S	S	S	NS	NS	NS
Comorbidities		S			NS		S	S	NS		NS			NS	
Sex	NS			S	NS		NS	NS	NS	NS	NS	S	NS	NS	NS
Primary payer					S		S	S	S						
Body mass index					NS		S	NS	NS				S		
Ethnicity/race					NS		S	NS	NS						
Education level	NS	S			NS			NS	S		NS				
Employment status					NS		NS	NS	NS						
Primary language					NS		NS	NS	NS						
Smoking status													NS		
Presence of family caregiver	NS														
Marital status	NS				NS		NS	NS	NS		NS				
Characteristic of the SCI															
AIS grade	S		S	S	S	S	S	S	S	S	S		S	S	S
Neurologic level of injury	S		S		S		S	S	S			S	NS	NS	S
ASIA LT sensory score											S			S	
ASIA PP sensory score											NS			NS	
ASIA motor score						S					S		NS	S	
Computed vibration score											S				
Brown-Sequard syndrome		NS													
Trauma-related factors															
Mechanism of injury	NS	NS			NS		S	NS	NS				NS	NS	
Intramedullary signal abnormality (MRI)						S									
Severity of the trauma											NS		S	S	
Presence of spinal fracture		NS													
Presence of concomitant TBI													NS	NS	
Work related SCI					NS		NS	NS	NS						

Level of bony injury												NS				
Treatment-related factors																
Surgical management		S										S				
Timing of spinal surgery											S			NS	NS	
Adm. of corticosteroids											NS	S				
Acute care hospitalization factors																
Length of stay			S		S		S	S	S				NS	S		S
Medical complications											S			S		
Functional status at discharge of acute care	S				S		S	S	S	S						S
Time to rescue													S*			
Early spasticity														S		
Shorter intensive care stay											S					
Inpatient functional rehabilitation factors																
Specialized multidisciplinary team													S			
Occurrence of medical complications	NS											S				
Length of stay	S				NS			NS	NS							NS
Time devoted to physiotherapy					S				S							
Time devoted to occupational therapy					NS				S							
Patient participation score in therapy									S	S						
Bedrest days for complications (PU)			S													
Time of social work					S											
Anxiety/depression score	S															
Time for therapeutic recreation					NS											
Ventilator use at admission							NS									
AIS motor score, LT/ PP sensory scores, computed vibration score, and AIS grade at discharge											S					
Days of interruption											NS					
Physiotherapy/Occupational therapy clinician experience								NS	NS							

Time of speech therapy					NS										
Time for nursing care					NS										
Time of psychology					NS										
Location of the specialized center					NS			NS	NS						
Discharge destination	NS														
Clinician experience index (education/experience vs. time in treatment)					NS										
Spasticity at follow-up (2 years post injury)		S													

SCI, Spinal Cord Injury; AIS, American Spinal Injury Association (ASIA) Impairment Scale; LT, light touch; PP, pinprick; MRI, magnetic resonance imaging; TBI, traumatic brain injury; PU, pressure ulcer.

NS, Factor assessed in the designated study, but not revealed as a significant variable (non-significant) in the final predictive model.

S, Factor identified as significant in the final predictive model adjusted for their respective covariates.

* Combination of time to rescue ≤ 30 min and rehabilitation treatment within 3 months after earthquake

Table 3: Summary of the articles included in this systematic review

Author, year	Population Type of study Level of Evidence	Outcome measure and timing of follow-up	Factors assessed	Results: Significant predictors of improved functional outcome
Abdul-Sattar <i>et al.</i> , 2014	90 patients with traumatic SCI from 10/2007 to 10/2010 admitted to inpatient rehabilitation center -AIS grades A to D -NLI: tetraplegia, paraplegia Prospective cohort study LoE : I	FIM motor score change from admission to d/c of functional rehabilitation	•Age (<50 vs. ≥50 years old) •Sex •Marital status (married vs. unmarried) •Level of education (<secondary level vs. ≥secondary level) •Presence of family caregiver •Mechanism of injury •Delay between SCI and admission to inpatient rehabilitation (<40 vs. >40 days) •Length of stay for inpatient rehabilitation (<123 vs. ≥123 days) •NLI (tetraplegia vs. paraplegia) •AIS grade (motor complete A-B vs motor incomplete C-D) at admission •FIM motor score at admission (<35.3, >35.3) •Depression score (HADS-D scale; <8 vs. ≥8) •Anxiety score (HADS-A; <8 vs. ≥8) •Complications (urinary tract infection, spasticity, pressure ulcer, pneumonia, deep venous thrombosis, pulmonary embolism, depression) •Discharge destination (home vs. other)	Factors associated with higher FIM motor score gain and effect measure (β) •Longer length of stay ($\beta=3.80$) •Shorter delay from injury to inpatient rehabilitation admission ($\beta=2.73$) •Motor incomplete injury ($\beta=2.62$) •Paraplegia ($\beta=2.49$) •Lower anxiety/depression score ($\beta=1.77$) •Lower FIM motor score at admission ($\beta=0.12$) Model Adjusted-R^2 value: 0.72
Dvorak <i>et al.</i> , 2005	70 patients with traumatic central cord syndrome -Admission to acute hospital within 72h of injury -AIS motor score	FIM motor score Minimum 2 years post-injury	•Age •Mechanism of injury (low vs. high energy) •Diagnosis (fracture vs. no fracture) •Presence of Brown-Sequard syndrome •Treatment (surgical vs. non-operative) •Presence of spasticity at follow-up	Factors associated with higher FIM motor score and effect measure (β) •Younger age ($\beta=0.34$) •Absence of spasticity ($\beta=0.27$) •Higher level of formal education ($\beta=0.23$) •Surgical treatment ($\beta=0.22$)

	assessment performed at admission -Inpatient or outpatient rehabilitation following acute hospitalization -NLI: C1-C7 Retrospective study on prospective database LoE: II		•Level of formal education •Comorbidity index	•Decreased comorbidities ($\beta=0.21$) Model R^2 value: not available
Post <i>et al.</i> , 2005	157 patients with acute SCI from 08/2000 to 07/2003 -Admission to inpatient rehabilitation center for more than 3 months -Age between 18 and 65 years -AIS grades A to D -NLI: tetraplegia (T1 or above), paraplegia (below T1) -Expected to remain wheel-chair dependent at least for long distances Multicenter prospective cohort study LoE : I	FIM motor score at discharge from inpatient rehabilitation	•Level of injury (T1 or above vs. below T1) •AIS grade (motor-complete A-B vs. motor-incomplete C-D) at admission •Number of days of bedrest required for: 1.Pressure ulcer 2.Urinary tract infection 3.Respiratory tract infection •Shorter delay from injury to admission to inpatient rehabilitation	Factors associated with higher FIM motor score and effect measure (β) • Shorter delay from injury to admission to inpatient rehabilitation ($\beta=0.35$) •Motor incomplete injury ($\beta=0.32$) •Level of injury below T1 ($\beta=0.25$) •Decreased need of bedrest days due to a pressure ulcer ($\beta=0.19$) Model Adjusted-R^2 value: 0.49

Pouw <i>et al.</i> , 2011	73 patients with traumatic or ischemic SCI from 01/2000 to 07/2009 -Admission to acute hospital -AIS grades A to D -NLI: T2-T11 -Initial neurological assessment within 40 days of injury Retrospective study on prospective database LoE : II	SCIM-II ≥12 months post-injury	•Initial AIS grade (complete A vs. incomplete B-C-D) •Aetiology of SCI (ischemic vs. traumatic) •Age •Sex	Predictors of higher SCIM-II score and effect measure (β) •Younger age ($\beta=0.403$) •Incomplete injury ($\beta=0.361$) •Sex: Male ($\beta=0.233$) Model Adjusted-R² value: 0.31
Whiteneck <i>et al.</i> , 2012	1376 patients with traumatic SCI from fall 2007 to 12/2009 -Age ≥12 years -AIS grades A to D -NLI: C1-C4, C5-C8, paraplegia -Admission to inpatient rehabilitation center Retrospective study on multicenter prospective cohort LoE : II	FIM motor score (Rasch-transformed) 12 months post-injury	Patients characteristics at admission to inpatient rehabilitation •Admission motor FIM Rasch-transformed •Admission cognitive FIM Rasch-transformed •Comorbidities (Comprehensive Severity Index) •Delay between SCI and admission to inpatient rehabilitation •Mechanism of injury •Age •Sex •Marital status (married vs non-married) •Race/ethnicity •Employment status •Work related SCI •Body mass index (<30 vs. ≥30)	Predictors of higher FIM motor score Rasch-transformed and effect measure (β) Patients characteristics at admission to inpatient rehabilitation •Less severe SCI: 1.Tetraplegia C1-C4, AIS grade A-B-C ($\beta= -27.749$) 2.Tetraplegia C5-C8, AIS grade A-B-C($\beta= -22.465$) 3.Paraplegia, AIS grade A-B-C ($\beta= -17.635$) 4.AIS D (reference) •Primary payer: 1.Medicaid ($\beta=-3.959$) 2.Private insurance (reference) •Higher admission FIM motor score Rasch-transformed ($\beta=0.612$) •Younger age ($\beta=0.153$)

			•Primary language (English vs. other) •Primary payer •Education level •Neurological status (Tetraplegia C1-C4, AIS grade A-B-C vs Tetraplegia C5-C8, AIS grade A-B-C vs Paraplegia, AIS grade A-B-C vs AIS grade D) •Length of rehabilitation stay Treatment characteristics •Clinician experience index (education/experience profile of clinician vs. time in treatment) •Time for occupational therapy •Time for psychology •Time for physical therapy •Time for nursing care •Time for speech language pathology •Time for social work/case management •Time for therapeutic recreation Rehabilitation center (n=6)	•Shorter delay between SCI and admission to inpatient rehabilitation ($\beta=0.116$) •Lower admission FIM cognitive score Rasch-transformed ($\beta=0.098$) Treatment characteristics •Decreased time for social work / case management ($\beta=0.144$) •Increased physical therapy total hours ($\beta=0.092$) Model Adjusted-R² value: 0.53
Wilson <i>et al.</i> , 2012	376 patients admitted to acute care with traumatic SCI from 08/2002 to 09/2009 -16 years and older -AIS grades A to D -Neurological examination within 3 days of injury -FIM motor score at 6 or 12 months post-injury	FIM motor score 6 months post-injury (N=66) or 12 months post-injury (N=310)	•Acute AIS grade •Acute ASIA motor score (≤ 50 vs. >50) •Age •MRI signal characteristics (normal vs. spinal cord edema vs. spinal cord hemorrhage)	Predictors of higher FIM motor score and effect measure (β) •Less severe acute AIS grade ($\beta=12.47$) •Acute ASIA motor score >50 ($\beta=9.17$) •Normal MRI signal ($\beta=4.83$) •Younger age ($\beta=0.33$) Model R² value: 0.52

Horn <i>et al.</i>, 2013	Retrospective study on combined dataset from two prospective cohorts LoE : II 859 patients with traumatic SCI from Fall 2007 to end 2010 -Admission to inpatient rehabilitation center -Age ≥ 12 years -AIS grades A to D -NLI: C1-C4, C5-C8, paraplegia Prospective cohort study LoE : I	FIM motor score (Rasch-transformed) at 12 months post-injury	<i>Patient characteristics at admission to inpatient rehabilitation</i> •Admission FIM motor score Rasch-transformed •Admission FIM cognitive score Rasch-transformed •Delay between SCI and admission to inpatient rehabilitation •Mechanism of injury (vehicular vs fall vs violence vs sports vs other) •Age •Sex •Marital status (married vs non-married) •Race/ethnicity (white vs black vs hispanic vs other) •Employment status (student vs working vs retired vs other) •Primary payer (Medicare vs Medicaid vs Worker's compensation vs private insurance) •Primary language (English vs. other) •Body mass index (<30 vs. 30-40 vs. >40) •Work-related injury • Ventilator use •Neurological status (Tetraplegia C1-C4, AIS grade A-B-C vs Tetraplegia C5-C8, AIS grade A-B-C vs	Predictors of higher FIM motor score Rasch-transformed and effect measure (β) <u>Model 1: Charlson Comorbidity Index included</u> <i>Patient characteristics at admission to inpatient rehabilitation</i> •Less severe SCI: 1.C1-C4 ABC ($\beta=-6.57$) 2.AIS D ($\beta=19.10$) •Primary payer: Medicaid ($\beta=-3.52$) •Mechanism of injury: MVA ($\beta=2.81$) •Higher admission FIM motor score ($\beta=0.75$) •Younger age ($\beta=0.16$) •Shorter delay between SCI and admission to inpatient rehabilitation ($\beta=0.14$) <u>Comorbidity measures</u> •Decrease in Charlson Comorbidity Index ($\beta=1.29$) Model R^2 value : 0.510 <u>Model 2: Maximum Comprehensive Severity Index included</u> <i>Patient characteristics at admission to inpatient rehabilitation</i> •Less severe SCI: 1.C1-C4 ABC ($\beta=-10.26$) 2.C5-C8 ABC ($\beta=-4.57$)

Ozelie <i>et al.</i>, 2012	1032 patients with traumatic SCI -Admission to inpatient rehabilitation center between fall 2007 and 12/2009 -Age ≥ 12 years -AIS grades A to D -NLI: C1-C4, C5-C8, paraplegia Retrospective study LoE : II	FIM motor score (Rasch-transformed) 12 months post-injury	Paraplegia, AIS grade A-B-C vs AIS grade D) Comorbidity measures •Case-mix group tier weight •Charlson Comorbidity Index •Maximum Comprehensive Severity Index Patient and injury characteristics at admission to inpatient rehabilitation •Admission FIM motor score Rasch-transformed •Admission FIM cognitive score Rasch-transformed •Delay between SCI and admission to inpatient rehabilitation •Mechanism of injury (vehicular vs fall/falling object vs violence vs sports vs other) •Age •Sex •Marital status (married vs non-married) •Education level (<high school vs high school diploma vs college vs other) •Race/ethnicity (white vs black vs hispanic vs other) •Employment status (student vs working vs retired vs other) •Primary payer (Medicare vs Medicaid	3. AIS D ($\beta=16.78$) •Body mass index ≤ 40 ($\beta=7.44$) •Non-black race ethnicity ($\beta=3.42$) •Primary payer: Private ($\beta=2.60$) •Mechanism of injury: MVA ($\beta=2.43$) •Higher admission FIM motor score ($\beta=0.58$) •Younger age ($\beta=0.13$) •Shorter delay between SCI and admission to inpatient rehabilitation ($\beta=0.13$) Comorbidity measures •Decrease in Maximum Severity of Illness Score ($\beta=0.09$) Model R^2 value: 0.525 Predictors of higher FIM motor score Rasch-transformed and effect measure (β) Patient and injury characteristics at admission to inpatient rehabilitation •Less severe SCI 1. C1-C4 ABC ($\beta=-24.601$) 2. C5-C8 ABC ($\beta=-20.188$) 3. Paraplegia ABC ($\beta=-16.866$) 4. AIS D (reference) •Primary payer 1. Medicaid ($\beta=-3.816$) 2. Worker's compensation ($\beta=-4.541$) 3. Private insurance (reference) •Higher admission FIM motor score ($\beta=0.476$) •Younger age ($\beta=0.182$) •Lower Comprehensive Severity Index ($\beta=0.108$) •Shorter delay from SCI to admission to inpatient rehabilitation ($\beta=0.097$) •Lower cognitive FIM score ($\beta=0.081$)

vs Worker's compensation vs private insurance)

•Primary language (English vs. other)

•Body mass index (<30 vs. ≥30)

•Work-related injury

•Neurological status (Tetraplegia C1-C4, AIS grade A-B-C vs Tetraplegia C5-C8, AIS grade A-B-C vs

Paraplegia, AIS grade A-B-C vs AIS grade D)

•Comorbidities (Comprehensive Severity Index)

Treatment characteristics

•Length of rehabilitation stay

•OT clinical experience

•Patient participation score in OT

Time for occupational therapy (OT)

•Strengthening/endurance

•Activities of daily living (bathing, bladder management, bowel management, dressing upper and lower body, self-feeding, grooming, toileting)

•Range of motion/stretching

•Education

•Therapeutic activities

•Interdisciplinary conferences

•Assessment

•Equipment evaluation

•Home management skills

•Transfers

•Modalities

•Assistive technology

•Balance

•Wheelchair mobility-power

•Communication

•Bed mobility

•Community reintegration outings

•Skin management

•Splint/cast fabrication

Treatment characteristics

•Higher patient participation score in OT ($\beta=3.650$)

•Increased time in OT

1. Assessment ($\beta=1.543$)

2. Home management skills ($\beta=0.916$)

3. Strengthening/endurance ($\beta=0.173$)

•Decreased time in OT

1. Communication ($\beta=-2.046$)

2. Bed mobility ($\beta=-0.929$)

3. Self-feeding ($\beta=-0.869$)

4. Assistive technology ($\beta=-0.439$)

Model R^2 value: 0.58

Teeter <i>et al.</i>, 2012	1032 patients with traumatic SCI -Admission to inpatient rehabilitation center between fall 2007 and 12/2009 -Age ≥ 12 years -AIS grades A to D -NLI: C1-C4, C5-C8, paraplegia Retrospective study of multicenter prospective database LoE : II	FIM motor score (Rasch-transformed) 12 months post-injury	•Wheelchair mobility- manual •Classes provided by OT •Airway/respiratory management Rehabilitation center Patient and injury characteristics at admission to inpatient rehabilitation •Admission FIM motor score Rasch-transformed •Admission FIM cognitive score Rasch-transformed •Delay between SCI and admission to inpatient rehabilitation •Mechanism of injury (vehicular vs fall/falling object vs violence vs sports vs medical/surgical or other) •Age •Sex •Marital status (married vs non-married) •Education level (<high school vs high school diploma vs college vs other) •Race/ethnicity (white vs black vs hispanic vs other) •Employment status (student vs working vs retired vs other) •Primary payer (Medicare vs Medicaid vs Worker's compensation vs private insurance) •Primary language (English vs. other) •Body mass index (<30 vs. >30) •Work-related injury •Neurological status (Tetraplegia C1-C4, AIS grade A-B-C vs Tetraplegia C5-C8, AIS grade A-B-C vs Paraplegia, AIS grade A-B-C vs AIS grade D)	Predictors of higher FIM motor score Rasch-transformed and effect measure (β) Patient and injury characteristics at admission to inpatient rehabilitation •Less severe SCI 1.C1-C4 ABC ($\beta=-18.912$) 2.C5-C8 ABC ($\beta=-12.454$) 3.Paraplegia ABC ($\beta=-9.312$) 4.AIS D (reference) •Primary payer 1.Medicaid ($\beta=-3.712$) 2.Worker's compensation ($\beta=-4.206$) 3.Private insurance (reference) •Higher education level 1.High school ($\beta=3.479$) 2.College ($\beta=4.550$) 3.<12 years/other (reference) •Higher admission FIM motor score ($\beta=0.570$) •Younger age ($\beta=0.238$) •Shorter delay between SCI and admission to inpatient rehabilitation ($\beta=0.086$) •Lower admission FIM cognitive score($\beta=0.078$) Treatment characteristics •Higher patient participation score in PT ($\beta=4.739$) •Increased time in PT for 1.Pre-gait ($\beta=1.595$) 2.Assessment ($\beta=1.323$) 3.Gait ($\beta=0.810$) •Decreased time in PT for

			•Comorbidities (Comprehensive Severity Index)	1. Airway / respiratory management ($\beta=-1.053$) 2. Wheelchair mobility – power ($\beta=0.837$) 3. Equipment evaluation/provision/education ($\beta=-0.827$) 4. Range of motion / stretching exercise ($\beta=-0.219$)
			Treatment characteristics •Length of rehabilitation stay •PT clinical experience •Patient participation score in PT •PT hours in specific treatment 1. airway / resp. management 2. aquatic exercises 3. assessment 4. bed mobility 5. classes provided by PT •education •equipment evaluation/provision/education •gait •interdisciplinary conferences •musculoskeletal treatment modalities •pre-gait •skin management •therapeutic exercise 1. balance 2. endurance 3. ROM/stretching 4. strengthening •transfers •upright activities •wheelchair mobility 1. manual 2. power •wound care	Model Adjusted-R ² value: 0.62
			Rehabilitation center	
Grassner <i>et al.</i> , 2016	70 patients with traumatic SCI from July 2004 to July 2014	Change in SCIM-II or SCIM-III total score from baseline (within 40 days of	•Timing of surgery (early <8hrs vs. late ≥ 8hrs after trauma) •Age •Sex	Predictors of gain in SCIM score and effect measure (β) •Less severe baseline AIS grade ($\beta=0.760$) •Lower baseline SCIM score ($\beta=0.308$)

	-Admission to acute hospital -Age ≥ 18 years -NLI between C2-T1 -AIS grade A to D -Initial GCS ≥ 14 -Detailed neurological examination in acute (within 40 days post-injury) and chronic (300-400 days post-injury) phases Retrospective study on a prospective cohort LoE : II	injury) to 12 months post-injury	•Cortisone treatment •Baseline AIS grade •Baseline SCIM score	•Younger age ($\beta=0.290$) •Early surgery (<8hrs) ($\beta=0.215$) Model R^2 value :0.513
Saboe et al. 1997	160 patients with traumatic SCI from 1983 to 1992 -Admission to acute hospital and inpatient rehabilitation -AIS grades A to D -NLI: C1-L5* - Initial neurological assessment with 96 hours of injury Prospective cohort study LoE: I	FIM total score 24 months post-injury	Admission to acute hospital •Age •Sex •Marital status (yes vs. no) •Education level (coded with 21-grade scale) •Medical comorbidities •Injury Severity Score •Level of bony injury (C1 to L5) •ASIA motor score •ASIA light touch sensory score •ASIA pinprick sensory score •AIS grade •Computed vibration score Inpatient stay in acute and rehabilitation hospital •Surgical vs. non-surgical treatment •Early use of steroids	Predictors of higher FIM total score and effect measure (β) Admission to acute hospital •Increased ASIA light touch sensory score ($\beta=0.75$) •Increased ASIA motor score ($\beta=0.36$) •Increased computed vibration score ($\beta=0.23$) •Lower AIS grade ($\beta=0.22$) •Younger age ($\beta=0.16$) Inpatient stay in acute and rehabilitation hospital •Shorter stay in ICU ($\beta=0.24$) •Absence of complications ($\beta=0.12$) •Surgical treatment ($\beta=0.10$) •Early use of steroids ($\beta=0.10$) Discharge from tertiary care facility •Increased ASIA motor score ($\beta=0.78$)

			•Complications (abdominal, bladder, chest, deep vein thrombosis) •Total stay in ICU •Total days of interruption of rehabilitation	Model Adjusted-R ² value: 0.75
			Discharge from tertiary care facility •ASIA motor score •ASIA light touch sensory score •ASIA pinprick sensory score •AIS grade •Computed vibration score	
Li et al., 2012	51 patients with traumatic SCI (due to earthquake) -NLI C1 to S5* -AIS grades A to D Prospective cohort study LoE : I	Change in Modified Barthel Index (MBI) between beginning and end of inpatient rehabilitation	•Age •Sex •NLI (above T7 vs. T7 and below) •Time to rescue (between earthquake and extrication) •Delay between SCI and admission to inpatient rehabilitation •Rehabilitation programming	Predictors of gain in MBI score and effect measure (B) •Rehabilitation programming ($\beta=10.04$) •NLI below T7 ($\beta=3.62$) •Sex: Male ($\beta=2.50$) •Younger age ($\beta=2.08$) •Combination of time to rescue ≤ 30 min and rehabilitation treatment within 3 months after earthquake ($\beta=2.06$) Model R ² value: not available
Richard-Denis et al. (2017)	159 patients admitted to a single acute care center for a traumatic SCI between Jan 2010 and Feb 2015 aged 16 years old and older. -NLI C1 to L1 -AIS grades A to D	SCIM III total score 6 months post-injury	•Surgical delay (in hours) •Presence of spasticity (early spasticity) •Sex •Age •Body mass index (as continuous data) •Smoking status •Mechanism of traumatic injury (high-velocity vs. non-high velocity) •Occurrence of medical complications	Predictors of higher total SCIM score and effect measure (B) Individuals with tetraplegia •AIS grade C-D ($\beta=27.3$) •Absence of medical complications ($\beta=22.7$) •Absence of early spasticity ($\beta=2.5$) •Shorter acute care length of stay ($\beta=0.3$) Model R ² value: 0.671

Kaminski et al. (2017)	Retrospective study on a prospective cohort LoE: II 76 patients admitted to a single acute care center for a traumatic SCI between April 2010 and Nov 2013 aged 16 years old and older. -NLI C1 to L1 -AIS grades A to D Retrospective study on a prospective cohort LoE: II	SCIM III total score 12 months post-injury	(pressure ulcers, urinary tract infection, pneumonia) • Occurrence of multiple complications • AIS grade (motor-complete (AIS A-B) vs. motor incomplete (AIS C-D) injury) at admission • AIS motor score at admission • Acute care length of stay • Presence of traumatic brain injury • Presence of moderate or severe traumatic brain injury • Neurologic level of injury at admission (C1-C8 (tetraplegia) vs. T1-L1 (paraplegia)) • Injury severity score (associated traumatic injuries) <i>Preoperative variables</i> • AIS grade • ASIA motor score • ASIA light touch score • ASIA pin prick score • Injury severity score (associated traumatic injuries) • Presence of traumatic brain injury • Surgical delay (in hours) • Age • Sex • Presence of comorbidity • Type of injury (sport, assault (closed or penetrating), fall, transport, other) • Level of injury (cervical vs. thoracolumbar)	<i>Individuals with paraplegia</i> • AIS grade C-D ($\beta=19.1$) • Absence of early spasticity ($\beta=6.3$) • Lower body mass index ($\beta=1.3$) • Lower injury severity score ($\beta=0.8$) Model R^2 value: 0.548 Predictors of higher total SCIM score and effect measure (β) • AIS-A ($\beta=-15.0$) • AIS-B ($\beta=-12.4$) • AIS-C ($\beta=-7.01$) • AIS-D (reference) • Lower injury severity score ($\beta=0.589$) • Higher ASIA light touch score ($\beta=0.283$) • Higher ASIA motor score ($\beta=0.134$) Model R^2 value: 0.573 Predictors of higher FIM motor score and

Mahmoud et al. 2017	532 patients admitted to one inpatient rehabilitation center from 2009 and 2014. - ≥16 years old - Traumatic and non-traumatic SCI - AIS A, B, C - Tetraplegia, paraplegia Retrospective study LoE: II	FIM motor score at discharge from inpatient rehabilitation	• FIM motor score at admission • Age • Sex • NLI (paraplegia vs. tetraplegia) • AIS grade (A, B, C) • Time to admission to inpatient rehabilitation (days) • Length of stay (inpatient rehabilitation)	effect measure (B) • Higher FIM motor score at admission ($\beta=0.62$) • Paraplegia ($\beta=0.16$) • Shorter time to admission to inpatient rehabilitation ($\beta=0.14$) Model R^2 value: 0.50

* NLI including non-spinal cord levels. Real numbers of participants with SCI is unknown, which might have influenced results of this review

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Table 4: Global rating of the relative importance of predictive factors of chronic functional outcome assessed in this systematic review

MAIN PREDICTIVE			<u>AIS grade of SEVERITY OF THE SCI</u>		
Strongly predictive	-Surgical management -Functional status at discharge from acute care -Acute care length of stay -<i>Specialized functional rehabilitation process</i>	-Age -Neurologic level of injury -ASIA motor score			
Moderately predictive	-Occurrence of medical complications during acute and rehabilitation -Time devoted to rehabilitation therapies during functional rehabilitation -Participation level of patients during functional rehabilitation therapies	-Primary payer -ASIA light touch sensory score -<i>Intramedullary signal abnormality (MRI)</i>			
Weakly predictive	-Timing of spinal surgery	-Trauma severity -Comorbidities -Body mass index -Education level -ASIA pinprick sensory score			
Very weakly or not predictive	- Administration of corticosteroids -Location of specialized functional rehabilitation facility -Functional rehabilitation length of stay -Therapist clinical experience	-Mechanism of traumatic injury -Concomitant TBI -Work-related SCI -Sex -Ethnicity/race -Employment status -Primary language -Marital status			
Inconclusive	- Discharge destination at discharge from functional rehabilitation -Days of interruption of functional rehabilitation -Intensive care length of stay -Ventilator use at admission to functional rehabilitation	-Brown Sequard syndrome -Early spasticity -Chronic spasticity -Smoking status -Presence of family caregiver -Computed vibration score -Level of bony injury -Depression /anxiety at admission to functional rehabilitation -ASIA motor score at discharge from functional rehabilitation			

16. Appendix 8: Manuscript submitted in Spinal Cord

Spinal cord

Oct 13th, 2017

Professor Lisa Harvey, Editor-in-chief

Dear Professor Lisa Harvey,

On behalf of the authors, I would like to submit to the journal *Spinal Cord* the following manuscript as Original article: **“The use of classification tree analysis to assess the influence of surgical timing on neurological recovery following traumatic complete cervical spinal cord injury”** by Facchinello Y., Richard-Denis A., Beauséjour M., Thompson C. and Mac-Thiong J.-M. This work is novel, original and has not been and will not be submitted or published elsewhere.

Following traumatic spinal cord injuries, early surgical decompression is often associated with better neurological outcome. However, no attempt was made to objectively quantify the surgical timing leading to better neurological recovery. This communication proposes the use of machine learning algorithms to define for the first time a surgical timing leading to improved neurological outcome in patients sustaining complete cervical spinal cord injury. We have no potential or real conflicts of interest related to this communication.

Yours sincerely,

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The use of classification tree analysis to assess the influence of surgical timing on neurological recovery following traumatic complete cervical spinal cord injury

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We have no potential or real conflicts of interest related to this communication.

32 Abstract

33

34 Study Design: A prospective cohort study

35 Objectives: Assess the influence of surgical timing on neurological recovery using
36 classification tree analysis in patients sustaining complete cervical traumatic spinal cord injury.

37 Settings : Hôpital du Sacré-Coeur de Montreal

38 Methods: 42 patients sustaining a complete cervical SCI treated in a single Level 1
39 Trauma Center specializing in spinal cord injury were followed for at least 6 months post-injury.
40 Neurological status was assessed from the American Spinal Injury Association impairment scale
41 (AIS) and neurological level of injury at admission to the acute care center and at follow-up 6
42 months after the injury. Age, surgical timing between trauma and surgery, AIS grade at
43 admission and energy of injury were the four parameters considered as influencing the
44 neurological recovery. Neurological recovery was quantified by the occurrence of improvement
45 by: 1) at least one AIS grade, 2) at least 2 AIS grades and 3) at least 2 neurological level of injury.

46 Results: Surgical timing had a significant influence on all three endpoints for neurological
47 recovery considered in this study. Early decompression surgery performed within 19 hours post-
48 injury was associated with better neurological outcome.

49 Conclusions : Neurological recovery of patients sustaining complete cervical traumatic
50 spinal cord injury can be improved by early decompression surgery performed within 19 hours
51 post-trauma. This study is the first to justify an optimized cut-off value defining the concept of
52 early decompression surgery.

53 Sponsorship : This work was supported by the U.S. Army Medical Research and Material
54 Command and by the Rick Hansen Institute.

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57 Keywords : traumatic spinal cord injury, neurological recovery, surgical timing, decision tree,
58 machine learning algorithms

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1. Introduction

Following traumatic spinal cord injuries (TSCI), motor and sensory functions can be severely impaired, leading to a loss of autonomy and a poor quality of life. The incidence of TSCI ranges from 10 to 80 cases per million inhabitants depending on the country while the prevalence varies from 250 to 950 cases per millions.¹

Surgical intervention is generally required following TSCI, in order to stabilize the spine, relieve the mechanical pressure to the spinal cord and potentially minimize the cascade of secondary lesions to the spinal cord.

Following TSCI, neurological recovery is one of the main concerns for patients as it is directly related to their independence, quality of life and productivity.²⁻⁴ Number of demographical and clinical parameters influence neurological recovery, such as the injury severity, age, occurrence of medical complications, injury mechanism and energy.⁵⁻⁸ Among those parameters, surgical delay, defined as the time interval between the trauma and surgical intervention, plays a significant role in the long-term functional and neurological recovery.^{9,10} Indeed, shorter surgical delays were showed to lead to better outcomes, less complications and decreased resource utilization.¹¹⁻¹⁵ However, the definition of early surgery is still debatable as values ranging from 8 to 72 hours can be found in the literature.^{11-14,16} It also must be noted that the definitions of early surgery found in the literature are arbitrary and no attempt was made to define an optimized surgical timing leading to better neurological outcome. Patients sustaining acute tetraplegia may particularly benefit from early surgery, especially in terms of improved neurological recovery as recently shown by Bourassa-Moreau et al¹³ and Fehlings et al.¹⁵

2. Methods

2.1. Participants

Methods Sponsorship: This work was supported by the U.S. Army Medical Research and Materiel Command and funded by the Rick Hansen Institute.

Study Design: This study was based on a prospective cohort of 42 patients who sustained a motor-complete, cervical TSCI between January 2010 and June 2016. All patients were enrolled on a voluntary

basis and signed the informed consent during the acute hospitalization at a single Level I trauma center specialized in TSCI. Patients were included if they sustained a TSCI between C1 and T1

levels with an initial AIS grade at admission of A or B and were followed for a minimum of 6 months after the trauma. This study was approved by the Institutional Review Board. All

applicable institutional and governmental regulations concerning the ethical use of human

volunteers were followed during the course of this research.

Keywords: traumatic spinal cord injury, neurological recovery, surgical timing, decision tree, machine learning algorithms

2.2. Variables

Parameters influencing the neurological recovery consisted in a reduced number of 4

2.2.1. Outcome variables

The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) were

used to assess the severity of injury in the form of American Spinal Injury Association

Impairment Scale (AIS) grades at 6 months follow-up minimum for every patient.¹⁹

Improvement by at least one AIS grade was considered as the primary endpoint to assess

neurological recovery. An improvement by at least 2 AIS grade²⁰ and by at least 2 neurological

levels of injury (NLI) improvement were considered as secondary outcomes.

Parameters influencing the neurological recovery consisted in a reduced number of 4

independent variables recognized as potential predictors of recovery following TSCI.^{5-7, 21-23}

2.2.2. Predictor variables

Age was considered as a continuous variable. Timing of surgery was defined as the interval of time

between the trauma and beginning of surgery and was also considered as a continuous variable. Parameters influencing the neurological recovery consisted in a reduced number of 4

independent variables recognized as potential predictors of recovery following TSCI.^{5-7, 21-23}

was considered as a continuous variable. Timing of surgery was defined as the interval of time

between the trauma and beginning of surgery and was also considered as a continuous variable

The energy of the trauma was considered as low (trivial trauma, fall from standing or walking, assault, etc) or high (motor-vehicle/motorcycle accident, pedestrian hit by vehicle, fall from more than 10ft, etc.). Finally, the initial AIS grade was used to assess the severity of injury for every patient at admission.

2.3. Statistical analysis

Statistical analyses were performed using the classification and regression tree (CART) analysis engine of the Salford Predictive Modeler (SPM) software (Version 8, Salford Systems, San Diego, CA, USA). The classification trees were constructed using the Gini splitting rule. A stopping rule was used to prevent the algorithm from creating subgroups of 5 patients or less. Overfitting was monitored by choosing the tree exhibiting the minimum relative cost value computed by the software. Trees were then pruned to prevent splitting rules based on the surgical timing from appearing more than once.

The relative importance of each predictor was computed for the three dependent variables (one AIS grade improvement; two or more AIS grade improvement; two or more NLI improvement). Variable importance reflects the relative influence of each predictor on the endpoint. The most important predictor during tree construction was assigned with a score of 100 and the other predictors were scaled down proportionally to their importance. The classification and regression tree analysis engine of the Salford Predictive Modeler software identifies surrogate splitter, as close approximations of the primary splitters appearing in the trees.²⁴ Surrogates splitter are used by the algorithm to handle eventual missing data and are taken into account when computing the variable importance.

Continuous data were reported as median and interquartile range (IQR) while categorical data were reported as percentages. Chi-square tests were used to assess whether the proportion of patients who improved neurologically was statistically different from the proportion of patients who did not improve as determined following the split based on the surgical timing. The significance level was set at $p < 0.05$.

3. Results

Table 1 presents the distribution of the 4 independent variables (input parameters) and 3 endpoints across the population considered in this study. One or more AIS grade improvement was observed in 57% of patients while 40% of patients improved by 2 AIS grades or more. Neurological level of injury improved by at least 2 levels in 17% of patients at follow-up. The median age (IQR) at admission was 43 (30-60) years old and the median surgical timing was 19h (13h-28h). High velocity traumas occurred in 30% of the cases. AIS grade at admission was A in 71% of the cases and B in the remaining 29%. The most frequent surgical delay ranges from 15 to 20 hours in our cohort, as shown in Figure 1.

Table 1 Around here

Figure 1 shows the distribution of the surgical timing across the population enrolled in the study. The most frequent timing observed ranges between 15 and 20 hours.

Figure 1 around here

Figure 2 presents the classification tree obtained considering one AIS grade improvement as the dependent variable. 57% of the complete dataset showed improvement of at least one AIS grade. This group was splitted based on the surgical delay with a cut off value of 19 hours. 75% of the patients that had surgery within 18.9 hours post-trauma improved by at least one AIS grade, forming the first terminal node. On the other hand, only 41 % of the patients that had surgery later than 18.9 h post-trauma improved by at least one AIS grade. This group was then divided based on the AIS grade at admission, where 67% of AIS B patients improved at least one AIS grade, as compared to 23% of AIS A patients. The surgical timing split the complete dataset into two groups showing significantly different proportions of patient that improved at least one AIS grade according to Chi-square test ($p=0.026$).

The surgical delay was found to be the parameter influencing the most the probability of AIS grade improvement, followed in order of importance by the initial AIS grade, energy of injury and age (as showed as the “importance of variable” box below).

Figure 2 around here

Figure 3 shows the classification tree obtained considering a neurological improvement of at least 2 AIS grades as the dependant variable. 40 % of the complete dataset of 42 patients improved 2 AIS grades or more. This group was divided based on the energy associated with the injury. Patients sustaining a high energy injury formed a terminal node in which 14 % of them improved 2 AIS grades of more. 54 % of the patients sustaining a low energy injury improved 2 AIS grades or more. The group of patients associated with low energy injury was then split based on the surgical timing, where 67 % of patients who had surgery within 18 hours post-trauma

improved by at least two AIS grades. This proportion dropped to 38% for surgical timings longer than 18 hours. The subgroups created following the split based on the surgical timing were significantly different ($p = 0.038$). Energy of injury was the most important variable followed by surgical timing and age. The AIS grade at admission had no influence on whether patients improved by 2 AIS grades or more.

Figure 3 around here

Figure 4 shows the influence of the surgical timing on the improvement of at least two NLI. 17 % of the complete dataset showed improvement of 2 NLI at follow-up. 30% of patients that had surgery within 20 hours post-trauma gained at least 2 NLI, while none that had surgery later than 20 hours post-trauma improved by at least 2 NLI. The two subgroups created following the split were significantly different ($p=0.016$). Surgical timing was the most important parameter in this tree. The other parameters had almost no influence on the proportion of patients gaining 2 NLI or more.

Figure 4 around here

4. Discussion

This study proposes the use of classification tree algorithms to assess the effect of surgical timing on neurological recovery and to justify a threshold value defining the concept of early surgical intervention frequently described in the literature. This study is the first to determine specifically a surgical timing leading to better outcomes for a particular subgroup of patients.

The delay prior to surgery influenced significantly neurological recovery in terms of AIS grade and NLI improvement. According to the results obtained in this study, a surgical intervention within 19 hours post-trauma improves the likelihood of neurological recovery for patients sustaining complete motor TSCI at the cervical level. A cut-off value approximating 19 hours was observed for all three outcomes, confirming the relevance of this observation. Our 19-hour surgical delay is in good agreement with previously published studies showing that an early surgical intervention improves the neurological recovery^{15, 25-27}. For instance, Umerani et al. (2014)²⁷ reported a mean surgical delay of 18h, which was associated to a greater proportion of patients improving by at least 2 AIS grades as compared to patients operated on average 53h post-SCI. These results are also similar to what was shown by Fehlings et al. (2012)¹⁵, where tetraplegic patients operated on average 14h post-SCI improved of at least 2 AIS grades in a greater proportion than who had later surgery. The value of 19 hours is also clinically relevant as it is a realistic target for health care workers considering all the factors contributing to a longer delay prior to surgery^{17, 18}.

The optimal surgical timing varied from 18 to 20 hours post-injury depending on the outcome measure considered. This observation shows that the optimal surgical timing depends on the outcome considered which might explain the large spread of early surgical timing values found in the literature^{10, 28}. The optimal surgical timing must therefore be defined considering the

250 severity of the SCI (complete or incomplete SCI), the neurological outcome considered, as well
 251 as the neurological level of injury.

252 The analysis presented in this communication considered age, AIS grade at admission, energy of
 253 the trauma and surgical timing as parameters potentially influencing the neurological recovery.
 254 A recent systematic review identifying factors associated to neurological outcome, Yousefifard
 255 et al. (2017)⁸ reported that many clinical, neurological and demographic characteristics can be
 256 used to assess the potential of recovery. Among the most common, younger age, less severe AIS
 257 grades at admission as well as lower velocity of trauma are considered by several studies among
 258 the most important factors influencing the neurological recovery following TSCI. In our study,
 259 the surgical timing was found to be one of the most important parameter affecting the 3
 260 outcome measures, showing that the neurological recovery can be strongly influenced by one of
 261 the only modifiable parameters in the acute treatment of TSCI.

262

263 It is worth noting that the proportion of patients who improved by one or at least two AIS
 264 grades, respectively 57% and 40%, might seem high as compared to previously published data^{13,}
 265 ^{15, 29, 30} Several hypotheses can be raised to explain this result. Patients with sensory incomplete
 266 tetraplegia (AIS B) have a better prognosis for neurological recovery (31). Although the majority
 267 of our cohort had a complete AIS A and that this factor did not come out as a predictor in the
 268 CART analyses, it can not be ruled out. Kirshblum SC et al (1998)³¹ also reported that most
 269 patients who had an AIS A injury, as assessed within 72h of trauma, and who improved by more
 270 than one AIS grade also sustained head injuries involving cognitive impairments, and were thus
 271 incorrectly diagnosed as AIS A. This could also have occurred in the present study, where the

initial AIS grade considered were mainly obtained within 72h post-SCI³¹ which could have lead to an overestimation of the severity of the injury.

Study limitations and recommendations

As shown in Figure 1, most patients had surgery between 15 and 20 hours after the TSCI, with a median of 19 hours. However, the cohort under study still exhibited a large spread of surgical timing ranging from 8 to 250 hours post-trauma, which could have allowed identification of an optimal timing of surgery outside the 15-20 hours range.

This study was performed on a limited number of patients, and further study with a larger sample should be done to reinforce our conclusion. However, our sample size was sufficient to reach our objectives and observe the significant influence of the timing of surgery on our endpoints.

While we performed our study with a limited number of predictors, we recognize that other parameters can also influence neurological recovery, and should be included in future studies involving a larger cohort of patients.

5. Conclusion

Surgical timing following TSCI has been thoroughly studied as it is related to a main treatment strategy (spine surgery) during the acute care of TSCI, and represents one of the infrequent modifiable parameters of the acute care hospitalization. The use of classification tree analysis was proposed to assess the influence of surgical timing on the neurological recovery in patients sustaining cervical motor-complete TSCI and to justify an optimal surgical timing leading to better neurological outcome. A surgical intervention performed within 19 hours post injury was

associated with significant improvement in neurological recovery. This study is the first to define a surgical timing value optimized for a specific subgroup of patients. The methodology described in this communication could be applied to a larger cohort involving patients with different severity and levels of TSCI.

6. Acknowledgment

This work was supported by the U.S. Army Medical Research and Material Command and by the Rick Hansen Institute.

7. Conflict of interest

The authors have no conflict of interest related to the work presented in this study.

8. References

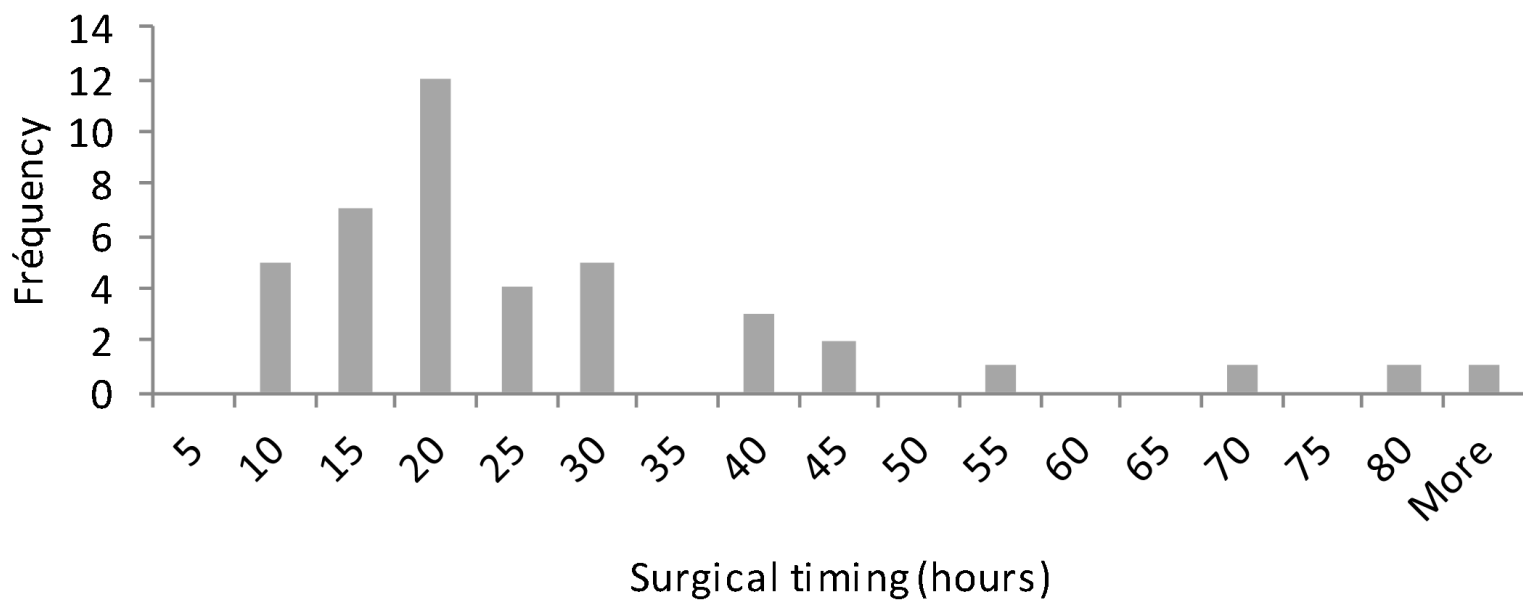
1. Singh A, Tetreault L, Kalsi-Ryan S, Nouri A, Fehlings MG. Global prevalence and incidence of traumatic spinal cord injury. *Clin. Epidemiol.* 2014;6:309-31.
2. Steeves JD, Lammertse D, Curt A, Fawcett JW, Tuszynski MH, Ditunno JF, et al. Guidelines for the conduct of clinical trials for spinal cord Guidelines injury (SCI) as developed by the ICCP panel: clinical trial outcome measures. *Spinal cord.* 2007;45.
3. Anderson KD. Targeting recovery: priorities of the spinal cord-injured population. *J. Neurotrauma.* 2004;21(10):1371-83.

- 314 4. Ditunno JF, Jr., Burns AS, Marino RJ. Neurological and functional capacity outcome
315 measures: essential to spinal cord injury clinical trials. *J. Rehabil. Res. Dev.* 2005;42(3 Suppl
316 1):35-41.
- 317 5. Pollard ME, Apple DF. Factors associated with improved neurological outcomes in
318 patients with incomplete tetraplegia. *Spine.* 2003;28.
- 319 6. Scivoletto G, Morganti B, Ditunno P, Ditunno JF, Molinari M. Effects of age on spinal cord
320 lesion patients rehabilitation. *Spinal cord.* 2003;41.
- 321 7. Scivoletto G, Morganti B, Molinari M. Neurologic recovery of spinal cord injury patients
322 in Italy. *Arch Phys Med Rehabil.* 2004;85(3):485-9.
- 323 8. Wilson JR, Cadotte DW, Fehlings MG. Clinical predictors of neurological outcome,
324 functional status, and survival after traumatic spinal cord injury: a systematic review. *J.*
325 *Neurosurg. Spine.* 2012;17(1 Suppl):11-26.
- 326 9. Yousefifard M, Rahimi-Movaghar V, Baikpour M, Ghelichkhani P, Hosseini M, Jafari A, et
327 al. Early versus late spinal decompression surgery in treatment of traumatic spinal cord injuries;
328 a systematic review and meta-analysis. *Emerg (Tehran).* 2017;5(1):e37.
- 329 10. El Tecle NE, Dahdaleh NS, Hitchon PW. Timing of Surgery in Spinal Cord Injury. *Spine.*
330 2016;41(16):E995-E1004.
- 331 11. Boakye M, Arrigo RT, Gephart MGH, Zygorakis CC, Lad S. Retrospective, Propensity
332 Score-Matched Cohort Study Examining Timing of Fracture Fixation for Traumatic
333 Thoracolumbar Fractures. *J. Neurotrauma.* 2012;29(12):2220-5.
- 334 12. Bourassa-Moreau E, Mac-Thiong JM, Feldman DE, Thompson C, Parent S. Non-
335 neurological outcomes after complete traumatic spinal cord injury: the impact of surgical timing.
336 *J. Neurotrauma.* 2013;30(18):1596-601.

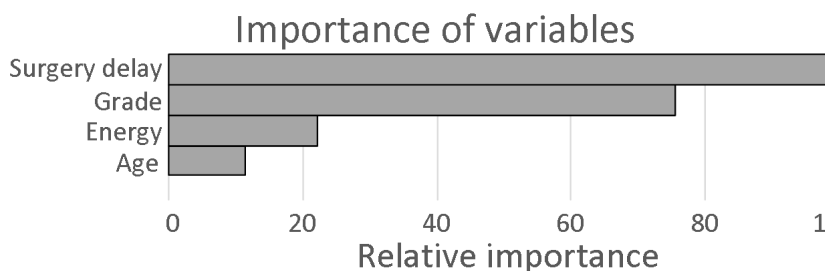
- 337 13. Bourassa-Moreau E, Mac-Thiong JM, Li A, Ehrmann Feldman D, Gagnon DH, Thompson
338 C, et al. Do Patients with Complete Spinal Cord Injury Benefit from Early Surgical
339 Decompression? Analysis of Neurological Improvement in a Prospective Cohort Study. *J.*
340 *Neurotrauma*. 2016;33(3):301-6.
- 341 14. Burke JF, Yue JK, Ngwenya LB, Winkler EA, Talbott J, Pan J, et al. 182 Ultra-Early (<12
342 Hours) Decompression Improves Recovery After Spinal Cord Injury Compared to Early (12-24
343 Hours) Decompression. *Neurosurgery*. 2016;63(CN_suppl_1):172-.
- 344 15. Fehlings MG, Vaccaro A, Wilson JR, Singh A, W. Cadotte D, Harrop JS, et al. Early versus
345 Delayed Decompression for Traumatic Cervical Spinal Cord Injury: Results of the Surgical Timing
346 in Acute Spinal Cord Injury Study (STASCIS). *PLOS ONE*. 2012;7(2):e32037.
- 347 16. Jug M, Kejzar N, Vesel M, Al Mawed S, Dobravec M, Herman S, et al. Neurological
348 Recovery after Traumatic Cervical Spinal Cord Injury Is Superior if Surgical Decompression and
349 Instrumented Fusion Are Performed within 8 Hours versus 8 to 24 Hours after Injury: A Single
350 Center Experience. *J. Neurotrauma*. 2015;32(18):1385-92.
- 351 17. Thompson C, Feldman DE, Mac-Thiong JM. Surgical management of patients following
352 traumatic spinal cord injury: identifying barriers to early surgery in a specialized spinal cord
353 injury center. *J. Spinal. Cord. Med*. 2016:1-7.
- 354 18. Furlan JC, Tung K, Fehlings MG. Process benchmarking appraisal of surgical
355 decompression of spinal cord following traumatic cervical spinal cord injury: opportunities to
356 reduce delays in surgical management. *J. Neurotrauma*. 2013;30(6):487-91.
- 357 19. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, et al.
358 International standards for neurological classification of spinal cord injury (Revised 2011). *J.*
359 *Spinal Cord Med*. 2011;34(6):535-46.

- 360 20. Park JH, Kim JH, Roh SW, Rhim SC, Jeon SR. Prognostic factor analysis after surgical
 361 decompression and stabilization for cervical spinal-cord injury. *Br. J. Neurosurg.* 2017;31(2):194-
 362 8.
- 363 21. Abdul-Sattar AB. Predictors of functional outcome in patients with traumatic spinal cord
 364 injury after inpatient rehabilitation: in Saudi Arabia. *NeuroRehabilitation.* 2014;35(2):341-7.
- 365 22. Richard-Denis A, Feldman D, Thompson C, Mac-Thiong JM. Prediction of functional
 366 recovery six months following traumatic spinal cord injury during acute care hospitalization. *J*
 367 *Spinal Cord Med.* 2017:1-9.
- 368 23. Wilson JR, Grossman RG, Frankowski RF, Kiss A, Davis AM, Kulkarni AV, et al. A Clinical
 369 Prediction Model for Long-Term Functional Outcome after Traumatic Spinal Cord Injury Based
 370 on Acute Clinical and Imaging Factors. *J. Neurotrauma.* 2012;29(13):2263-71.
- 371 24. Breiman L, Friedman J, Stone CJ, Olshen RA. Classification and regression trees: CRC
 372 press; 1984.
- 373 25. Mirza SK, Krengel WFI, Chapman JR, Anderson PA, Bailey JC, Grady MS, et al. Early
 374 Versus Delayed Surgery for Acute Cervical Spinal Cord Injury. *Clin. Orthop Relat. Res.*
 375 1999;359:104-14.
- 376 26. Papadopoulos SM, Selden NR, Quint DJ, Patel N, Gillespie B, Grube S. Immediate spinal
 377 cord decompression for cervical spinal cord injury: feasibility and outcome. *J Trauma.*
 378 2002;52(2):323-32.
- 379 27. Umerani MS, Abbas A, Sharif S. Clinical Outcome in Patients with Early versus Delayed
 380 Decompression in Cervical Spine Trauma. *Asian Spine J.* 2014;8(4):427-34.
- 381 28. Piazza M, Schuster J. Timing of Surgery After Spinal Cord Injury. *Neurosurg. Clin. N. Am.*
 382 2017;28(1):31-9.

- 383 29. Marino RJ, Ditunno JF, Jr., Donovan WH, Maynard F, Jr. Neurologic recovery after
 384 traumatic spinal cord injury: data from the Model Spinal Cord Injury Systems. *Arch. Phys. Med.*
 385 *Rehabil.* 1999;80(11):1391-6.
- 386 30. Fawcett JW, Curt A, Steeves JD, Coleman WP, Tuszynski MH, Lammertse D, et al.
 387 Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel:
 388 spontaneous recovery after spinal cord injury and statistical power needed for therapeutic
 389 clinical trials. *Spinal cord.* 2007;45(3):190-205.
- 390 31. Kirshblum SC, O'Connor KC. Predicting neurologic recovery in traumatic cervical spinal
 391 cord injury. *Arch. Phys. Med. Rehabil.* 1998;79(11):1456-66.
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- 397 9. Figure and table legends
- 398 Table 1 Input parameters and outcomes considered in this study
- 399 Figure 1 Distribution of surgical timing across the cohort
- 400 Figure 2 Classification tree describing the influence of the 4 parameters under study on the one
 401 AIS grade neurological improvement
- 402 Figure 3 Classification tree describing the influence of the 4 parameters under study on at least
 403 2 AIS grades neurological improvement
- 404 Figure 4 Classification tree describing the influence of the 4 parameters under study on the gain
 405 of at least two neurological level of injury
- 406
 407
 408



Complete dataset
N=42
Grade improve :
Yes : 57%
No : 43 %



SX Delay

SX Delay < 19 h
N=20
Grade improve
Yes 75 %
No : 25 %

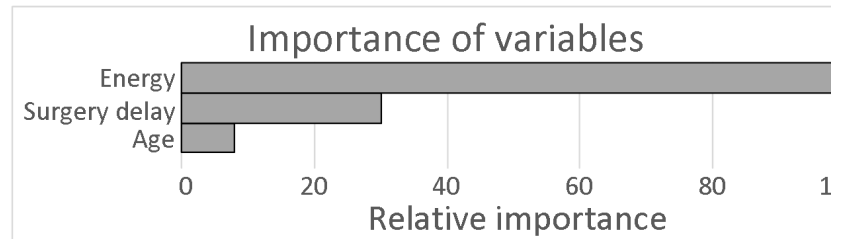
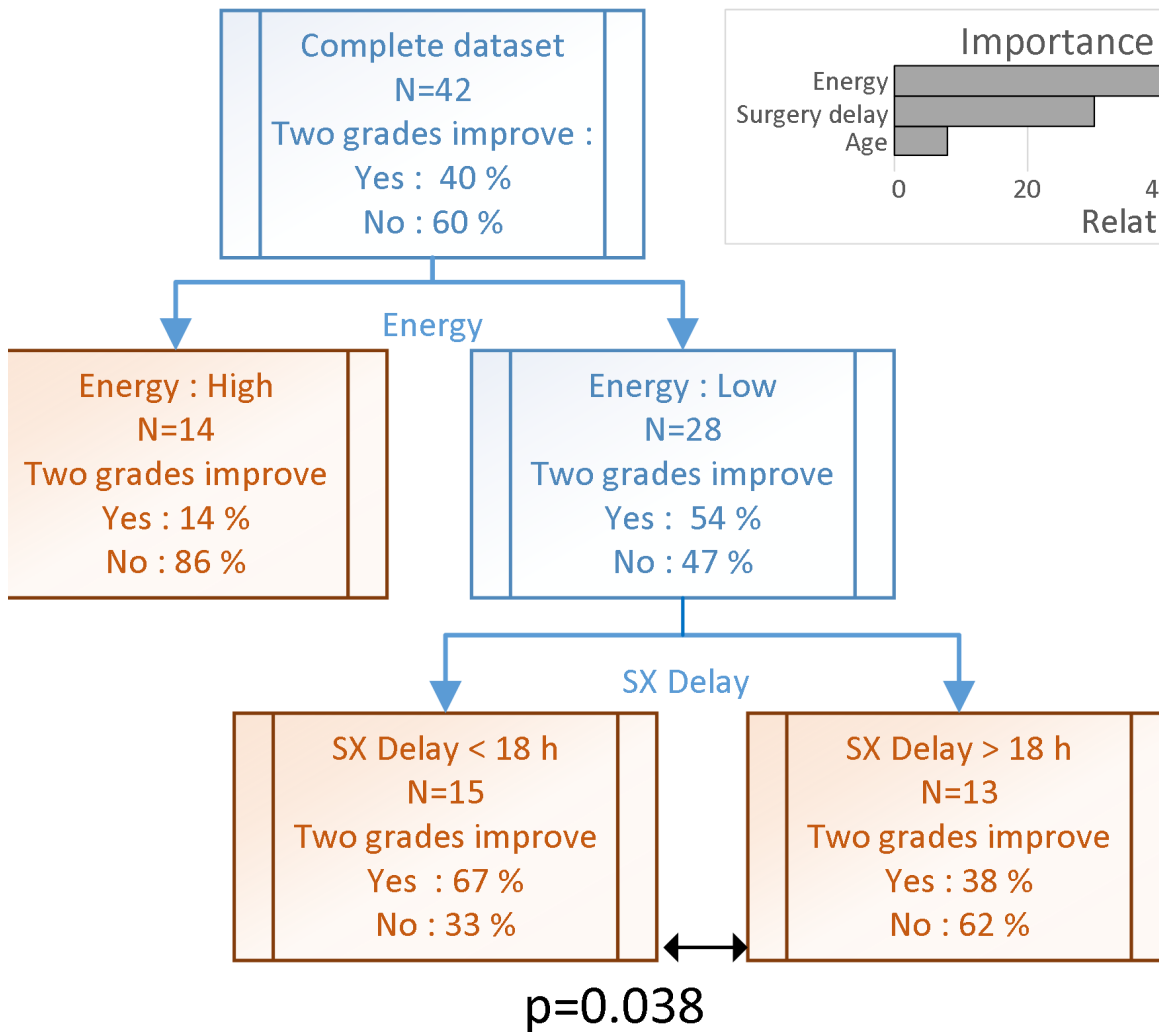
SX Delay > 19 h
N=22
Grade improve
Yes : 41 %
No : 59 %

$p=0.0257$

AIS GRADE

Grade A
N=13
Grade improve
Yes : 23 %
No : 77 %

Grade B
N=9
Grade improve
Yes : 67 %
No : 33 %



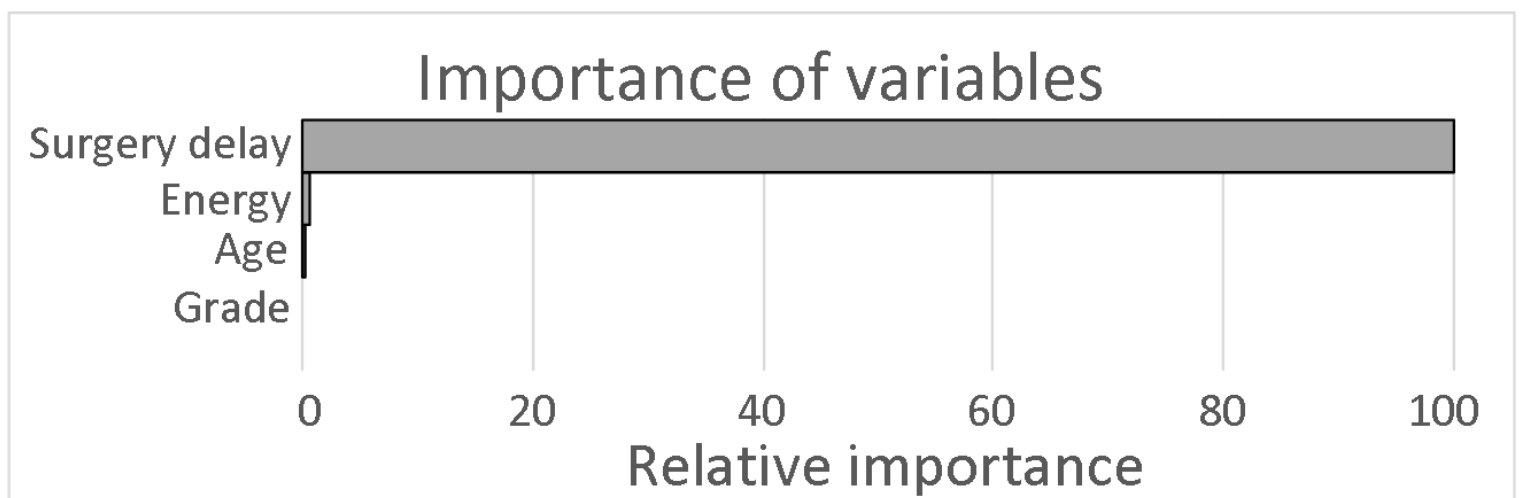
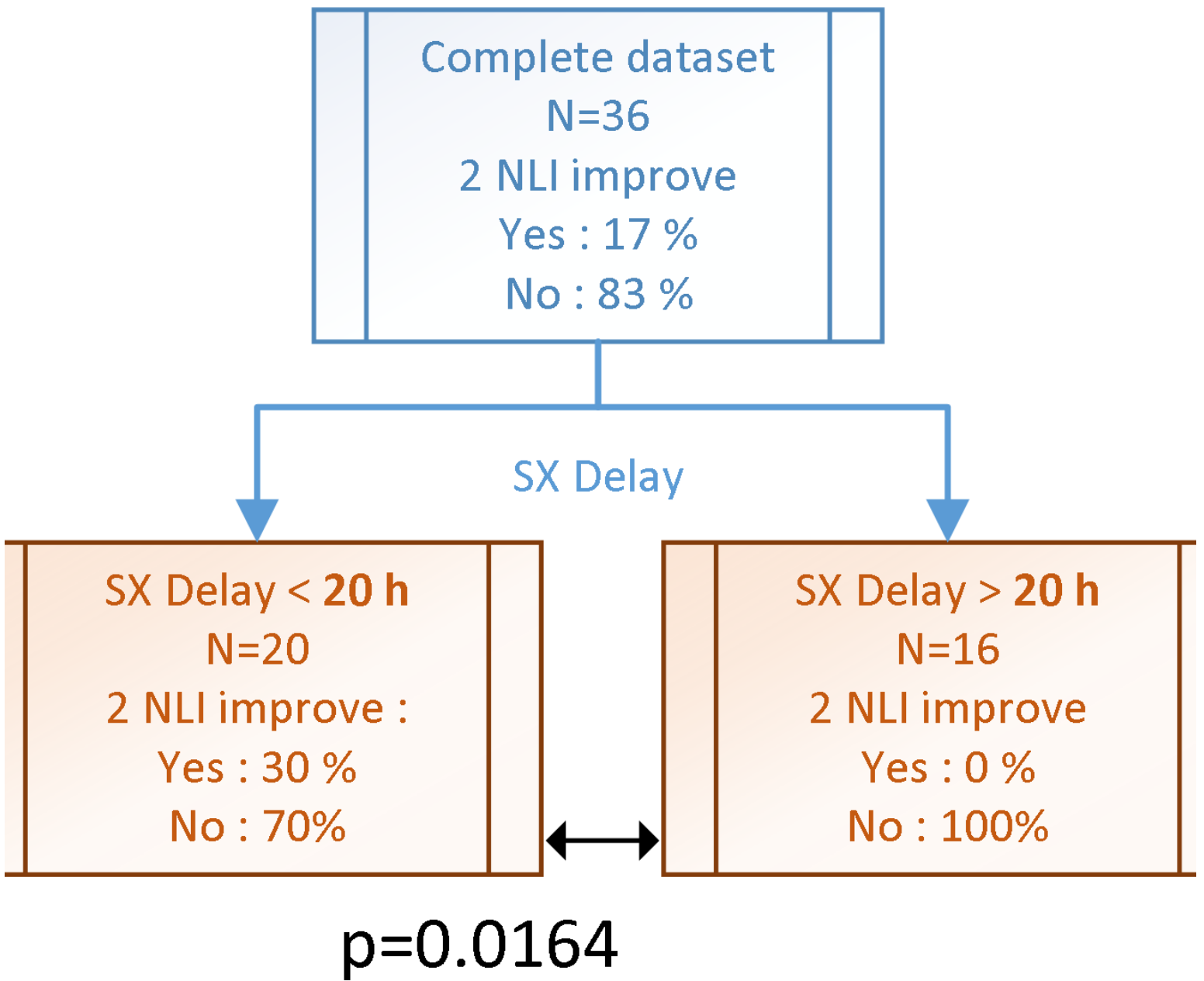


Table 1 Input parameters and outcomes considered in this study

<u>Outcome measures</u>		
1 or more AIS Grade improvement		57%
2 or more AIS Grades improvement		40%
2 or more NLI improvement		17%
<u>Input parameters</u>	-	
Age (years)	Median (IQR)	43(30-61)
Delay from injury to surgical incision (hours)	Median (IQR)	19(13-28)
Energy associated with the injury	High	30%
	Low	70%
ASIA Impairment Scale (AIS)	AIS A	71%
	AIS B	29%

17. Appendix 9: Manuscript published in Archives of Physical Medicine and Rehabilitation

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of Physical Medicine and Rehabilitation
Manuscript Draft

Manuscript Number:

Title: Relationships between Specific Functional Abilities and Health-Related Quality of Life in Chronic Spinal Cord Injury

Article Type: Original Research

Keywords: Spinal cord injury; Health-related quality of life; Functional abilities

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Abstract: Objective: To assess which specific functional abilities are most important in the health-related quality of life (HRQoL) of patients in the chronic phase of traumatic spinal cord injury (TSCI).

Design: Cross-sectional study

Participants: A prospective cohort of 195 patients that had sustained a TSCI from C1 to L1, and consecutively admitted to a single Level 1 SCI-specialized trauma center between 2010 and 2016 was studied

Interventions: none

Main outcome measures: The 3rd version of the Spinal Cord Injury Measure (SCIM-III) and Short-Form 36 version 2 (SF-36v2) questionnaires were administered concurrently during routine follow-up visit between 6 to 12 months after the trauma. Correlation coefficients were calculated between SCIM-III scores (total, subgroups and individual items scores), and SF-36v2 summary scores (Physical component score, PCS; Mental component score, MCS). All analyses were repeated separately for subjects with tetraplegia and paraplegia

Results: The total SCIM-III score correlated moderately with the PCS in the entire cohort, correlated strongly with PCS in tetraplegics and did not correlate with PCS in paraplegics. Mobility subgroup and individual items scores showed the strongest correlations with the PCS in the entire cohort as well as in tetraplegic patients, followed by self-care and sphincter management. Correlations between SCIM-III scores and MCS for all patients were negligible.

Conclusion: This is the first study to objectively evaluate the relative importance of specific functional abilities in the HRQoL in TSCI patients. This work is significant because it determines which specific functional abilities are mostly related to HRQoL, and highlights the differences between tetraplegic and paraplegic patients, such findings

that could help clinicians to guide the patient's treatment and rehabilitation plan.

Relationships between Specific Functional Abilities and Health-Related Quality of Life in Chronic Spinal Cord Injury

Declaration of interest:

None to declare.

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Relationships between Specific Functional Abilities and Health-Related Quality of Life in Chronic Spinal Cord Injury

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Key words: Spinal cord injury; Health-related quality of life; Functional abilities;

Abbreviations: AIS, American Spinal Injury Association impairment scale; MCS, mental component score; NLI, neurological level of injury; PCS, physical component score; HRQoL, health-related quality of life; QoL, quality of life; SCI, spinal cord injury; SCIM-III, spinal cord independence measure version 3; SF-36v2, Short Form 36 version 2; TSCI, traumatic spinal cord injury;

Introduction

Traumatic spinal cord injury (TSCI) is a debilitating condition that creates a plethora of challenges to the patient, their support system, as well as to society. It implies many different levels of long-term disability, which require significant adaptation as people with spinal cord injury often see their life change substantially after the trauma. It involves considerable costs and effort from all parties involved¹. In order to adequately measure improvements in care regarding life satisfaction in this population, there has been much interest towards quality of life (QoL) research in the recent years^{2,3}. Health-related quality of life (HRQoL) is considered a useful tool in TSCI research as it encompasses many dimensions focusing on health that are important to consider when evaluating progress and responses to interventions⁴.

In addition, there are still controversies regarding long-term priorities of patients with a TSCI. Simpson et al.⁵ suggested in a systematic review that the two health priorities cited as most important by patients were motor function and bowel/bladder function, while Lo et al.⁶ found that arm function, bowel/bladder function and walking were most important. Similarly, Manns et al.⁷ observed that physical function and independence were highly associated with the QoL of patients. Although these studies emphasized on understanding which general life domains are prioritized by patients, they mainly rely on a subjective assessment of patients.

Alternatively, other authors have assessed the impact of function impairment using validated objective measures of function, on QoL or health/life satisfaction. Accordingly, different authors have observed positive associations with the motor subscale of the Functional Independence Measure (mFIM)⁸⁻¹¹, FIM total score¹², Barthel Index¹³, and total score of the 3rd version of the Spinal Cord Independence Measure (SCIM-III)^{1,14}. Unfortunately, these studies did not look into which specific functional abilities would be mostly related to patient's QoL, despite the use of validated questionnaires involving multiple items specifically assessing multiple aspects of the functional status. Further analysis in this direction would be significant as it would guide clinicians to better elaborate patient's treatment and rehabilitation plan.

Therefore, this study aims at objectively exploring the relationships between specific functional abilities for performing activities of daily living independently, based on the SCIM-III questionnaire, and HRQoL as assessed by the Short Form 36 version 2 (SF-36v2) following a TSCI.

Material and Methods

Patients

A prospective cohort of 195 patients sustaining a TSCI and consecutively admitted to a single Level 1 SCI-specialized trauma centre between April 2010 and September 2016 was studied. All patients were recruited on a voluntary basis at time of admission and were followed after discharge from the trauma centre. They were included if they sustained an acute TSCI with a neurological level of injury between C1 and L1 that

required surgical management in our institution. They were included if aged 17 years or older and presented to the follow-up visit between 6 and 12 months post-injury.

Exclusion criteria were 1) penetrating trauma causing the spinal cord injury, and 2) absent or incomplete functional and QoL assessment between 6 and 12 months after the injury. The study was approved by the institutional review board.

Data collection:

Socio-demographic and clinical data were retrieved from our institution's SCI prospective database in order to describe the total cohort of patients. Collected data are shown in Table 1 and included age, sex, initial grade of severity of neurological deficits, neurological level of injury (tetraplegia from C1 to C8; paraplegia from T1 to L1), mechanism of injury (sports; fall; motor vehicle accident; other), trauma severity (measured by the Injury Severity Score - ISS), surgical delay between trauma and surgery (dichotomized as < 24h or > 24 h post-trauma), presence of concomitant traumatic brain injury, length of stay in acute care facility and discharge destination after acute care (home, intensive functional rehabilitation or other). The neurological examination was performed according to the International Standards for neurological classification of spinal cord injury¹⁵, in order to determine the American Spinal Injury Association impairment scale grade (AIS) and the neurological level of injury (NLI).

Functional status and HRQoL questionnaires were administered at the same moment during routine follow-up visit between 6 to 12 months after the trauma. Functional status was assessed by the SCIM-III that evaluates level of independence in 19 different items

related to activities of daily living (Table 2). The 19 items are separated in three areas of function: self-care (feeding, grooming, bathing and dressing; sub-score from 0 to 20), respiration and sphincter management (sub-score from 0 to 40) and mobility (bed and transfers, indoor/outdoor ambulation; sub-score from 0 to 40). The total SCIM-III score can reach 100, where higher scores correspond to higher levels of independence. The SCIM-III is a valid and reliable questionnaire that showed higher specificity with regards to TSCI¹⁶.

HRQoL was assessed by the SF-36v2 questionnaire which reliability and validity has also been demonstrated in the TSCI population¹⁷. The SF-36v2 consists of 36 items assessing eight distinct health domains: 1) physical functioning; 2) role physical; 3) body pain; 4) general health; 5) vitality; 6) social functioning; 7) role emotional and 8) mental health¹⁸. The physical component score (PCS) and the mental component score (MCS) derived from the weighted eight health domains were calculated for all patients included in the analysis. These summary scores have been widely used in the past to assess the HRQoL of TSCI patients².

Statistical analysis

Descriptive statistics were used to outline the characteristics of the population.

Continuous data were described using means and standard deviations, while percentages and proportions were used for categorical data. The relationship between the functional performance and QoL scores was assessed using Spearman's rank-order correlations analyses. More specifically, correlations were performed between the SF-36v2

component scores (PCS and MCS) and: 1) the SCIM-III total score; 2) the SCIM-III sub-scores (self-care; respiration and sphincter management; mobility and transfers); 3) each of the SCIM-III 19 single items for the total cohort of patients. Results were reported using the Spearman's Rho coefficient and corresponding p value. As a second step, all analyses were repeated separately for subjects with tetraplegia and paraplegia. All statistical analyses were performed using the IBM SPSS Statistics 21 software (Chicago, IL). The level of statistical significance was set at an alpha of 0.05. Statistically significant correlation coefficients were considered clinically large if greater than 0.5, moderate if greater than 0.3, and small if greater than 0.1, according to suggestions from Cohen et al.^{19,20}

Results

Patients socio-demographic and clinical characteristics are showed in Table 1. Sixty-five percent of the cohort sustained tetraplegia. Results from the correlation studies between SCIM-III sub-scores and total score, and the QoL (SF-36v2 component scores) are shown in Table 3. Results from the correlations between and individual SCIM-III items and SF-36v2 component scores are shown in Table 4.

Considering the complete cohort, significant moderate positive correlations were found between PCS and mobility, total SCIM-III score, and self-care. While the mobility sub-score was most importantly correlated to PCS, the correlation with respiration / sphincter management sub-score was significant but small. MCS was negatively correlated with

SCIM-III sub-scores and total score, but correlation coefficients were small although significant (Table 3).

Similar trends were observed between SCIM-III scores (total and sub-scores) and PCS and MCS when analysing separately tetraplegic patients (Table 3, 4). Moreover, all correlation coefficients increased while reaching a large correlation between mobility and PCS. However, there was no significant correlation for paraplegic patients between the self-care and respiratory / sphincter management sub-scores and PCS, while only a significant moderate correlation was found between the mobility sub-score and PCS.

When correlating individual SCIM-III items with PCS and MCS, all individual items (except item 5 – respiration) were significantly correlated to the PCS in the total cohort, particularly for items 14-12-13 (mobility outdoors-indoors-moderate distances). Large correlation coefficients were obtained with respect to items 14 (mobility outdoors) and 12 (mobility indoors), while other significant correlations were moderate (Table 3). In accordance with correlations found between SCIM-III sub-scores and PCS, the strength of correlation was largest for items related to mobility, followed by items for self-care and by items for respiration and sphincter management. In general, individual SCIM-III items were not correlated with MCS, although small significant correlation coefficients were observed inconsistently (Table 4).

In the tetraplegic group, mobility indoors (item 12), mobility for moderate distances (item 13), mobility outdoors (item 14) and stair management (item 15) were largely correlated

with PCS. All other items (except item 5) showed moderate correlation coefficients, but these coefficients were closer to the cut-off value used to detect large correlations^{19,20}, when compared to the results for the total cohort. Similarly to the total cohort, correlation coefficients were largest for items related to mobility, followed by items for self-care and respiration / sphincter management for individuals with tetraplegia.

In the paraplegic subgroup, moderate significant correlations with PCS were found for lower body bathing (item 2B), mobility indoors (item 12), mobility for moderate distances (item 13), mobility outdoors (item 14) and stair management (item 15).

Discussion

This is the first study that evaluates the relationship between specific functional abilities and HRQoL for TSCI patients. While some studies investigated the global functional status with validated tools and their relationship with QoL, this study is unique since it separates items of the widely used and validated SCIM-III questionnaire in order to objectively assess which specific functional ability is primarily correlated to QoL. It establishes an order of significance for different abilities according to patient's perceived QoL measured in a precise point in time in the chronic phase of SCI.

Our results on the association between total SCIM-III score and HRQoL are in line with previous studies. In particular, Tramonti et al.¹⁴ found a large significant correlation ($r = 0.72$, $p < 0.001$) between the total SCIM-III score and the physical functioning (PF)

subscale of the SF-36v2 for 40 patients with SCI injury, 45 % of which were caused by trauma. Based on a larger cohort including 197 patients with both paraplegic and tetraplegic patients, we further confirmed the findings of Tramonti et al.¹⁴ Accordingly, in a post-hoc sub-analysis, we found that the total SCIM-III score correlated strongly with PF ($Rho = 0.741$, $p < 0.001$ in all patients, $Rho = 0.780$, $p < 0.001$ in tetraplegic patients and $Rho = 0.618$, $p < 0.001$ in paraplegic patients). Other reports also show findings in accordance to the trend observed in our study. Of the 357 patients surveyed, Mittman et al. studied a cohort of patients with a SCI for which more than 75 % occurred secondary to a traumatic event. They also found a robust relationship between the SCIM-III total score and a HRQoL score. However, in aiming to compare the SCI population with other disability groups, they used the Health Utility Index-Mark III score that has not been validated in SCI adults¹. The other authors that investigated the relationship between function status and QoL relied on functional scores that are not SCI-specific^{8,10-13}. Even though the QoL measures vary from one study to another, their results all show positive association between functional independence and QoL as well. The fact that this finding recurs, regardless of method and compared scores, serves to support our results and adds to the relevance the deeper analysis of the importance of functional status presented in this study.

Our study highlights the relative order of importance for sub-scores and individual items with respect to the HRQoL. PCS was mainly correlated with the mobility sub-score, followed by the self-care sub-score, and by the respiration and sphincter management sub-score. The trend was observed particularly in tetraplegic patients. Mobility was the

only sub-score that correlated with PCS in paraplegic patients, which is consistent with the conclusions of Simpson et al.⁵ regarding the high priority for walking in this population. They nevertheless suggested that arm and hand function was a priority considered more important than mobility for recovery in tetraplegic patients. However, in the two largest survey studies they included in their analysis, there was only one mobility-related question^{21,22}. In contrast, the SCIM-III questionnaire evaluates nine different items related to mobility (Table 4). This discrepancy could account for the differing order of importance between our objective evaluation of functional abilities and assessments from previous subjective survey studies.

It is well recognized that mobility is an important contributor to QoL in SCI population²³. Dependence on others for mobility is known to greatly affect QoL in the chronic SCI setting²⁴. In our study for both tetraplegic and paraplegic patients, mobility on even surface (items 12, 13, 14) was more strongly correlated with PCS than items related to transfers (items 16, 17). This result is in agreement with a previous study suggesting that walking was a top priority, followed by standing, transferring and stair climbing, regardless of level of injury²³. Therefore, our study suggests that higher mobility is better correlated to quality of life than higher arm/hand function for both tetraplegic and paraplegic subjects.

The self-care sub-score may be an important endpoint after a cervical TSCI as activities related to self-care are highly dependent on upper extremity function and hand dexterity⁵. It is therefore not surprising that a large correlation coefficient was observed between

self-care sub-score and PCS. Similarly, the correlations between individual items for self-care and PCS almost reached 0.5.

As suggested by Simpson et al.⁵, bowel and bladder management is usually considered as an important priority, although less important than motor function. However, no correlation was found between respiration/sphincter management sub-score nor individual items and QoL among paraplegic patients in our cohort. Potential explanations could reside in the small variability in paraplegic patients for items 6-7-8 that precludes adequate correlation analysis. In the subgroup of paraplegic patients, 82 % scored $\geq 9 / 15$ on item 6, 59 % scored $\geq 8 / 10$ on item 7 and 94 % scored $\geq 8 / 10$ on item 8. Sphincter dysfunction associated to TSCI remains very disturbing for patients, as it may seriously impact the self-esteem and social activities²⁵. Some studies have also reported cultural variation on the perception of sphincter dysfunction on the quality of life which is also important to consider^{26,27,28}.

Respiratory dysfunction may greatly vary according to the severity and the level of the spinal cord injury. In most severe cases, respiratory insufficiency may lead to permanent mechanical ventilation support³⁰. It is thus not surprising that respiratory dysfunction was previously showed to impact the QoL of SCI patients²⁹. Accordingly, Charlifue et al.³¹ reported better health perception and improved QoL in non-mechanically ventilated patients versus those requiring mechanical ventilation. A recent study by Postma et al.³⁰ showed that more severely impaired respiratory function was associated with lower HRQoL, taking into account Functional Vital Capacity, cough strength, dyspnea and

pulmonary infection burden. On the opposite, the SCIM-III evaluates independence in respiration regardless of such quantitative pulmonary function parameters. No correlation was found between the respiration item and the SF-36v2 summary scores in our cohort. This could be explained by the fact that the great majority of the cohort was completely independent for respiration management, again resulting in a small variability in our cohort which limits the use of correlation studies.

What could be seen as counter-intuitive is the absence of significant correlations between the SCIM and MCS, reflecting the absence of heightened mental health in patients with better function status. This is in agreement with Tramonti et al.¹⁴ who did not find any correlation between the SCIM-III total score and mental health assessed from the SF-36v2. It is also in agreement with previous studies showing the absence of a relationship between QoL mental health summary scores and neurological function^{2,32,33}. These findings suggest that mental health after a TSCI strongly depends on other factors that were not considered in the current study. For example, it is known that many psychological factors influence QoL such as depression³⁴, pain³⁵, locus of control, sense of coherence, hope, purpose in life or feelings of self-worth³⁶. Therefore, in the future, thorough study of the impact of function on MCS should ideally include these factors as potential co-variables.

The current study showed that it is of paramount importance to analyse tetraplegic and paraplegic patients distinctly when evaluating impact of function on QoL, considering the magnitude of difference between the strength of correlation with SCIM sub-scores.

Different priorities for patients lead to distinct goals in the rehabilitation effort. For tetraplegics, mobility indoors, mobility for moderate distances 10-100 meters and stair management are major items helping to determine potential for discharge at home, and mobility outdoors is decisive for patient's ability to participate in the community. Also, feeding and ability to dress, as well as toilet use are significant factors in planning for degree of assistance needed at home or long-term care facilities after discharge from rehabilitation center. In paraplegic patients, considering that the disability primarily involves lower limbs, it was expected to find stronger correlation with bathing lower body than with other self-care items, because such task requires a significant contribution from the lower limbs.

Limitations

Our main limitation is related to the objective questionnaires that were used to assess function and QoL in this study. Although our global objective was to determine specific functional abilities that are related to the QoL, we recognize that our results are limited to the outcome measures that were used (SF-36v2 and SCIM). However, the SCIM-III has proven to be reliable and valid in the TSCI patient population^{16,37}, and useful for post-injury rehabilitation programs³⁸. Its simplicity for patients, use of validated items and ability to establish objective information makes it an ideal functional outcome questionnaire.

In line with the goal of objectively establishing priorities in the TSCI population, we chose to use the SF-36 questionnaire because it has been widely used and therefore

translated for more than 60 countries, which allows for comparison with many other populations¹⁸. Finally, a future study including a higher number of subjects may improve the correlation precision on items exhibiting weak score variability.

Conclusion

This is the first study to objectively evaluate the relative importance of specific functional abilities in TSCI patients. Independence in mobility items are the most important functional abilities related to improved PCS, followed by self-care items and sphincter management. Functional abilities assessed from the SCIM-III were not significantly related to MCS.

References

1. Mittman N, Hitzig S, Craven C. Predicting health preference in chronic spinal cord injury. *J Spinal Cord Med* September 2014;37(5):548–55
2. Leduc BE, Lepage Y. Health-related quality of life after spinal cord injury. *Disabil Rehabil* 2002;24(4):196-202
3. Dijkers MPJM. Quality of life after spinal cord injury: a meta-analysis of the effects of disablement components. *Spinal Cord* 1997;35:829-40
4. Ku HJ. Health-related Quality of Life in Patients with Spinal Cord Injury: Review of the Short Form 36-Health Questionnaire Survey. *Yonsei Medical Journal* 2007;48(3):360-70
5. Simpson E et al. The health and life priorities of individuals with spinal cord injury: A systematic review. *J Neurotrauma* 2012;29(8):1548–55
6. Lo C, Tran Y, Anderson K, Craig A, Middleton J. Functional Priorities in Persons with Spinal Cord Injury: Using Discrete Choice Experiments To Determine Preferences. *J Neurotrauma* 2016;33(21):1958-68
7. Manns PJ et al. Components of quality of life for persons with a quadriplegic and paraplegic spinal cord injury. *Qual Health Res* 2001;11(6):795-811
8. Barker R.N. et al. The relationship between quality of life and disability across the lifespan for people with spinal cord injury. *Spinal Cord* 2009;47:149-55
9. van Koppenhagen et al. Changes and Determinants of Life Satisfaction After Spinal Cord Injury: A Cohort Study in the Netherlands. *Am J Phys Med Rehabil* 2008;89(9):1733-40

10. van Leeuwen CMC, Kraaijeveld S, Lindeman E, Post MWM. Associations between psychological factors and quality of life ratings in persons with spinal cord injury: a systematic review. *Spinal Cord* 2012 ;50 :174–87
11. Rivers CS, Fallah N, Noonan VK, Whitehurst DG, Schwartz C, Finkelstein J, Craven BC, Ethans K, O'Connell C, Truchon C, Ho C, Linassi AG, Short C, Tsai E, Drew B, Ahn H, Dvorak MF, Paquet J, Fehlings MG, Noreau L. The RHSCIR Network, Health conditions: impact on function, health-related quality of life, and life satisfaction following traumatic spinal cord injury: prospective observational registry cohort study. *Archives of physical medicine and rehabilitation*. July 2017; ahead of print
12. Gurcay E, Bal A, Eksioglu E, Cakci A. Quality of Life in Patients with Spinal Cord Injury. *International Journal of Rehabilitation Research* 2010;33:356-8
13. Chang F-H, Wang Y-H, Jang Y, Wang C-W. Factors associated with quality of life among people with spinal cord injury: application of the International Classification of Functioning. Disability and Health Model. *Arch Phys Med Rehabil* 2012;93:2264-70
14. Tramonti F, Gerini A, Stampacchia G. Individualised and health-related quality of life of persons with spinal cord injury. *Spinal Cord* 2014;52:231-35
15. Kirshblum SC et al. Reference for the 2011 revision of the International Standards for Neurological Classification of Spinal Cord Injury. *J Spinal Cord Med* 2011;34(6):547-54

16. Itzkovich M, Catz A et al. The Spinal Cord Independence Measure (SCIM) version III: Reliability and validity in a multi-center international study. *Disability and Rehabilitation* 2007;29(24):1926-33
17. Forchheimer M, McAweeney M, Tate DG. Use of the SF-36 among persons with spinal cord injury. *Am J Phys Med Rehabil* 2004;83(5):390-5
18. Aaronson NK, Acquadro C, Alonso J, Apolone G, Bucquet D, Bullinger M, Bungay K, Fukuhara S, Gandek B, S. Keller S, Razavi D, Sanson-Fisher R, M. Sullivan M, S. Wood-Dauphinee S, A. Wagner S, Ware JE. International quality of life assessment (IQOLA) project. *Quality of Life Research* 1992;1(5):349-51
19. Cohen J, Cohen CP, West SG, Aiken LS. *Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences*. J Royal Stat Soc 2003;52
20. . *Statistical Power Analysis for the Behavioural Sciences*. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988
21. Anderson KD. Targeting recovery: Priorities of the spinal cord-injured population. *J Neurotrauma* 2004;21:1371–83
22. Snoek GJ, IJzerman MJ, Hermens HJ, Maxwell D, Biering-Sorensen F. Survey of the needs of patients with spinal cord injury: impact and priority for improvement in hand function in tetraplegics. *Spinal Cord* 2004;42(9):526-32
23. Brown-Triolo DL, Roach MJ, Nelson K, Triolo RJ. Consumer perspectives on mobility: Implications for neuroprosthesis design. *Journal of Rehabilitation Research and Development* 2002;39(6):659-669

24. Riggins MS et al. The relationship between quality of life and change in mobility 1 year postinjury in individuals with spinal cord injury. *Arch Phys Med Rehabil* 2011;92:1027-33
25. Krogh K, Christensen P, Sabroe S, Laurberg S. Neurogenic bowel dysfunction score. *Spinal Cord* 2006;44:625–31
26. Erdem D, Hava D, Keskinoglu P, Bircan Ç, Peker O, Krogh K, Gülbahar S. Reliability, validity and sensitivity to change of neurogenic bowel dysfunction score in patients with spinal cord injury. *Spinal Cord* 2017; ahead of print
27. Liu CW, Huang CC, Yang YH, Chen SC, Weng MH, Huang Mh. Relationship between neurogenic bowel dysfunction and health-related quality of life in persons with spinal cord injury. *J Rehabil Med* 2009;41:35–40
28. Westgren N, Levi R. Quality of life and traumatic spinal cord injury. *Arch Phys Med Rehabil* 1998;79:1433–9
29. Brown R, DiMarco AF, Hoit JD, Garshick E. Respiratory dysfunction and management in spinal cord injury. *Respiratory care* 2005;51(8):853-70
30. Postma K, Post MWM, Haisma JA, Stam HJ, M P Bergen MP, Bussmann JBJ. Impaired respiratory function and associations with health-related quality of life in people with spinal cord injury. *Spinal Cord* 2016;54:866–71
31. Charlifue S, Apple D, Burns SP, Chen D, Cuthbert JP, Donovan WH, Lammertse DP, Meade MA, Pretz CR. Mechanical ventilation, health, and quality of life following spinal cord injury. *Arch Phys Med Rehabil* 2011;92(3):457-63
32. Abrantes-Pais FN et al. Psychological or physiological. Why are tetraplegic patients content? *Neurology* 2007;69:261-7

33. Ames H et al. Does functional motor incomplete (AIS D) spinal cord injury confer unanticipated challenges? Rehabil Psychol 2017;62(3):401-6
34. Glennie RA, Batke J, Fallah N, Cheng CL, Rivers CS, Noonan VK, Dvorak F, Fisher CG, Kwon BK, Street JT. Journal of Neurotrauma 2017, 34(20): 2877-82
35. Ataoglu E, Tiftik T, Kara M, Tunç H, Ersöz M, S Akkuş S. Effects of chronic pain on quality of life and depression in patients with spinal cord injury. Spinal Cord 2013;51:23–26
36. van Leeuwen C, Post M, van Asbeck F, Bongers-Janssen H, van der Woude L, de Groot S, Lindeman E. Life satisfaction in people with spinal cord injury during the first five years after discharge from inpatient rehabilitation, Disability and Rehabilitation 2012;34(1):76-83
37. Bluvstein V, Catz A et al. SCIM III is reliable and valid in a separate analysis for traumatic spinal cord lesions. Spinal Cord 2011;49:292-6
38. Ackerman P, Morrison SA, McDowel S, Vazquez L. Using the Spinal Cord Independence Measure III to measure functional recovery in a post-acute spinal cord injury program. Spinal Cord 2010;48:380-7

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Table 1. Socio-demographic and clinical characteristics of the cohort of patients with a traumatic spinal cord injury

(HSCM, Hôpital du Sacré-Coeur de Montréal; ISS, Injury Severity Score; LOS, length of stay)

		All patients	Tetraplegic	Paraplegic
N		195	127	68
Age	Mean (SD)	48.8 (18.0)	52.7 (17.7)	41.9 (16.5)
Sex	Male (%)	79.7	78.1	82.4
Initial AIS grade	A (%)	35.6	22.7	60.3
	B (%)	9.6	10.2	7.4
	C (%)	14.2	17.1	8.8
	D (%)	40.6	50.0	23.5
Mechanism of injury	Sports (%)	16.8	16.4	16.2
	Fall (%)	45.2	46.9	42.6
	MVA (%)	27.9	28.1	27.9
	Other (%)	10.1	8.6	13.3
ISS	Mean (SD)	22.9 (8.9)	21.5 (9.1)	25.7 (7.7)
Surgical delay	<24h (%)	46.6	37.6	63.2
Traumatic brain injury	Presence (%)	50.0	56.1	60.3
LOS HSCM	Mean (SD)	25.7 (18.0)	26.7 (19.9)	24.2 (13.7)
Discharge destination	Home (%)	15.7	19.5	8.8
	IFR (%)	77.2	71.9	86.8
	Other (%)	7.1	8.6	4.4

Table 2. SCIM-III items and description

1	Feeding (cutting, opening containers, pouring, bringing food to mouth, holding cup with fluid)
2 A	Bathing Upper body (soaping, washing, drying body and head, manipulating water tap)
2 B	Bathing Lower body (soaping, washing, drying body and head, manipulating water tap)
3 A	Dressing Upper body (clothes, shoes, permanent orthoses; dressing, wearing, undressing)
3 B	Dressing Lower Body (clothes, shoes, permanent orthoses; dressing, wearing, undressing)
4	Grooming (washing hands and face, brushing teeth, combing hair, shaving, applying makeup)
5	Respiration
6	Sphincter Management - Bladder
7	Sphincter Management - Bowel
8	Use of Toilet (perineal hygiene, adjustment of clothes before/after, use of napkins or diapers)
9	Mobility in Bed and Action to Prevent Pressure Sores
10	Transfers: bed-wheelchair (locking wheelchair, lifting footrests, removing and adjusting arm rests, transferring, lifting feet)
11	Transfers: wheelchair-toilet-tub (if uses toilet wheelchair: transfers to and from; if uses regular wheelchair: locking wheelchair, lifting footrests, removing and adjusting armrests, transferring, lifting feet)
12	Mobility Indoors
13	Mobility for Moderate Distances (10-100 meters)
14	Mobility Outdoors (more than 100 meters)
15	Stair Management
16	Transfers: wheelchair-car (approaching car, locking wheelchair, removing arm and footrests, transferring to and from car, bringing wheelchair into and out of car)
17	Transfers: ground-wheelchair

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Table 3. Spearman correlation coefficients between categories of the SCIM-III and the SF-36v2 PCS and MCS scores for patients with a TSCI

** $p < 0.01$

* $p < 0.05$

	SCIM-III Category	PCS	MCS
		rho coefficient	rho coefficient
Total cohort	Self-care	0.421**	-0.114
	Respiration and sphincter management	0.370**	-0.118
	Mobility	0.516**	-0.147*
	Total	0.482**	-0.124
Tetraplegia	Self-care	0.519**	-0.132
	Respiration and sphincter management	0.444**	-0.202*
	Mobility	0.556**	-0.149
	Total	0.541**	-0.154
Paraplegia	Self-care	0.225	-0.052
	Respiration and sphincter management	0.069	0.138
	Mobility	0.397**	-0.161
	Total	0.236	.041

ble

Table 4. Spearman correlation coefficients between individual items of the SCIM-III and the SF-36v2 PCS and MCS scores for the total cohort of patients with a TSCI, and separated based on the presence of tetraplegia or paraplegia.

** p<0.01

* p<0.05

	SCIM-III Item	All Patients		Tetraplegic		Paraplegic	
		PCS	MCS	PCS	MCS	PCS	MCS
		r_s	r_s	r_s	r_s	r_s	r_s
Self-care	1	0.359**	-0.173*	0.489**	-0.200*	0.040	-0.065
	2a	0.388**	-0.143*	0.479**	-0.159	0.205	-0.085
	2b	0.425**	-0.106	0.468**	-0.103	0.369**	-0.123
	3a	0.319**	-0.101	0.472**	-0.139	-0.181	0.206
	3b	0.327**	-0.110	0.475**	-0.160	-0.077	0.072
	4	0.281**	-0.080	0.388**	-0.058	-0.022	-0.106
Respiration and sphincter management	5	0.103	-0.123	0.119	-0.153	---	---
	6	0.326**	-0.121	0.404**	-0.205*	0.063	0.084
	7	0.296**	-0.087	0.400**	-0.211*	0.045	0.137
	8	0.400**	-0.160*	0.479**	-0.209*	0.170	-0.032
Mobility	9	0.307**	-0.117	0.356**	-0.095	0.273*	-0.172
	10	0.331**	-0.158*	0.406**	-0.134	0.159	-0.243*
	11	0.334**	-0.106	0.400**	-0.106	0.181	-0.086
	12	0.502**	-0.170*	0.555**	-0.230**	0.344**	-0.071
	13	0.484**	-0.134	0.513**	-0.146	0.361**	-0.107
	14	0.533**	-0.165*	0.568**	-0.160	0.405**	-0.159
	15	0.476**	-0.106	0.530**	-0.141	0.337**	-0.066
	16	0.356**	-0.203**	0.435**	-0.204*	0.169	-0.177
	17	0.355**	-0.178*	0.464**	-0.209*	0.102	-0.089

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Conflict of interest

The authors declare that they have no conflict of interest.

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Abstract

Study design

Prospective cohort study.

Objectives

To evaluate the relationship between quality of life (QOL) after a traumatic spinal cord injury (TSCI) and acute predictors, with a particular emphasis on the initial severity of the neurological injury. Secondarily, to compare the QOL after a TSCI with the general population.

Setting

A single Level-1 SCI-trauma centre.

Methods

A cohort of 119 individuals admitted after a cervical TSCI between April 2010 and September 2016 was studied. QOL was assessed using the SF-36v2 questionnaire 6–12 months following the injury, and compared to the general population. The relationship between the initial severity of the neurological injury and the SF-36 summary scores was assessed using linear multivariable regression analyses.

Results

Individuals sustaining less severe neurological injury (grade D) exhibited higher PCS than individuals with grades A, B or C injury. Individuals with initial grade A injury showed increased MCS than individuals with incomplete grade B, C or D injury, with 42.9% scoring higher than the general population. The initial grade was significantly associated with chronic PCS and MCS.

Conclusions

The initial severity of the neurological injury after a cervical TSCI may be used to estimate QOL in the subacute period following the injury. Individuals with complete tetraplegia may report good mental QOL despite severe physical impairment. Our findings could help clinicians to determine realistic expectations for patients in terms of QOL, and optimize the rehabilitation plan based on the initial evaluation after a TSCI.

Introduction

Traumatic spinal cord injuries (TSCI) lead to severe neurological deficits and functional limitations [1]. Accurate estimation of the future outcome early after the injury is of utmost importance [2]. In fact, clinicians working in acute trauma hospitals need to discuss with patients and their families about the neurological deficits and potential for recovery early after the injury [3]. Moreover, the medical and surgical management also greatly depends on the long-term prognosis of patients. This is particularly true in cervical TSCI leading to severe functional deficits in the setting of tetraplegia. While neurological and functional outcomes after a TSCI have been widely studied [2, 4, 5], studies on quality of life (QOL) are more sparse because predicting long-term QOL is highly complex. Indeed, QOL is a multidimensional phenomenon defined by the World Health Organization as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” [6], consisting in the evaluation of a person’s life as a whole [7, 8]. Therefore, QOL may provide a broad bio-psychosocial aspect of the outcome in a more holistic way than the neurological and functional aspects.

While the initial severity of the injury (American Spinal Injury Impairment Scale or AIS grade) is recognized as the main predictive factor of long-term functional and neurological outcomes following a TSCI [2, 9], its association with QOL remains largely unclear. Up to now, an association between QOL and the severity of the neurological deficits after an SCI has only been found when both aspects are assessed simultaneously during the chronic phase [10,11,12,13]. Kivisild et al. [14] evaluated the relationship between the completeness of the SCI in the acute phase and chronic QOL, but they only adjusted their regression analyses for age and gender, thus failing to consider other potential predictors available at the initial evaluation following TSCI.

It remains difficult for clinicians to estimate future QOL early after a TSCI based on the initial severity of the injury, while taking into account other potential acute predictors of mid to long-term QOL. Accurate estimation of QOL based on acute predictors could facilitate interactions between caregivers, optimize the elaboration of a coordinated rehabilitation plan and improve counselling for patients and their families [11]. Accordingly, this study aims to evaluate the relationship between QOL 6–12 months after

a cervical TSCI and the initial severity of the neurological injury, while accounting for other potential predictors collected at admission of acute care. Secondly, we compared the QOL for our cohort of cervical TSCI patients with mean normative QOL observed in the general Canadian population.

Methods

Subjects

A total of 189 patients with a cervical TSCI were admitted between April 2010 and September 2016 in an acute Level I SCI-specialized trauma centre (Hôpital Sacré-Coeur de Montréal, Quebec, Canada) were potentially eligible. After consenting to enrol in the study, patients were followed prospectively during inpatient care and at the outpatient clinic appointments after discharge. Patients were included in the study if they sustained an acute TSCI at the cervical level (C1–C8) requiring surgical management at our institution, were aged 16 years or older, and attended the follow-up visits between 6 and 12 months post-SCI. Subjects were excluded if they had a penetrating trauma since these individuals are generally managed differently, as opposed to the general TSCI population. A total of 70 patients were excluded because they were loss to follow-up (Fig. 1). The study was approved by the institutional review board and all patients were enrolled on a voluntary basis.

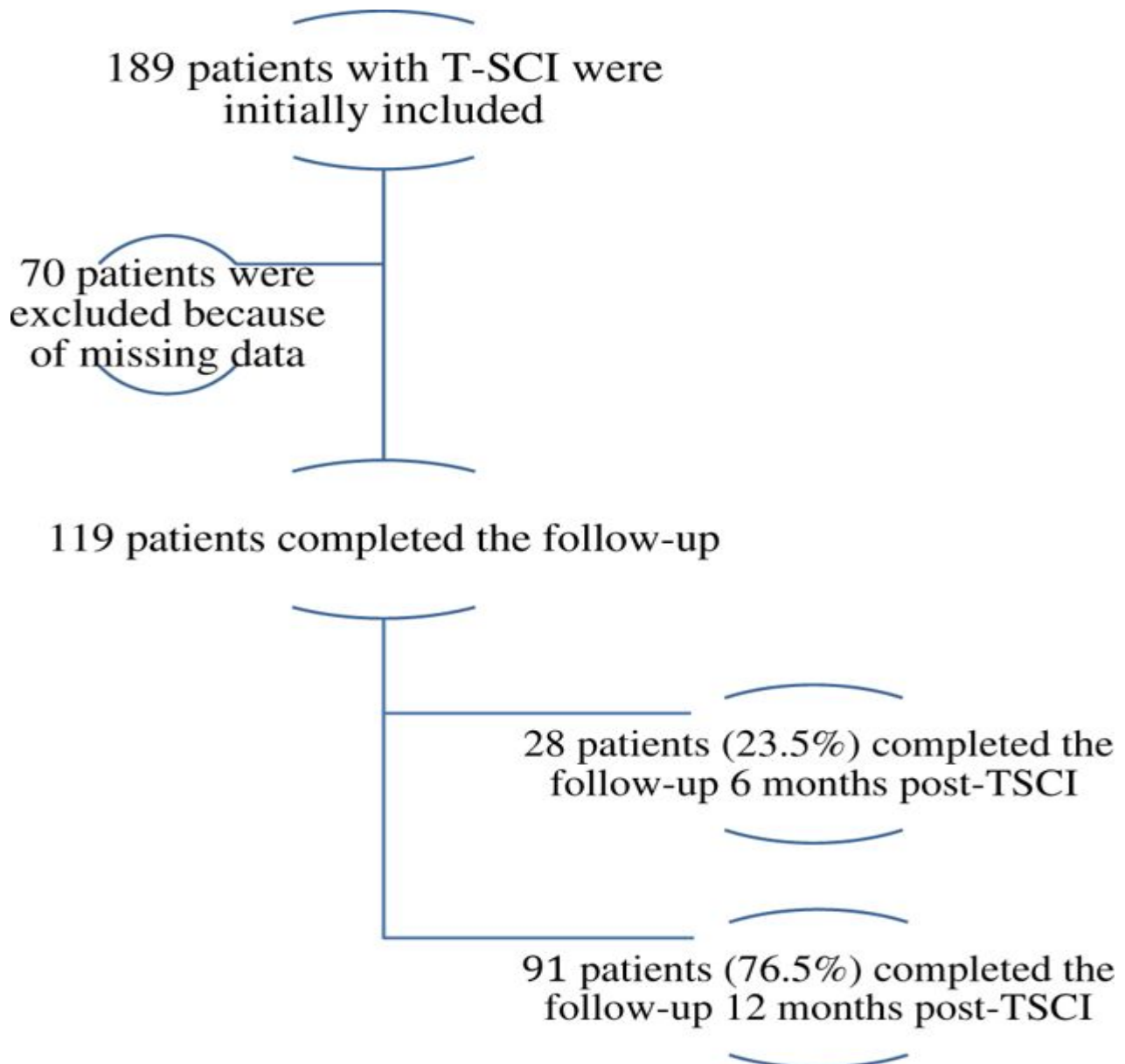


Fig 1. Description of the inclusion process of patients in this prospective study

[Full size image](#)

Data collection

Socio-demographic, clinical and trauma-related data were collected prospectively during the acute care hospitalization. Socio-demographic data included age, sex, household income (<40,000\$; 40,000–100,000\$; >100,000\$), employment status (active worker vs. unemployed / retired / student), education level (less than college vs. college or beyond) and household status (alone vs. living with spouse vs. living with family member other than spouse). Household income was subdivided based on subgroups frequently used by Statistics Canada for the population of Quebec [15]. The severity of the TSCI was assessed upon arrival to the SCI-centre and was reported using the American Spinal Injury Association (ASIA) impairment scale (AIS) grade (A to D), according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) [16]. The neurological level of injury was dichotomized as high tetraplegia (C1–C4) or low tetraplegia (C5–C8). Trauma severity and the presence of associated injuries were assessed

using the Injury Severity Score (ISS) [17]. The presence of concomitant traumatic brain injury (TBI) was also documented. The burden of comorbidities was also assessed using the Charlson Comorbidity Index (CCI), which weighs 19 comorbidities based on the adjusted relative risk of 1-year mortality and assigns them a score from 1 (conditions with a smaller relative risk; e.g. myocardial infarct) to 6 (conditions with a higher relative risk; e.g. AIDS) [18].

Outcome assessment

As a theoretical concept, QOL is a complex and dynamic phenomenon that has no simple single definition [19]. Few concepts in healthcare are often used to define the concept of QOL as a qualitative measure [20]. As mentioned in the introduction section, this study will use the concept of health-related QOL defined by the World Health Organization as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” [6]. We thus used the multidimensional health-related QOL measure, the SF-36v2 questionnaire as our main outcome measure. The SF-36v2 is a valid and reliable tool that is widely used [13, 20]. The SF-36v2 consists of 36 items assessing eight distinct health domains, which are physically and emotionally based: [21]

1.

Physical functioning (PF; limitations in performing physical activities)

2.

Role physical (RP; limitations in typical role activities due to physical health problems)

3.

Body pain (BP; limitations in usual activities due to pain)

4.

General health (GH; one’s perceptions of overall health)

5.

Vitality (VT; feelings of energy / fatigue)

6.

Social functioning (SF; interference of physical or emotional problems in performing social activities)

7.

Role emotional (RE; limitations in typical role activities due to emotional problems)

8.

Mental health (MH; emotional and cognitive well-being).

Two summary scores can be derived, one for the physical component score (PCS) and the other for the mental component score (MCS). PCS is derived from the scores on the PF, RP, BP and GH domains, whereas the MCS is calculated using the VT, SF, RE and MH subscores [13, 21]. The eight individual domain scores range between 0 and 100, and the component summary scores (PCS and MCS) are standardized around a mean of 50 (standard deviation of 10) for the norm-based scoring according to the general US population, using the software provided by Optum (Eden Prairie, MN, USA). The SF-36v2 was administered at the routine follow-up visit between 6 and 12 months after the trauma.

Statistical analyses

Non-parametric analyses were used since the distribution was not normal for independent variables according to the Kolmogorov–Smirnov tests. Direct comparisons for each individual domain and component summary scores between individuals based on the initial AIS grade (A vs. B vs. C vs. D) were performed using Kruskal–Wallis *H*tests followed by post-hoc tests with pairwise comparisons in case of rejection of the null hypothesis (group similarity). The level of significance was not corrected for multiple testing, considering that such a correction may lead to significant weaknesses (for instance increased type 2 error) and should not be used unless it is imperative to avoid type 1 error or a general null hypothesis (all null hypotheses are true simultaneously) is required, which is not the case in this study [22, 23]. Continuous data were reported as means $\pm$ standard deviation (SD) as well as median and interquartile range (IQR), while categorical data were presented as percentages. The proportion of cervical TSCI patients with PCS and/or MCS reaching the mean normative PCS and/or MCS observed in the general Canadian population [24] (PCS: <50.5 vs. ≥ 50.5 ; MCS: <51.7 vs. ≥ 51.7) was also compared based on each initial AIS grade using χ^2 tests.

As noted in Table 1, a non-negligible proportion of patients (30% = 36/119 subjects) refused to provide information pertaining to some socio-demographic characteristics, particularly the household income, employment status, education level and household status. Individuals with complete data (83 subjects) and incomplete data (36 subjects) were similar in terms of all baseline characteristics (socio-demographic, initial trauma and clinical evolution), except for a higher proportion of women who did not provide information with regard to household income, employment status, education level and household status. There were 37% females in the group that did not answer all questions, as compared to 16% females in the group that answered all questions ($p = 0.01$).

Table 1 Baseline characteristics of the final cohort and comparison of individuals who completed the study ($N = 119$) and individuals who were loss to follow-up ($n = 70$)

[Full size table](#)

Considering the presence of missing data for 36 subjects (for the independent variables), multiple (10) imputation analysis was performed using a Markov chain Monte Carlo (MCMC) algorithm. General linear models (GLM with identity link) were performed on the imputed cohort since the distribution of the standard error was normally distributed for our data. GLMs were first used to analyze the relationship between the initial severity of the TSCI (AIS grade) and the PCS (as the dependent variable). Then, a second GLM was performed to adjust for important confounding variables: (1) age; (2) gender; (3) neurological level of injury; (4) ISS; (5) presence of concomitant TBI; (6) CCI; (7) education level; (8) household income; (9) employment status; (10) household status. The same process was done for MCS (as dependant variable).

All statistical analyses were performed using the IBM SPSS Statistics 21 software (Chicago, IL), and the level of significance was 0.05. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

Results

Table 1 presents the baseline characteristics of the cohort, including socio-demographic, traumatic and clinical characteristics. A total of 189 patients (150 males and 39 females; mean age $\pm$ SD: 55.1 ± 18.5 years old) were admitted for a TSCI in our centre between April 2010 and September 2016, while 70 (37%) subjects were loss to follow-up. Losses to follow-up were significantly older and more likely to be unemployed (Table 1). The final cohort therefore consisted of 119 subjects: 93 males and 26 females with a mean age of 51.7 ± 18.0 years.

SF-36v2 scores were obtained 1 year after the TSCI for 91 patients (77%) and 6 months after the TSCI for 28 patients (24%). Baseline characteristics were similar between these patients ($p > 0.05$) (Table 1). Table 2 shows the PCS and associated subscores (PF, RP, BP and GH) for all patients according to the initial AIS grade. A Kruskal–Wallis H test revealed statistically significant differences for PCS ($H = 38.238$; $p < 10^{-4}$), PF ($H = 47.696$; $p < 10^{-4}$) and RP ($H = 16.408$; $p = 0.001$) based on the initial AIS grade. Post-hoc tests showed that PF and PCS were 10–20 points higher with an initial AIS D SCI, when compared with more severe AIS A, B and C grades ($p < 0.05$). Post-hoc tests also showed that RP was increased in AIS D injury, reaching statistical significance when compared to AIS A and C injuries ($p < 0.05$).

Table 2 Physical domain and summary scores derived from SF-36v2 based on initial AIS grade (median; interquartile range)

[Full size table](#)

Table 3 presents the MCS and associated subscores (VT, SF, RE and MH) according to the initial AIS grade. The Kruskal–Wallis H test revealed a significant difference in MCS

($H = 11.195$; $p < 0.05$), while there were no differences observed for the four subscores contributing to the MCS. Post-hoc tests showed that MCS was significantly increased in AIS A SCI when compared with AIS D SCI ($p < 0.05$).

Table 3 Mental domain and summary scores derived from SF-36v2 based on initial AIS grade (median; interquartile range)

[Full size table](#)

Only one patient with AIS C injury (1% of entire cohort) reached a PCS higher than the average Canadian PCS ($PCS \geq 50.5$) [24]. Conversely, 16 patients (13%) scored higher than the average Canadian MCS ($MCS \geq 51.7$), including 12 patients presenting with AIS A injury [24]. The proportion of patients with a MCS higher than the average Canadian MCS was significantly increased for AIS A injury when compared to AIS B, C and D injuries ($X^2 = 28.322$; $p < 10^{-3}$): 43% for AIS A vs. 8%, 10.6% and 2% for AIS B, C and D, respectively.

The GLM showed that more severe initial AIS grade was significantly associated with lower PCS (Table 4). This model was significant ($p = 0.01$), and explained 38% of the variance in PCS ($R^2 = 0.381$). The initial AIS grade was also significantly associated with MCS in the GLM, but in the opposite direction (more severe AIS with higher MCS) (Table 4). This model was significant ($p = 10^{-3}$) and explained 11% of the variance in MCS ($R^2 = 0.114$).

Discussion

Cervical TSCI can result in severe functional limitations and deterioration in physical, emotional and social areas of health. To our knowledge, this is the first study to document general expectations in terms of QOL using the SF-36v2 questionnaire, according to the initial severity of the TSCI and taking into account other relevant clinical variables available at admission to acute care. This study showed that the initial AIS grade was significantly associated with PCS and MCS in the subacute period following a cervical TSCI. This study also suggests that the severity of the injury influences PCS and MCS differently.

In accordance with previous studies [12,13,14], a more severe AIS grade of cervical TSCI was associated with lower PCS in our study, indicating that physical QOL is significantly better with substantial preserved motor function. Completeness of the TSCI—assessed from the AIS grade—reflects the degree of the neurological deficits and potential for recovery [25]. It is also proportionally associated with resulting functional limitations [2], which may limit the level of participation of an individual in various activities [26]. Improvement in physical abilities, such as arm/hand function and ability to ambulate

independently, is one of the most important priorities for patients after an SCI, as it fosters independence, participation, and consequently affects positively QOL [27].

Conversely, more severe AIS grade was negatively associated with MCS. Interestingly, 13.4% of individuals with cervical TSCI reported a MCS higher than the average reported for the general Canadian population. This observation might seem counterintuitive, but previous studies have showed similar results for the SCI population [28, 29]. Our finding could be explained in part by the following hypotheses. First, the algorithm for computing the SF-36 summary scores may have contributed to this result since PCS and MCS are both calculated from various physical and mental domains, and are thus negatively correlated [30]. Calculation of PCS involves positive weights for physical domains (physical functioning, role-physical, bodily pain, general health and vitality scales), but also negative weights for mental domains (social functioning, role-emotional and emotional well-being scales) [30]. As a result, for two individuals with the same physical domain subscores, the PCS will be higher in the subject with lower mental domain subscores, as mental domain subscores negatively weigh the PCS [30]. This highlights the importance of interpreting component scores of the SF-36v2 questionnaire in combination with domain scores [31]. Accordingly in Table 3, vitality/role emotional and mental health scores were relatively higher in individuals with complete AIS A cervical TSCI, reinforcing that individuals with more severe TSCI may develop higher mental QOL.

Second, the relatively high MCS observed in some patients is also in agreement with previous studies showing that QOL could be discordant with the level of disabilities when using other QOL questionnaires [32, 33]. Individual characteristics may also contribute to the fact that some patients with neurological deficits may report good QOL despite severe disability. As the common understanding of a good QOL implies good health and a sense of well being, it seems intuitive that disabled individuals experience poorer QOL due to their limitations and role performance [33]. Accordingly, the concept of the 'disability paradox' has developed [33]. The disability paradox highlights the importance of personal experience with disability in defining the self, one's view of the world, social context and social relationships. Some individuals with disabilities may be able to produce and maintain a sense of balance between the body (physical function dimensions), mind (rational and intellectual capacities of the self) and spirit (having a purpose of life extending beyond the self), and therefore report good QOL despite their major disabilities. Some individuals may achieve this process through rediscovering spirituality in giving them strength, direction and meaning in life. Some individuals will develop a deep need to give and get involved in reciprocal relationships, or compare themselves with others in similar conditions providing positive or negative role models [32, 33]. As suggested by Albrecht et al. [33], individuals experiencing disability can find an enriched meaning in their lives secondary to the disability condition, and may reconstitute personal meaning in their social roles [33]. For instance, some individuals may find satisfaction in using available resources to conquer each day challenges and help others sustaining similar disabilities. In some countries, more severe disability may also lead to higher transfer incomes (compensation payments from insurances or government), which could potentially influence perceived QOL [34, 35]. On the other hand, individuals sustaining milder neurological deficits may experience unanticipated medical/psychological challenges (such as pain and higher depressive symptoms), and be more inclined to report lower QOL based on functional and neurological outcomes [36].

Rehabilitation approaches targeting improvement of QOL following a cervical TSCI may thus be adapted based on the initial severity of the injury. While all patients require education and should be followed by a multidisciplinary team addressing the emotional and cognitive issues after a TSCI [20, 37], this study suggests that the need for psychological support should not be underestimated in individuals with less severe neurological deficits (AIS D cervical TSCI). These individuals can benefit from a holistic approach focussing on developing a harmonious set of relationships within the person's social and environmental context at least as much as individuals with more severe deficits.

Overall, patients in our study reported decreased QOL when compared to the general Canadian population on all eight domains, as well as on the PCS and MCS of the SF-36v2, regardless of the initial severity of the neurological impairment. This is consistent with previous literature reporting a negative impact of the severity of the chronic neurological deficit on the QOL, especially for physical domains [12,13,14, 38]. However, the PCS of one patient with AIS C tetraplegia initially after the TSCI was higher than the mean values reported for the general Canadian population, despite the lack of improvement in neurological status during follow-up [24]. This supports that numerous factors other than the severity of the TSCI also influence QOL [27, 39].

Limitations

One of the main limitations of this study is the small number of patients from a single hospital centre, limiting its generalizability. The loss to follow-up reaching 37% is also a recognized limitation. However, baseline characteristics of losses to follow-up were similar to those completing the study, although patients lost to follow-up were older and less likely to be active workers. Older age is typically associated with decreased mobility, which may explain the difficulty to comply with scheduled follow-up visits. A total of 17% individuals lost to follow-up did not provide their working status, in comparison to one patient in the final cohort with adequate follow-up. Consequently, our findings are mainly applicable to younger active workers.

The authors acknowledge that the relationship between TSCI severity and MCS is complex. Because QOL is a multidimensional dynamic process [20, 40], clinical evolution may certainly influence QOL later in the process, in addition to personality, mood state, coping, pain and environmental factors [20]. This may explain the relatively low percentage of variance explained by the MCS model, when compared to the PCS model. Since the aim of this study was to help clinicians estimate QOL according to the initial evaluation following a cervical TSCI, factors related to clinical evolution were not considered. However, this study may be used by the medical and rehabilitation team to counsel patients about their expectations in QOL early during the acute care, and optimize modifiable factors influencing QOL during the rehabilitation process [26, 32].

The period of time after injury can also be related to QOL, as previous studies showed its effect on adjustment after TSCI [40]. Approximately 75% of our patients were administered the SF-36 12 months post-injury, while remaining patients were assessed 6 months post-SCI. However, time to follow-up is unlikely to have significantly biased the

results for two different reasons. First, Table 1 shows that the baseline characteristics were similar between patients seen after 6 months vs. 12 months follow-up. Second, additional univariate linear regression analyses involving the timing of follow-up and MCS or PCS did not show any significant relationship ($p = 0.81$ for MCS and $p = 0.44$ for PCS). Finally, Mortenson et al. [40] previously showed that QOL scores were not significantly different between 3 months and 15 months post-SCI.

Conclusions

This study suggests that a severe initial AIS grade is associated with lower PCS and higher MCS in the subacute phase following cervical TSCI. Severe neurological deficits may limit functional independence, participation and perception of general health, and consequently decrease the PCS. However, psychological challenges represented by such injury are not necessarily associated to the importance of physical limitations, as individuals with less severe AIS grades may present lower MCS. Our findings could be useful for clinicians working in acute care settings to improve early counselling between the medical/surgical and rehabilitation teams, along with the patients and family, in order to set realistic goals early during the first days after the injury. Overall, individuals with cervical TSCI present lower subacute QOL scores compared to the general Canadian population, when evaluated using the SF-36 questionnaire.

Data sharing

According to our ethic board committee, public data sharing is not allowed. Most of our data is included in the Rick Hansen Registry. However, specific request for data sharing can be addressed to the corresponding author.

RESULTS

Individuals sustaining less severe neurological injury (grade D) exhibited higher PCS than individuals with grades A, B or C injury. Individuals with initial grade A injury showed increased MCS than individuals with incomplete grade B, C or D injury, with 42.9% scoring higher than the general population. The initial grade was significantly associated with chronic PCS and MCS.

REFERENCES

1. Sezer N, Akkus S, Ugurlu FG. Chronic complications of spinal cord injury. *World J Orthop.* 2015;6:24–33.
2. Richard-Denis A, Feldman D, Thompson C, Mac-Thiong JM. Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization. *J Spinal Cord Med.* 2017;41:1–9.
3. Consortium for Spinal Cord M. Early acute management in adults with spinal cord injury: a clinical practice guideline for health-care professionals. *J Spinal Cord Med.* 2008;31:403–79.
4. Kirshblum SC, O'Connor KC. Predicting neurologic recovery in traumatic cervical spinal cord injury. *Arch Phys Med Rehabil.* 1998;79:1456–66.
5. van Middendorp JJ, Hosman AJ, Donders AR, Pouw MH, Ditunno JF Jr, Curt A, et al. A clinical prediction rule for ambulation outcomes after traumatic spinal cord injury: a longitudinal cohort study. *Lancet.* 2011;377:1004–10.
6. Organization WH Health statistics and information systems. WHOQOL: measuring Quality of life: WHO; 2018. <http://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/>. Accessed 15 Apr 2018.
7. Diener E, Emmons RA, Larsen RJ, Griffin S. The satisfaction with life scale. *J Pers Assess.* 1985;49:71–5.
8. Veenhoven R. Social conditions for human happiness: a review of research. *Int J Psychol.* 2015;50:379–91.
9. Wilson JR, Grossman RG, Frankowski RF, Kiss A, Davis AM, Kulkarni AV, et al. A clinical prediction model for long-term functional outcome after traumatic spinal cord injury based on acute clinical and imaging factors. *J Neurotrauma.* 2012;29:2263–71.
10. Dijkers M. Quality of life after spinal cord injury: a meta analysis of the effects of disablement components. *Spinal Cord.* 1997;35:829–40.
11. Cushman DM, Thomas K, Mukherjee D, Johnson R, Spill G. Perceived quality of life with spinal cord injury: a comparison between emergency medicine and physical medicine and rehabilitation physicians. *PM R.* 2015;7:962–9.
12. Lidal IB, Veenstra M, Hjeltne N, Biering-Sorensen F. Health-related quality of life in persons with long-standing spinal cord injury. *Spinal Cord.* 2008;46:710–5.
13. Forchheimer M, McAweeney M, Tate DG. Use of the SF-36 among persons with spinal cord injury. *Am J Phys Med Rehabil.* 2004;83:390–5.
14. Kivisild A, Sabre L, Tomberg T, Ruus T, Korv J, Asser T, et al. Health-related quality of life in patients with traumatic spinal cord injury in Estonia. *Spinal Cord.* 2014;52:570–5.
15. Quebec Gd. Quebec handy numbers. In: Quebec Idlsd, editor. *Bibliothèque et Archives nationales du Québec* ed: Institut de la statistique du Québec; 2017.
16. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, et al. International standards for neurological classification of spinal cord injury (revised 2011). *J Spinal Cord Med.* 2011;34:535–46.
17. Baker SP, O'Neill B. The injury severity score: an update. *J Trauma.* 1976;16:882–5.
18. Charlson M, Wells MT, Ullman R, King F, Shmukler C. The Charlson comorbidity index can be used prospectively to identify patients who will incur high future costs. *PLoS ONE.* 2014;9:e112479.
19. Chappell PWS. Quality of life following spinal cord injury for 20-40 Year old males living in Sri Lanka. *Asia Pac Disabil Rehabil J.* 2003;14:168–78.
20. Post M, Noreau L. Quality of life after spinal cord injury. *J Neurol Phys Ther.* 2005;29:139–46.
21. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;30:473–83.
22. RA A. When to use the Benferroni correction. *Ophtalmic Physiol Opt.* 2014;34:502–08.
23. Perneger TV. What's wrong with Bonferroni adjustments. *BMJ.* 1998;316:1236–8.
24. Hopman WM, Towheed T, Anastassiades T, Tenenhouse A, Poliquin S, Berger C, et al. Canadian normative data for the SF-36 health survey. Canadian Multicentre Osteoporosis Study Research Group. *CMAJ.* 2000;163:265–71.
25. Fawcett JW, Curt A, Steeves JD, Coleman WP, Tuszynski MH, Lammertse D, et al. Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP

- panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. *Spinal Cord*. 2007;45:190–205.
26. Noreau L, Fougereyrollas P, Post M, Asano M. Participation after spinal cord injury: the evolution of conceptualization and measurement. *J Neurol Phys Ther*. 2005;29:147–56.
 27. Erosa NA, Berry JW, Elliott TR, Underhill AT, Fine PR. Predicting quality of life 5 years after medical discharge for traumatic spinal cord injury. *Br J Health Psychol*. 2014;19:688–700.
 28. Haran MJ, Lee BB, King MT, Marial O, Stockler MR. Health status rated with the Medical Outcomes Study 36-Item Short-Form Health Survey after spinal cord injury. *Arch Phys Med Rehabil*. 2005;86:2290–5.
 29. Abrantes-Pais Fde N, Friedman JK, Lovallo WR, Ross ED. Psychological or physiological: why are tetraplegic patients content? *Neurology*. 2007;69:261–7.
 30. Farivar SS, Cunningham WE, Hays RD. Correlated physical and mental health summary scores for the SF-36 and SF-12 Health Survey, V.I. *Health Qual Life Outcomes*. 2007;5:54.
 31. Taft C, Karlsson J, Sullivan M. Do SF-36 summary component scores accurately summarize subscale scores? *Qual life Res*. 2001;10:395–404.
 32. Bonanno GA, Kennedy P, Galatzer-Levy IR, Lude P, Elfstrom ML. Trajectories of resilience, depression, and anxiety following spinal cord injury. *Rehabil Psychol*. 2012;57:236–47.
 33. Albrecht GL, Devlieger PJ. The disability paradox: high quality of life against all odds. *Soc Sci Med*. 1999;48:977–88.
 34. Diener ESE. Measuring quality of life: economic, social, and subjective indicators. *Soc Indic Res*. 1997;40:189–216.
 35. Clayton KS, Chubon RA. Factors associated with the quality of life of long-term spinal cord injured persons. *Arch Phys Med Rehabil*. 1994;75:633–8.
 36. Ames H, Wilson C, Barnett SD, Njoh E, Ottomanelli L. Does functional motor incomplete (AIS D) spinal cord injury confer unanticipated challenges? *Rehabil Psychol*. 2017;62:401–6.
 37. Martz E, Livneh H, Priebe M, Wuermsier LA, Ottomanelli L. Predictors of psychosocial adaptation among people with spinal cord injury or disorder. *Arch Phys Med Rehabil*. 2005;86:1182–92.
 38. Westgren N, Levi R. Quality of life and traumatic spinal cord injury. *Arch Phys Med Rehabil*. 1998;79:1433–9.
 39. Ebrahimzadeh MH, Soltani-Moghaddas SH, Birjandinejad A, Omid-Kashani F, Bozorgnia S. Quality of life among veterans with chronic spinal cord injury and related variables. *Arch Trauma Res*. 2014;3:e17917.
 40. Mortenson WB, Noreau L, Miller WC. The relationship between and predictors of quality of life after spinal cord injury at 3 and 15 months after discharge. *Spinal Cord*. 2010;48:73–9.

. Appendix 11: Manuscript published in J Spinal cord Med (2018)

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Determining priorities in functional rehabilitation related to quality of life one-year following a traumatic spinal cord injury.

Abstract

Context/Objective: To determine the relationship between the different functional aspects (as determined by the Spinal Cord Independence Measure) and quality of life (QOL) following a traumatic spinal cord injury (TSCI), considering clinical confounding factors.

Design: Retrospective review of a prospective cohort

Setting: A single Level-1 trauma center specialized in SCI care

Participants: 142 individuals sustaining an acute traumatic SCI

Interventions: Not applicable

Outcome Measures: The four QOL domains as assessed by the WHOQoL-bref questionnaire six to twelve months post-injury.

Results: The mobility subscore was the single functional aspect significantly associated with each of the domains of QOL (physical, psychological, social and environmental). Males may experience worst chronic social and environmental-QOL compared to females. The level of injury may also influence environmental-QOL.

Conclusion: Mobility training (mobility in bed, mobility with or without technical aids, transfers and stair management) should be an important part of the rehabilitation process in order to optimized chronic QOL following a TSCI.

Key words: spinal cord injury; mobility; quality of life; function; trauma

Abbreviations: TSCI, traumatic spinal cord injury; QOL, quality of life

1 Introduction

2
3 Traumatic spinal cord injuries (TSCI) lead to severe functional limitations and secondary
4 complications affecting physical, emotional and social areas of health.¹ The evaluation of
5 outcomes following TSCI thus requires considering quality of life (QOL), in order to improve the
6 management of TSCI patients in a holistic approach. The rehabilitation process is a critical part
7 of the coping process following such a severe injury. It comprises multidisciplinary therapies
8 throughout the continuum care encompassing various functional aspects (self-care, respiratory
9 and sphincter management, as well as mobility training) with the ultimate goal of reaching the
10 highest functional status possible.

11
12 Previous studies have showed that functional outcome may influence directly and/or indirectly
13 QOL following TSCI. A meta-analysis by Djikkers et al. (1997) has reported moderate correlation
14 between the severity of functional impairment and QOL,^{2,3} while Erosa et al. (2013) showed in a
15 longitudinal study that greater functional impairment was a significant predictor of decreased
16 participation, which is an important indicator for QOL.⁴ Unfortunately, these studies did not
17 identify which specific functional aspects mainly influence QOL, while this information would
18 help determining functional rehabilitation priorities. As a result, there is no consensus on the
19 prioritization of the different aspects of the functional training during rehabilitation following
20 TSCI.

21
22 Accordingly, this study aims to identify which specific functional aspect may be prioritized
23 during the rehabilitation process in order to optimize QOL following a TSCI. Thus, this study
24 will investigate the relationship between different functional aspects (as determined by the third

25 version of the Spinal Cord Independence Measure (SCIM)) and the QOL (as evaluated by
the

26 WHOQOL-bref)

27 **Methods**

28 ***Patients***

A prospective cohort of 142 patients consecutively admitted to a single Level I SCI-specialized trauma center between March 2011 and October 2016 (113 males and 29 females; mean age $\pm$ SD: 48.5 $\pm$ 18.7 years old) for a TSCI was studied. Patients entered the cohort at the time of admission after consent and were followed until discharge from the acute SCI-center. They were included if they sustained an acute cervical (C1 to C8) or thoraco-lumbar (T1 to L1) TSCI requiring surgical management at our institution; were aged 16 years and older; and presented at their follow-up visit in the chronic phase between 6 and 12 months post-TSCI. Patients were excluded if they sustained a penetrating trauma, did not come to any follow-up visit or failed to fill out one or both of the QOL and functional assessments. The study was approved by the institutional review board and all patients were enrolled on a voluntary basis.

29

30 ***Data collection***

Socio-demographic, clinical and trauma information were collected prospectively and updated on a daily basis during the acute care hospitalization. Socio-demographic data included age, sex, household income (< 40,000\$; 40,000-100,000\$; >100,000\$), employment status at time of the injury (active worker vs. unemployed/retired/student), education level (less than college vs. college or more) and people living in the household / marital status (alone vs. married/common-law vs. family member/other). The body mass index (BMI) was also calculated. The burden of comorbidities was also assessed using the Charlson Comorbidity Index, which weighs the different comorbidities based on the adjusted relative risk of one-year mortality.⁵

The initial severity of the TSCI was assessed upon arrival to the SCI-center within 72 hours of the TSCI and was reported using the American Spinal Injury Association impairment scale (AIS) grade (A to D) as well as the initial ASIA motor score. The neurological level of injury was stratified as high (C1-C4) and low tetraplegia (C5-C8), and high (T1-T7) and low paraplegia (T8-L1). Trauma severity assessed from the Injury Severity Score (ISS),⁶ presence and severity of concomitant traumatic brain injury (none vs. mild vs. moderate vs. severe) as well as the presence of central cord syndrome were also documented. The mechanism of injury (sports vs. assault-blunt vs. fall vs. transport vs. other) and trauma velocity (high vs. low) were noted. The surgical delay, defined as the time (in hours) between the injury and the time of incision, was also considered. Hospital length of stay was defined as the number of days from admission to discharge from the acute SCI-center.

31 The third version of the Spinal Cord Independence Measure (SCIM) questionnaire was used to
32 assess functional status in the chronic phase post-SCI. The SCIM is a valid and reliable disability
33 scale specifically aimed at assessing the ability of patients with a spinal cord injury to perform
34 daily living activities independently.⁷ The SCIM assesses three domains: self-care (6 items
35 evaluating feeding, grooming, bathing and dressing); respiration and sphincter management (4
36 items); and mobility and transfers (9 items evaluating bed, indoor and outdoor mobility).⁷ The
37 score for the self-care aspect can range between 0 and 20, while the respiration / sphincter
38 management and mobility / transfers scores both range between 0 and 40. The total SCIM score
39 can thus vary between 0 and 100, with higher score referring to higher functional status. The
40 three SCIM subscores (self-care; respiration and sphincter management; mobility and transfers)
41 as well as the total SCIM score were assessed.

Outcome assessment

QOL was assessed using the scores obtained on the four domains assessed using the WHOQoL-Bref questionnaire, which is a valid and reliable tool that is widely used for health-related QOL evaluation and has been validated in the SCI population.⁸ The WHOQOL-Bref questionnaire consists of 24 items assessing 4 distinct health domains: 1) physical health (7 items); 2) psychological health (6 items); 3) social relationships (3 items) and 4) environment (8 items). Higher scores referring to higher health-related QOL. Both the WHOQOL-Bref and the SCIM were administered at the routine follow-up visit during the chronic phase post-SCI, between 6 and 12 months after the trauma.

Statistical analyses

IBM SPSS Statistics Version 19 software package was used for statistical analyses. Our cohort was described using means $\pm$ standard deviation for continuous variables, and proportions or percentages for categorical variables.

Multivariate linear regression analyses (general linear model) were used to evaluate the strength of association between the independent variables and each domain of the WHOQOL-Bref questionnaire (dependent variable). The three SCIM functional subscores and the total SCIM were designated as the main independent variables, while the socio-demographic data, the characteristics of the injury, the surgical delay, the acute care length of stay were considered as covariates. A backward elimination method was used to obtain the final regression model. The association between the independent variables and the score on each of the WHOQOL-Bref domains was expressed using the beta (β) coefficient with its 95% confidence interval (CI), and the R^2 was used as an indicator of the percentage of the variance explained by each model.

Results

Our cohort included 142 patients who sustained a TSCI. Their socio-demographic, trauma and clinical information are presented in Table 1.

The final regression model for each WHOQOL-bref domain is showed in Table 2. A total of 23 independent variables were included for each multivariate regression model. The SCIM-mobility subscore was the only functional aspect significantly associated with QOL. It was also the only factor associated with each WHOQOL-Bref domain considering covariates. More specifically, a higher SCIM mobility subscore was the single significant factor associated with higher physical and psychological scores on the WHOQOL-Bref questionnaire, explaining 6% and 18% of total variance for each model. Higher scores on the SCIM mobility subscale predicted higher scores on the social aspect of the WHOQOL-Bref questionnaire, while being a male was associated with a lower social-QOL score. The environmental-QOL score was significantly influenced by four factors. Higher SCIM-mobility scores, female sex, higher trauma severity (higher ISS) and lower (caudal) neurological level of injury were associated with higher environmental-QOL score. All final models were significant ($P < 10^{-3}$) and the last two models (dependent variables: social- and environmental-QOL) explained 13% and 24% of the total variance.

Discussion

Reaching an optimal QOL is of utmost importance for individuals with TSCI as they generally sustain important deficits and limitations. The rehabilitation process is therefore critical, as it provides the training and knowledge required to maximize functional recovery. However, even if the importance of rehabilitation training is well recognized,⁹ the impact of specific functional training on the QOL following TSCI remains uncertain. To our knowledge, this is the first study evaluating the relationship between specific functional abilities and QOL following a TSCI, while considering various confounding variables using multivariate analyses.

Results of this study suggest that improved mobility is significantly associated with higher scores on the WHOQOL-Bref questionnaire for all four QOL domains (physical, psychological, social and environmental) in the chronic phase after TSCI. Mobility in the SCIM questionnaire refers to the ability to mobilized in bed, to move on various distances, indoor or outdoor, with or without technical aids or wheelchair.⁷ It also refers to the ability to manage stairs and transfer in various situations.⁷ Individuals with TSCI generally experience severe mobility problems due to muscular weakness/paralysis, but also to spasticity, balance disorders, contractures and pain.^{8,9} A

part of the mobility training thus consists in optimizing these factors, while working with technical aids and specialized equipment when applicable (such as robotic technologies and locomotor training).^{10,11} Improved mobility was showed to represent a priority for subjects with TSCI,¹² but may also consists as an important determinant of the participation level of an individual in his environment.⁴⁻⁶ For instance, mobility restrictions may limit the ability to live

108 independently, to return to work and to previous leisure activities. Low mobility is also
109 associated with weaker social engagement, which can accentuate psychological issues and

ultimately impeding fulfillment of the social role and one's sense of identity.¹³ Thus, mobility training, in comparison with other functional aspect (self-care, respiratory and sphincter management), may particularly improve the social disadvantage related to TSCI. In this regard, the rehabilitation program should also early integrate interventions promoting social reintegration.^{4,14}

QOL is a broad concept involving several personal attributes, adaptability, personal perception and values^{15,16} which were not considered in this study and may explain the low percentage of variance observed. Therefore, the severity of functional impairments can only be considered as one of many factors influencing QOL following TSCI.³ However, results of this study remains of critical importance. Indeed, identifying which specific functional ability is independently associated to QOL will help to better plan the rehabilitation process and resources utilization. Keeping in mind that the rehabilitation process should be approached in a multidisciplinary holistic way, results from this study suggest that mobility training must take an important place. Accordingly, mobility training should be started early as possible. Not only as an early improved mobility may prevent medical complications,¹⁷ but can also facilitate progression of mobility throughout the subsequent phases rehabilitation.⁹ This information is particularly important, as there is no consensus on the optimal acute care rehabilitation plan following TSCI. As the

128 rehabilitation process mobilizes a lot of resources, the identification of which functional aspect
129 mostly influences QOL is definitely an asset. However, future multi-centered studies are needed
130 to establish evidence-based practice recommendations based on our findings.

131

132 Results of the GLM also suggest that most of the baseline characteristics (characteristics of the
133 individual and of the injury showed in Table 1) are not associated to physical and psychological

QOL, which is in accordance with previous studies.^{3,4} This result may be surprising as social and environmental domains of QOL rely on interpersonal relationships and interactions with the environment (social support, sexual activity, home environment, opportunities to acquire new skills and accessibility).⁸ However, we found that males were more likely to experience decreased social and environmental QOL. Several clinical studies have showed contradictory results regarding QOL outcomes between males and females, and various theories were proposed to explain the differences.¹⁸⁻²⁰ Biological factors (genes, hormones, etc.),¹⁹ factors stemming from women's social role (social network and support, non-paid work at home, etc.) and mixed factors such as health-related lifestyles, mental health disorders may also contribute to the differences between males and females.²¹ To that extent, we have performed additional comparative analyses between males and females, showing that males were less educated than women ($p=0.02$). Education and mental development are recognized important attributes of improved QOL, as it may empower a person, help being more proactive and gain control of their lives.^{22,23} It should be however kept in mind that education was not revealed as an independent predictive factor of QOL in our multivariate regression analyses, which suggests that impact of the education level on QOL is potentially more important for males. Previous studies have also showed similar results in the SCI population.^{24,25}

153 ***Limitations***

154 A recognized limitation of this study is the relatively low proportion of variance of QOL
155 explained by the mobility function. The percentage is however still noticeable, considering that
156 qualitative measure of QOL may account for around 50% of the variance for people with
157 disabilities.²⁶ It thus confirms, as expected, that other factors not considered in this study

influence QOL. For instance, the functional status prior to the injury, social functioning and various psychological factors are recognized to influence chronic QOL following TSCI.^{3,27} Future studies should also account for social and psychological factors, along with their dynamic interactions with participation and QOL. Presence of neurogenic pain⁴ and employment status post-injury are also variables that may have influenced results of this study. Nevertheless, this study has assessed important predictors of QOL as reported in healthy individuals: sex, marital status, age, education level and disability.²⁸ Finally, it is possible that items from the SCIM and the WHOQol-Bref questionnaire may be measuring similar mobility aspects, which may have participated to results of this study. However, others functional aspects also measured by the SCIM and thus considered in this study (such as self-care and sphincter management) may also be correlated to some WHOQol-Bref items. Thus, potential collinearity between domains of the SCIM and WHOQol-Bref questionnaire is less likely to limit conclusions of this study.

Conclusions

The occurrence of traumatic spinal cord injury (TSCI) is associated with severe deficits and significant functional impairments. Long-term quality of life (QOL) is a critical outcome following TSCI as it illustrates an individual in its physical, psychological and social aspects. The rehabilitation process following TSCI aims to optimize the chronic functional outcome through various types of assessment and training. However, priorities among the different aspects of functional training remain unknown. We have thus evaluated the relationship between the different aspects of the functional outcome (as assessed by the SCIM-III questionnaire) and the four domains of QOL as evaluated by the WHOQOL-bref questionnaire. Results of this study, based on a review of a prospective database including 142 patients, showed that the mobility subscore was the single functional aspect significantly associated with each of the four WHOQOL-bref domains (physical, psychological, social and environmental). Mobility was previously showed to be a life priority following TSCI, as higher mobility may facilitate independent living and the return to previous activities. Furthermore, a higher mobility status may facilitate participation and empower individuals in fulfilling their social role. Mobility training should thus constitute an important part of the rehabilitation plan following a TSCI. This

188 result may also guide decisions-makers in planning rehabilitation resources, always keeping in
189 mind that a multidisciplinary holistic approach aiming for better participation and integration in
190 the community is an asset following TSCI.
191

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References

1. Tulskey DS, Kistala PA. The Spinal Cord Injury--Quality of Life (SCI-QOL) measurement system: Development, psychometrics, and item bank calibration. *J Spinal Cord Med* 2015;38(3):251-6.
2. Dijkers M. Quality of life after spinal cord injury: a meta analysis of the effects of disablement components. *Spinal cord* 1997;35(12):829-40.
3. Mortenson WB NL, Miller WC. The relationship between and predictors of quality of life after spinal cord injury at 3 and 15 months after discharge. *Spinal cord* 2010;48(1):73-9.
4. Erosa NA, Berry JW, Elliott TR, Underhill AT, Fine PR. Predicting quality of life 5 years after medical discharge for traumatic spinal cord injury. *Br J Health Psychol* 2014;19(4):688-700.
5. Charlson ME, Charlson RE, Peterson JC, Marinopoulos SS, Briggs WM, Hollenberg JP. The Charlson comorbidity index is adapted to predict costs of chronic disease in primary care patients. *J Clin Epidemiol* 2008;61(12):1234-40.
6. Baker SP, O'Neill B. The injury severity score: an update. *J Trauma* 1976;16(11):882-5.
7. Itzkovich M, Gelernter I, Biering-Sorensen F, Weeks C, Laramie MT, Craven BC, *et al.* The Spinal Cord Independence Measure (SCIM) version III: reliability and validity in a multi-center international study. *Disabil Rehabil* 2007;29(24):1926-33.

8. Jang Y, Hsieh CL, Wang YH, Wu YH. A validity study of the WHOQOL-BREF assessment in persons with traumatic spinal cord injury. *Arch Phys Med Rehab* 2004;85(11):1890-5.
9. Nas K, Yazmalar L, Sah V, Aydin A, Ones K. Rehabilitation of spinal cord injuries. *World J Orthop* 2015;6(1):8-16.
10. Harkema SJ, Schmidt-Read M, Lorenz DJ, Edgerton VR, Behrman A. Balance and ambulation improvements in individuals with chronic incomplete spinal cord injury using locomotor training-based rehabilitation. *Arch Phys Med Rehab* 2012;93(9):1508-17.
11. Wirz M, Zemon DH, Rupp R, Scheel A, Colombo G, Dietz V, *et al.* Effectiveness of automated locomotor training in patients with chronic incomplete spinal cord injury: a multicenter trial. *Arch Phys Med Rehab* 2005;86(4):672-80.
12. Simpson LA, Eng JJ, Hsieh JT, Wolfe DL, Spinal Cord Injury Rehabilitation Evidence Scire Research T. The health and life priorities of individuals with spinal cord injury: a systematic review. *J Neurotrauma* 2012;29(8):1548-55.
13. Rosso AL, Taylor JA, Tabb LP, Michael YL. Mobility, disability and social engagement in older adults. *J Aging Health* 2013;25(4):617-37.
14. Noreau L, Fougereyrollas P, Post M, Asano M. Participation after spinal cord injury: the evolution of conceptualization and measurement. *J Neurol Phys Ther* 2005;29(3):147-56.
15. Wilson JR, Grossman RG, Frankowski RF, Kiss A, Davis AM, Kulkarni AV, *et al.* A clinical prediction model for long-term functional outcome after traumatic spinal cord injury based on acute clinical and imaging factors. *J Neurotrauma* 2012;29(13):2263-71.
16. Moghimian M, Kashani F, Cheraghi MA, Mohammadnejad E. Quality of Life and Related Factors Among People With Spinal Cord Injuries in Tehran, Iran. *Arch trauma Res* 2015;4(3):e19280.

17. Minkel JL. Seating and mobility considerations for people with spinal cord injury. *Phys Ther* 2000;80(7):701-9.
18. Farrace E AW. Do women face worse: a metaanalysis of gender differences in traumatic brain injury outcome. *J Neurosurg* 2000;93(4):539-45.
19. Furlan JC, Krassioukov AV, Fehlings MG. The effects of gender on clinical and neurological outcomes after acute cervical spinal cord injury. *J Neurotrauma* 2005;22(3):368-81.
20. Gunnarsson T, Fehlings MG. Acute neurosurgical management of traumatic brain injury and spinal cord injury. *Curr Opin Neurol* 2003;16(6):717-23.
21. Guallar-Castillon P; Sendino AR; Banegas J; Lopes-Garcia E R-aF. Differences in quality of life between women and men in the older population of Spain. *Soc Sci Med* 2005;60(6):1229-40.
22. Kumar N, Gupta B. Effect of Spinal Cord Injury on Quality of Life of Affected Soldiers in India: A Cross-Sectional Study. *Asian Spine J* 2016;10(2):267-75.
23. Rivers CS, Fallah N, Noonan VK, Whitehurst DG, Schwartz CE, Finkelstein JA, *et al.* Health Conditions: Effect on Function, Health-Related Quality of Life, and Life Satisfaction After Traumatic Spinal Cord Injury. A Prospective Observational Registry Cohort Study. *Arch Phys Med Rehab* 2018;99(3):443-51.
24. Dowler R, Richards JS, Putzke JD, Gordon W, Tate D. Impact of demographic and medical factors on satisfaction with life after spinal cord injury: a normative study. *J Spinal Cord Med* 2001;24(2):87-91.
25. Putzke JD, Richards JS, Hicken BL, DeVivo MJ. Predictors of life satisfaction: a spinal cord injury cohort study. *Arch Phys Med Rehab* 2002;83(4):555-61.

26. Chappell p ws. Quality of life following spinal cord injury for 20-40 Year old males living in sri lanka. Asia Pac Disab Rehab J. 2003;14(2):168.
27. Van Leeuwen CM, Kraaijeveld S, Lindeman E, Post MW. Associations between psychological factors and quality of life ratings in persons with spinal cord injury: a systematic review. Spinal Cord 2012;50(3):174-87.
28. Ruggeri M NM, Bonetto C, Cristofalo D, Lasalvia A, Salvi G, et al. Changes and predictors of change in objective and subjective quality of life. Br J Psychiatry 2005;187(2):121-30.

Table 1: Baseline characteristics of the total cohort of patients with traumatic spinal cord injury (N=142)

Socio-demographic	Age	Mean $\pm$ SD	48.5 $\pm$ 18.7
	Sex	% Male	79.6
	Household income	% 0-40,000\$	18.3
		% 40,000-100,000\$	35.2
		% >100,000\$	12.7
		% Unknown / refused to answer	33.8
	Employment status	% Active worker	58.5
		% Unemployed, student, or retired	39.4
		% Unknown / refused to answer	2.1
Initial trauma	Education level	% Less than college	61.3
		% More than college	31.7
		% Unknown / refused to answer	7.0
	Marital status	% Living alone	21.1
		% Spouse / Partner	52.8
		% Family member or other	23.9
		% Unknown / refused to answer	2.1
	Charlson Comorbidity Index (CCI)	% 0	87.3
		% 1	7.0
		% 2	4.9
		% 3	0.0
		% 4	0.0
		% 5	0.0
		% 6	0.7
	Body Mass Index (BMI)	Mean $\pm$ SD	26.6 $\pm$ 7.6
Initial trauma	AIS grade	% A	38.7
		% B	9.2
		% C	13.4
		% D	38.7
	Neurological level of injury (NLI)	% C1-C4	38.0
		% C5-C8	29.6
		% T1-T7	7.7
		% T8-L1	24.6
Initial trauma	Mechanism of injury	% Sports	16.2
		% Assault-blunt	7.0
		% Fall	43.0
		% Transport	31.0
		% Other	2.8
	High velocity trauma	% High	56.3
		% Low	35.9
		% Unknown	7.7
Initial trauma	Injury Severity Scale (ISS)	Mean $\pm$ SD	23.1 $\pm$ 8.3
	Severity of	% No TBI	48.6

	concomitant traumatic brain injury (TBI)	% Mild % Moderate % Severe	48.6 2.1 0.7
	Central cord syndrome (%)		23.2
	Surgical timing (hours)	Mean ±SD	103.1±374.0
	Length of stay in acute care (days)	Mean ±SD	24.6 ±14.3

AIS: ASIA (American Spinal Injury Association) Impairment Scale

Table 2: Results of the multivariate regression analyses using General Lineal Models (GLM) for each of the WHOQOL-Bref domains (physical, psychological, social and environmental) (N=142)

Dependent variables for each final GLM	Significant variable(s) in the final model	Beta (95%CI)	R ² value of the final model	Final model P-value
Model 1 : Physical	SCIM_mobility	0.23 (0.08-0.37)	0.062	0.003
Model 2 Psychological	SCIM_mobility	0.46 (0.26-0.67)	0.123	<10 ⁻³
Model 3 : Social	SCIM_mobility Male	0.52 (0.27-0.76) -8.19 (-15.83- -0.55)	0.128	<10 ⁻³
Model 4 : Environmental	SCIM_mobility Male Level of injury C0-C4 C5-C8 13.27 (2.39-24.16) T8-L1 category ISS	0.58 (0.35-0.80) -8.75 (-15.26—2.25) 9.16 (2.37-15.95) 10.41 (3.30-17.52) T1-T7 reference 0.40 (0.06-0.75)	0.240	<10 ⁻³

ISS, Injury severity score; SCIM, Spinal Cord Independence Measure

. Appendix 12: Manuscript published in J Spinal cord Med (2018)

The Journal of Spinal Cord Medicine

**The impact of early spasticity on the intensive functional rehabilitation phase and community reintegration following traumatic spinal cord injury
--Manuscript Draft--**

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Abstract:	Context/Objectives: To determine the impact of spasticity presenting during the acute care hospitalization on the rehabilitation outcomes following a traumatic spinal cord injury (TSCI). Design: Retrospective cohort study Setting: A single Level 1 trauma center specialized in SCI care Participants: 150 individuals sustaining an acute TSCI. Interventions: Not applicable Outcome Measures: The total inpatient functional rehabilitation length of stay. The occurrence of medical complications and the discharge destination from the inpatient functional rehabilitation facility were also considered. Results: 63.3% of the cohort presented signs and/or symptoms of spasticity during acute care. Individuals with early spasticity developed medical complications during acute care and intensive functional rehabilitation (IFR) in a higher proportion. They were also hospitalized significantly longer and were less likely to return home after rehabilitation than individuals without early spasticity. Early spasticity was an independent factor associated with increased total inpatient rehabilitation length of stay. Conclusion: The development of signs and symptoms of spasticity during acute care following a TSCI may impede functional rehabilitation outcomes. Higher vigilance towards the prevention of medical complications and aggressive treatment using non-pharmaceutical interventions is recommended. Future studies should investigate the impact of aggressive management using pharmaceutical treatment in these individuals.

The impact of early spasticity on the intensive functional rehabilitation phase and community reintegration following traumatic spinal cord injury

Abstract

Context/Objectives: To determine the impact of spasticity presenting during the acute care hospitalization on the rehabilitation outcomes following a traumatic spinal cord injury (TSCI).

Design: Retrospective cohort study

Setting: A single Level 1 trauma center specialized in SCI care

Participants: 150 individuals sustaining an acute TSCI.

Interventions: Not applicable

Outcome Measures: The total inpatient functional rehabilitation length of stay. The occurrence of medical complications and the discharge destination from the inpatient functional rehabilitation facility were also considered.

Results: 63.3% of the cohort presented signs and/or symptoms of spasticity during acute care. Individuals with early spasticity developed medical complications during acute care and intensive functional rehabilitation (IFR) in a higher proportion. They were also hospitalized significantly longer and were less likely to return home after rehabilitation than individuals without early spasticity. Early spasticity was an independent factor associated with increased total inpatient rehabilitation length of stay.

Conclusion: The development of signs and symptoms of spasticity during acute care following a TSCI may impede functional rehabilitation outcomes. Higher vigilance towards the prevention of medical complications and aggressive treatment using non-pharmaceutical interventions is recommended. Future studies should investigate the impact of aggressive management using pharmaceutical treatment in these individuals.

Key Words: spinal cord injury; spasticity; rehabilitation; acute care; trauma

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Introduction

Spasticity is a complex neurological syndrome characterized by a velocity-dependant hypertonia following a central nervous system lesion.¹ It affects 40 to 80% of individuals suffering from traumatic spinal cord injury (TSCI) and adversely so in 28 to 48% of individuals.² Spasticity is not only restricted to muscular hypertonia, but is rather part of a complex spectrum of signs and symptoms including spasms and clonus.^{3, 4}

Spasticity occurs during recovery from spinal shock, which corresponds to the depression of the spinal reflexes below the level of injury.^{4, 5} The onset of muscle hypertonia, spasms and clonus will generally occur in the next weeks following the injury presumably due to neuronal hyper sensibility and axonal sprouting.⁶ Spasticity may lead to pain, mobility disorders, affect daily activities and decrease quality of life.⁷⁻⁹ Spasticity was also previously reported as a top concern for patients in the chronic phase following a TSCI.^{10, 11}

The acute hospitalization is a critical step in the rehabilitation process, along with the intensive functional rehabilitation (IFR) hospitalization and the reintegration to the community.^{12, 13} In the province of Quebec, when an extended period of intensive inpatient rehabilitation is required and ‘specialized’ training is completed in IFR (sphincter management, SCI education, etc.), individuals are sent to an affiliated transitional rehabilitation facility. This transitional rehabilitation facility can provide additional mobility and functional training, while being less expensive than IFR.¹² The course of the acute care hospitalization has been shown to influence functional outcome following a TSCI,¹⁴ but the impact of the development of early spasticity (during acute care) remains unknown. Considering that chronic spasticity can affect long-term

outcomes following TSCI,^{11, 15, 16} it is hypothesized that early development of spasticity after a TSCI can alter the functional rehabilitation process and community reintegration. Awareness of the implications of early spasticity could help clinicians in preventing complications, planning the rehabilitation process and improve long-term outcome. It could also help to clarify the indications for spasticity treatment, which currently remain subjective.¹⁷

The objective of this study was to determine the impact of spasticity presenting during the acute care hospitalization on the rehabilitation outcomes following a TSCI. Outcomes measures were the occurrence of medical complications and the rehabilitation length of stay (LOS), as well as the discharge orientation for individuals that have or not developed early spasticity. Multivariable linear regression analyses were used to analyze the relationship between the presence of early spasticity and the total inpatient functional rehabilitation LOS considering important confounding factors. As a secondary objective, multivariate logistic regression analyses were used to determine the impact of early spasticity on the discharge orientation after IFR.

Methods

Subjects

We conducted a retrospective cohort study of prospectively collected data including 156 consecutive patients admitted to a single Level 1 SCI-specialized trauma center between April 2010 and April 2017, and transferred to the affiliated IFR center for a TSCI. Patients were included if they sustained an acute TSCI between level C1 to L1 requiring surgical management at our institution and were aged 16 years or more. Patients were excluded if information regarding discharge destination after IFR was missing (6 subjects). The final cohort thus consisted in 150 patients. The study was approved by the institutional review board.

Our cohort was subdivided into two groups based on the development of spasticity during the acute care hospitalization. Group 1 included 55 (36.7%) individuals with a TSCI (“no early spasticity group”) who did not develop spasticity during the acute care hospitalization, while Group 2 (“early spasticity group”) included 95 individuals (63.3%) who developed spasticity during the acute care hospitalization. The development of spasticity was noted during the acute care hospitalization based on physical findings assessed by the attending treating team and symptoms reported by the patient. The diagnosis of spasticity required one of the following three criteria: 1) presence of increased velocity-dependant muscle tone at physical examination (Modified Ashworth scale score of >1); 2) spasm and/or clonus noted at physical examination, and; 3) spasms and/or clonus reported by the subject.

Data collection

Socio-demographic, clinical and trauma-related information were retrieved from a prospective database of all consecutive TSCI patients collected during the acute care hospitalization. Socio-demographic data included age and body mass index. The burden of comorbidities was assessed using the Charlson Comorbidity Index (CCI), which weighs 19 comorbidities based on the adjusted relative risk of one-year mortality.¹⁸ The severity of the TSCI was assessed upon arrival to the acute SCI-center and was reported using the American Spinal Injury Association (ASIA) impairment scale (AIS) grade (A to D), according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI).¹⁹ The neurological level of injury was categorized as high tetraplegia (C1-C4), low tetraplegia (C5-C8) or paraplegia (T1-L1). Trauma severity and the burden of associated traumatic injuries were assessed using the Injury Severity Score – ISS.²⁰ The presence and severity of concomitant traumatic brain injury were also documented.

Data concerning the following complications that arose during the acute care hospitalization was collected: overall respiratory complications (e.g. pneumonia, acute respiratory distress syndrome; pulmonary embolism; bronchitis; atelectasis; pulmonary oedema; pneumothorax; etc.), urinary tract infections (UTI) and pressure ulcers (PU). The occurrence of respiratory complications was diagnosed using clinical features and confirmed by a radiologist using chest X-rays.²¹ UTI were diagnosed using criteria from the 2006 Consortium for Spinal Cord Medicine Guidelines for healthcare providers.²² Finally, the presence of PU was diagnosed based on the clinical guidelines defined by the National Pressure Ulcer Advisory Panel (NPUAP).²³ A complication rate was calculated, referring to the proportion of patients who developed one of the above-mentioned complications during their stay at the acute specialized SCI center, and was expressed as a

percentage. The presence of PU was also considered separately since the presence of spasticity in the chronic phase has been associated with increased prevalence of PU in a previous study.⁷ Surgical delay was defined as the time (in hours) between the trauma and the spinal surgery (time of skin incision). Length of stay (LOS) was defined as the number of days from admission to discharge either from acute care (acute care LOS), or IFR center (IFR LOS). The total inpatient rehabilitation LOS referred to the number of days either in IFR and transitional rehabilitation, when applicable.

Outcome variables

The total inpatient rehabilitation LOS consisted in our main outcome variable. The discharge destination after IFR was categorized into: 1) discharge home; 2) transitional inpatient rehabilitation facility; 3) long-term nursing home and others (readmission to acute care hospital, death, etc.). This data was collected retrospectively through a review of the IFR clinical chart. Individuals that are discharged home generally benefit from multidisciplinary rehabilitation on an outpatient basis, based on their needs assessment during the IFR stay.

Data on new medical complications (ITU, PU and pneumonia) occurring during the IFR hospitalization was collected using the same criteria as those during the acute care. The occurrence of multiple complications was also assessed for patients having experienced more than one complication.

Statistical analyses

In order to compare the two groups (early vs. no early spasticity), we first used non-parametrical analyses (Mann-Whitney tests for continuous variables and chi-square tests for categorical

variables), considering that Kolmogorov-Smirnov tests revealed a non-normal distribution. We used IBM SPSS Statistics Version 24 software package for all statistical analyses. The level of significance was set to 0.05 for all statistical analyses.

A General Linear Model (GLM) based on multivariable linear regression analyses was performed, using main effects and a backward elimination method to analyze the relationship between the presence of “early spasticity” (main independent variable) and the total inpatient rehabilitation LOS (dependent variable), accounting for clinical confounding factors available during acute care. Nine variables were entered in the multivariate model as covariables: 1) AIS grade; 2) neurological level of injury; 3) presence and severity of concomitant traumatic brain injury; 4) age (as continuous); 5) injury severity score (ISS) (as continuous); 6) comorbidities (CCI); 7) BMI (as continuous); 8) presence of complications during acute care; 9) surgical delay (as continuous). The strength of association of the independent variable included in the final GLM was expressed by the beta coefficient (β coefficient) with their respective 95% confidence interval (95%CI) and p-values. The R-square value refers to the percentage of variance of the outcome variable explained by the independent variables included in the final GLM.

Finally, as secondary objective, a multinomial logistic regression analyses were performed to determine the impact of the development of early spasticity during the acute care hospitalization on the discharge destination after IFR. The outcome (dependent) variable for this model was categorized into three categories: 1) discharge home; 2) discharge to transitional inpatient rehabilitation, and 3) discharge to long-term nursing care or others (readmission to acute care hospital, death, etc.). Again, the main independent variable was the development of early spasticity (Group 1 vs. Group 2). Seven other variables were entered in the multivariate model as covariables:

1) AIS grade; 2) neurological level of injury; 3) presence and severity of concomitant traumatic brain injury; 4) age (as continuous); 5) injury severity score (ISS) (as continuous); 6) comorbidities (CCI); 7) BMI (as continuous). Main effects statistic models were used with the orientation in transitional inpatient rehabilitation center as reference category for the dependent variable in model A, and discharge home as the reference category from model B. The strength of association with the discharge orientation is expressed in terms of odd ratios with 95% confidence interval (95%CI) and p-values. Non-significant independent variables at the likelihood ratio test were excluded from the final model. The goodness-of-fit of the final model is expressed by the Nagelkerke R^2 value.

Results

Patient characteristics

The study cohort consisted in 150 patients with a mean age of 51.3 ± 18.2 years old. Baseline characteristics of the total cohort, and separately for Groups 1 and 2 are showed in Table 1. A total of 95 (63.3%) subjects developed spasticity during the acute care hospitalization (Group 2), while 55 (36.7%) did not (Group 1). A total of 56.8% of individuals with a complete TSCI (AIS grade A) developed spasticity during acute care, in comparison with 66.7%, 77.1% and 59.6% for individuals sustaining an AIS grade B, C and D injury respectively ($p=0.26$). Similarly, 59.3% of individuals with a C1-C4 cervical TSCI developed spasticity during the acute care, while 65.6% and 66.7% of individuals with lower cervical TSCI or paraplegia did, respectively ($p=0.70$).

There were no significant differences between the two groups in terms of age, BMI, comorbidities, associated traumatic injuries (ISS), surgical delay and characteristics of the TSCI (NLI and AIS grade) (Table 1). However, individuals with early spasticity (Group 2) developed a significantly higher proportion of medical complications during the acute stay than individuals without (Table 1). The incidence of PU during acute care was also significantly higher in the early spasticity group (Table 1). Finally, the acute care LOS reached almost 30 days in the early spasticity group, while it was closer to 20 days in the non-early spasticity group (Table 1).

Comparison of the IFR clinical course is showed in Table 2. Individuals with early spasticity showed a tendency, to develop more medical complications during the IFR, but the difference was not significant (Table 2). Individuals in Group 2 were hospitalized almost 20 days longer in the IFR center than individuals in Group 1 (Table 2). Almost 80% of subjects with early spasticity

were discharged home after IFR, as compared to 58.9% in the non-early spasticity group (Table 2). On the other hand, individuals in Group 2 were more likely to require an extended period of rehabilitation in a transitional inpatient rehabilitation facility than Group 1. Post-hoc tests revealed that both discharge home and transitional inpatient rehabilitation facility were significantly different between the two groups, with the latter contributing the most to the difference observed (with a adjusted standardized residual of 2.6). Ultimately, the final destination (after inpatient rehabilitation process) was significantly different between the two Groups (Table 2). According to post-hoc tests results, individuals from Group 2 could ultimately return to a private residence in a lower proportion than Group 1 (adjusted standardized residuals of 2.4). These individuals were also sent in a higher proportion in a long-term nursing home (adjusted standardized residuals of 2.0) (Table 2).

Early spasticity was also revealed as a significant factor associated with increased total inpatient rehabilitation LOS, independently of the characteristics of the individual and of the TSCI considered in this study (Table 3). The AIS-grade and the presence of acute medical complication were also significantly associated with increased total inpatient rehabilitation LOS.

Finally, the final multinomial logistic regression model is shown in Table 4. From the eight independent variables included in the analyses, five were excluded (ISS, BMI, CCI, NLI and presence of concomitant traumatic brain injury) because they were not associated with the main outcome (discharge destination) in the likelihood ratio tests ($p > 0.05$). Three independent variables (age, presence of early spasticity and AIS grade) were thus included in the final model. Model A shows the impact of each independent variable on the likelihood of being discharged home and in a nursing home, as compared to being discharged in a transitional inpatient rehabilitation facility.

Model B shows the impact for each independent variable on the likelihood of being discharged in a transitional inpatient rehabilitation facility and in a nursing home, as compared to being discharged home.

Absence of early spasticity increased 5 times the odds of being discharged home as compared to discharge in a transitional inpatient rehabilitation facility (Table 4 A). Absence of early spasticity decreased the odds ($OR=0.2$) of being discharged to a transitional inpatient rehabilitation facility after IFR as compared to discharge home (Table 4 B). The goodness of fit of both models was fair, explaining 27.3% of the variance (Nagelkerke $R^2=0.273$).

Discussion

Spasticity is an important clinical issue for individuals with TSCI, as it may be associated to pain, interfere with mobility and decrease quality of life.^{7, 24} As the acute care hospitalization is the first step of the continuum of care following a TSCI, its process may influence subsequent rehabilitation phases and reintegration to community. However, the impact of the occurrence of spasticity during acute care on the rehabilitation process remains largely unknown. This study is the first, to our knowledge, to demonstrate the negative impact of the presence of early spasticity on the IFR outcomes and community reintegration.

A majority of our cohort (63.3%) developed velocity-dependant hypertonia, spasms and/or clonus during their acute care hospitalization. The incidence of spasticity obtained in this study is in the lower range previously reported in the SCI population (65-78%).^{2, 7} This result was expected since previous studies have investigated the incidence of spasticity in the sub acute or chronic phases following TSCI. This study may suggest that a great majority of individuals who will develop spasticity will experience signs and symptoms within the first month following the injury. This study may also help in defining the natural history of spasticity, which remains largely unknown in the TSCI population. Our cohort was similar to the Canadian SCI population in terms of baseline characteristics (age, level and severity of the TSCI), acute care and IFR LOS, as well as discharge destination after IFR.¹³

Results also showed that individuals with early spasticity were hospitalized significantly longer (both acute care and IFR) as compared to their counterparts, despite similar baseline and injury characteristics. The occurrence of spasticity early in the continuum of care may thus interfere with

the rehabilitation process significantly enough to also influence the discharge destination after IFR. Indeed, individuals with early spasticity were more likely to require an extended inpatient rehabilitation in a transitional facility than individuals who have not developed spasticity in acute care. Moreover, spasticity increased the odds five-fold of transferring to an inpatient transitional rehabilitation center after IFR as opposed to discharging home, after considering confounding factors related to the characteristics of the individual and the TSCI.

Many hypotheses may explain these results. First, motor behaviours related to spasticity are showed to interfere with functional recovery following a TSCI, such as the presence of muscle hypertonia, antagonist muscle co-activation and spasms activity. [ENREF 16](#)²⁵ These motor behaviours may further decrease mobility and performance in daily living activities.^{26, 27} Thus, the occurrence of early spasticity may create a further challenge to functional recovery from the beginning of the rehabilitation process, as compared to individuals who will not develop spasticity or develop it later in the process. This highlights the impact of spasticity relatively to the continuum of care, and the importance of a proper acute rehabilitation process following a TSCI.

Spasticity may also indirectly impact the rehabilitation process due to its association with the incidence of medical complications. Indeed, individuals with early spasticity sustained a higher proportion of medical complications during acute care. The association between spasticity and medical complication has already been demonstrated in previous work.^{7, 27} However, it is difficult to determine in which direction these two factors are related. Their association may be bilateral, as spasticity may lead to PU and contractures, which can ultimately lead to immobility and other complications;²⁷ while the nociceptive input related to complications may increase signs and symptoms of spasticity.¹ Both processes may have contributed to results of this study. The

association between spasticity and medical complications is also likely to have participated to the longer LOS (both in acute care and the IFR) observed in this study.²⁸ The acute rehabilitation team should maintain a high vigilance towards the prevention/treatment of medical complications, particularly for PU in acute care, for individuals with early spasticity.

As spasticity and motor recovery are both related to neural plasticity,²⁹ one may question if early spasticity may be an indication for aggressive treatment. Although this relationship remains poorly understood, the stroke literature suggested that early interventions may create a transient plastic state of the neuromotor system, allowing higher motor re-learning and neuro-functional recovery.²⁹ It is thus possible that aggressive management of early spasticity may be beneficial. Future studies in the SCI population are needed to investigate this hypothesis. Spasticity management in SCI population remains quite subjective and is generally based on the reduction of ‘passive problems’ (preventing contracture, reducing pain, facilitating splint wearing, easing positioning and hygiene, etc.).¹⁷ It is recognized that pharmaceutical treatment with Baclofen (frequently used in TSCI care) may have no positive effect on daily living activities and may impede ability of SCI patients to walk or stand.^{17, 30} Thus, authors of this study may suggest aggressive management of early spasticity with non-pharmaceutical interventions (positioning, range of motion, stretching, weight-bearing, muscle strengthening, electrical stimulation, cold/heat application, splinting/orthosis.¹⁷ Pharmaceutical treatment may be considered for refractory and problematic spasticity.⁷ However, injection techniques with chemodenervation agents may deserve more attention for regional early spasticity, as this technique is used in other neurological conditions (acute traumatic brain injuries).³¹

Limitations

The main limitations of this study relate to its retrospective nature and the low number of patients. This study also took place in a single hospital center limiting generalizability. The authors also acknowledge that information pertaining to the severity and clinical signs/symptoms of spasticity could have helped in better understanding its relationship with the IFR outcomes. A prospective cohort study is thus recommended. Finally, this study cannot draw any conclusions on the impact of the occurrence of early spasticity *in terms of time* after the injury, since the acute care LOS was significantly different between the two groups. On the other hand, this study aimed to investigate the impact of early spasticity *with regards to the rehabilitation phases* as part of the continuum of care following a TSCI. Using timeline of spasticity in terms of rehabilitation phases may help in guiding clinicians to ultimately better define the objectives and the role acute rehabilitation, which still remain unclear.

Conclusion

Spasticity may lead to decreased functional outcome and reduced quality of life in the chronic phase following a TSCI. However, the impacts of developing signs and/or symptoms of spasticity during acute phase following TSCI remain unclear. Yet, the acute care hospitalization is a critical step involved in the rehabilitation process and continuum of care for this clientele. Results of this study showed that the occurrence of spasticity during the acute care hospitalization was associated to a significant longer rehabilitation LOS and increased the odds of being discharged to an inpatient transitional rehabilitation center as opposed to discharged home after the IFR. Presence of early spasticity was also revealed as a significant factor associated with increased total inpatient rehabilitation LOS, independently of the characteristics of the individuals and the trauma. Individuals with early spasticity may experience challenges from additional motor control deficits related to spasticity and sustain a higher incidence of medical complications. This may impede the rehabilitation process from the acute care phase and thus explain poorer IFR outcomes. Higher vigilance towards the prevention of complications in patients who develop spasticity during the acute care phase is recommended. Aggressive treatment using non-pharmaceutical interventions is also recommended. Future studies may investigate if an aggressive management using pharmaceutical treatment (oral medication or injection techniques) of early spasticity may be beneficial.

References

1. Hinderer SR, Dixon K. Physiologic and clinical monitoring of spastic hypertonia. *Phys Med Rehabil Clin N Am*. 2001;12(4):733-46.
2. Hsieh JT, Wolfe DL, Miller WC, Curt A, Team SR. Spasticity outcome measures in spinal cord injury: psychometric properties and clinical utility. *Spinal Cord*. 2008;46(2):86-95.
3. Ivanhoe CB, Reistetter TA. Spasticity: the misunderstood part of the upper motor neuron syndrome. *American journal of physical medicine & rehabilitation / Association of Academic Physiatrists*. 2004;83(10 Suppl):S3-9.
4. Dietz V, Sinkjaer T. Spastic movement disorder: impaired reflex function and altered muscle mechanics. *The Lancet Neurology*. 2007;6(8):725-33.
5. Hiersemenzel LP, Curt A, Dietz V. From spinal shock to spasticity: neuronal adaptations to a spinal cord injury. *Neurology*. 2000;54(8):1574-82.
6. Ditunno JF, Little JW, Tessler A, Burns AS. Spinal shock revisited: a four-phase model. *Spinal cord*. 2004;42(7):383-95.
7. Adams MM, Hicks AL. Spasticity after spinal cord injury. *Spinal Cord*. 2005;43(10):577-86.
8. Bhimani RH, Anderson LC, Henly SJ, Stoddard SA. Clinical measurement of limb spasticity in adults: state of the science. *The Journal of neuroscience nursing : journal of the American Association of Neuroscience Nurses*. 2011;43(2):104-15.
9. Adams MM, Ginis KA, Hicks AL. The spinal cord injury spasticity evaluation tool: development and evaluation. *Archives of physical medicine and rehabilitation*. 2007;88(9):1185-92.
10. Lechner HE, Frotzler A, Eser P. Relationship between self- and clinically rated spasticity in spinal cord injury. *Archives of physical medicine and rehabilitation*. 2006;87(1):15-9.

11. Walter JS, Sacks J, Othman R, Rankin AZ, Nemchausky B, Chintam R, et al. A database of self-reported secondary medical problems among VA spinal cord injury patients: its role in clinical care and management. *J Rehabil Res Dev*. 2002;39(1):53-61.

12. Moutquin J. Lésions médullaires traumatiques et non-traumatiques: analyse comparative des caractéristiques et de l'organisation des soins et services de réadaptation au Québec. In: INESSS, editor.: *Bibliothèque et archives nationales du Québec, ETMIS*; 2013. p. 1-44.

13. Noonan VK, Kwon BK, Soril L, Fehlings MG, Hurlbert RJ, Townson A, et al. The Rick Hansen Spinal Cord Injury Registry (RHSCIR): a national patient-registry. *Spinal Cord*. 2012;50(1):22-7.

14. Richard-Denis A, Beausejour M, Thompson C, Nguyen BH, Mac-Thiong JM. Early predictors of global functional outcome after traumatic spinal cord injury: a systematic review. *J Neurotrauma*. 2018.

15. Dvorak MF, Fisher CG, Hoekema J, Boyd M, Noonan V, Wing PC, et al. Factors predicting motor recovery and functional outcome after traumatic central cord syndrome: a long-term follow-up. *Spine (Phila Pa 1976)*. 2005;30(20):2303-11.

16. Milicevic S, Piscevic V, Bukumiric Z, Nikolic AK, Sekulic A, Corac A, et al. Analysis of the factors influencing functional outcomes in patients with spinal cord injury. *J Phys Ther Sci*. 2014;26(1):67-71.

17. Graham LA. Management of spasticity revisited. *Age Ageing*. 2013;42(4):435-41.

18. Charlson M, Wells MT, Ullman R, King F, Shmukler C. The Charlson comorbidity index can be used prospectively to identify patients who will incur high future costs. *PLoS One*. 2014;9(12):e112479.

19. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, et al. International standards for neurological classification of spinal cord injury (revised 2011). *J Spinal Cord Med*. 2011;34(6):535-46.

20. Baker SP, O'Neill B. The injury severity score: an update. *J Trauma*. 1976;16(11):882-5.
21. Medicine CfSC. Respiratory management following spinal cord injury: a clinical practice guideline for health-care professionals. *J Spinal cord Med*. 2005;28:259-93.
22. Medicine CfSC. Bladder management for adults with adults with spinal cord injury: a clinical practice guideline for health-care providers. *J Spinal cord Med*. 2006;29(5):527-73.
23. NPUAP-EPUAP I. NPUAP pressure ulcer stages/categories. 2007.
24. Pandyan AD, Gregoric M, Barnes MP, Wood D, Van Wijck F, BurrIDGE J, et al. Spasticity: clinical perceptions, neurological realities and meaningful measurement. *Disabil Rehabil*. 2005;27(1-2):2-6.
25. McKinley W, Santos K, Meade M, Brooke K. Incidence and outcomes of spinal cord injury clinical syndromes. *The journal of spinal cord medicine*. 2007;30(3):215-24.
26. Carr JH SR, Ada L. Spasticity: research findings and implications for intervention. *Physiotherapy*. 1995;81(8):1.
27. Kheder A, Nair KP. Spasticity: pathophysiology, evaluation and management. *Pract Neurol*. 2012;12(5):289-98.
28. Richard-Denis A, Feldman D, Thompson C, Mac-Thiong JM. Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization. *The journal of spinal cord medicine*. 2017:1-9.
29. Li S. Spasticity, Motor Recovery, and Neural Plasticity after Stroke. *Front Neurol*. 2017;8:120.
30. Montane E, Vallano A, Laporte JR. Oral antispastic drugs in nonprogressive neurologic diseases: a systematic review. *Neurology*. 2004;63(8):1357-63.

31. Zafonte R, Elovic EP, Lombard L. Acute care management of post-TBI spasticity. J Head Trauma Rehabil. 2004;19(2):89-100.

Table3. Clinical factors associated with the total inpatient rehabilitation length of stay: results of the final general linear model (n-150)

Predictive factors		β (95%CI)	P value
Early spasticity			
Absence (Group 1)		-39.7 (-69.7;-9.7)	0.01**
Presence (Group 2)		Ø	
Initial AIS grade			
AIS-A		100.0 (65.0;135.1)	0.000*
AIS-B		75.2 (30.3;120.1)	0.001**
AIS-C		51.7 (15.0;88.4)	0.006**
AIS-D		Ø	
Complications during acute care			
Absence		-34.9 (-64.5;-5.2)	0.02**
Presence		Ø	
R-square = 31.9%			

AIS, American Spinal Injury Association Impairment Scale.

Ø: Reference category.

*P is significant if <0.05.

18. Appendix 13: Status of tasks reported on the statement of work

Major Task 1: Finalize research protocol.

Completed.

Major Task 2: Participant recruitment and follow-up.

Subtask 1: Recruitment of patients.

Completed.

Subtask 2: Follow-up of patients.

Completed: We have redefined the initial "two-year follow-up visit" as a long-term follow-up visit, to be performed at least 2 years after the spinal cord injury. We have tried to limit the loss to the follow-up rate and should not bias our data because we estimate that a recovery tray is reached about one year after the injury. As of September 30, 2017, 64 patients had completed the long-term follow-up visit. We recovered 5 long-term follow-ups in January-February 2019 due to our new system to reach patients.

Major Task 3: Data collection

Subtask 1: Socio-demographic and clinical data collection

Completed.

Subtask 2: Neurological, functional and quality of life data

Completed.

Aim 1 - Costs and length of stay vs. surgical delay.

Major Task 4: Evaluate costs and length of stay with respect to surgical delay.

Completed. We published a manuscript: Richard-Denis A, Feldman DE, Thompson C, Bourassa-Moreau E, Mac-Thiong JM. Costs and length of stay for the acute care of patients with motor-complete spinal cord injury following cervical trauma: the impact of early transfer to specialized acute SCI center. Am J Phys Med Rehabil 2017.

Aim 2 - Complications vs. surgical delay.

Major Task 5: Evaluate global and specific complication rates with respect to surgical delay.

Completed. This aim has been partially addressed when comparing the impact of early transfer and peri-operative management in our SCI-center to late, post-surgery transfer to our SCI (Richard-Denis et al., 2017, J Spinal Cord Med). This was performed in patients with motor-complete tetraplegia exclusively.

Aim 3 - Neurological recovery, function and quality of life vs. surgical delay.

Major Task 6: Evaluate neurological recovery, function and quality of life with respect to surgical delay.

Subtask 1: Neurological recovery

Completed.

We have published a manuscript: Richard-Denis A, Feldman DE, Thompson C, Mac-Thiong JM. The impact of acute management on the occurrence of medical complications during the specialized spinal cord injury acute hospitalization following motor-complete cervical spinal cord injury. J Spinal Cord Med 2017.

Subtask 2: Functional recovery

Completed.

We have published a manuscript: Facchinello Y, Beauséjour M, Richard-Denis A, Thompson C, Mac-Thiong JM. The use of regression tree analysis for predicting the functional outcome following traumatic spinal cord injury. J Neurotrauma. Surgical timing was not revealed as a significant predictor using CART analyses.

Subtask 3: Quality of life

Completed.

We have published a manuscript: Goulet J, Richard-Denis A, Thompson C, Mac-Thiong JM. Relationships between specific functional abilities and health-related quality of life in chronic spinal cord injury. Arch Phys Med Rehabil. October 17, 2017. We Also published: Richard-Denis A, Thompson C, Mac-Thiong JM. Quality of life in the subacute period following a cervical traumatic spinal cord injury based on the initial severity of the injury: a prospective cohort study. Spinal Cord. Nov 2018