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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

15. SUBJECT TERMS

Spinal cord injury; surgery; delay; recovery; trauma; complications; length of stay; costs

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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

Recruitment of patients was completed in September 2014.

b) Follow-up of patients

Follow-up of patients is still in progress. Fifty-seven patients have completed their 2-year follow-up 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, their 2-year follow-up and the outcome data collection should be completed.

d) Data analysis

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

e) Publications and conferences

To date, we have presented 3 abstracts at the 4th ASIA and ISCoS Joint Scientific Meeting held in Montreal (Canada) in May 2015, and 5 abstracts at the ASIA 2016 Annual Scientific Meeting in April 2016. One manuscript related to neurological recovery was published in Journal of Neurotrauma, and another manuscript on the barriers to early surgery was published in Journal of Spinal Cord Medicine. A third manuscript on the costs and hospitalization duration is in press in American Journal of Physical Medicine and Rehabilitation.

What was accomplished under these goals?

For the third year of funding, the major goals were to pursue and complete the 1-year and 2-year 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). We have obtained a 1-year no-cost extension, so funding end date is now September 29, 2017.

a) Recruitment of patients

Recruitment is completed since September 2014. Information related to this goal was provided in previous Annual reports.

b) Follow-up of patients

With respect to patients' follow-up, as of September 30, 2016, 84 patients had their 6-month follow-up completed, 87 patients came for their 1-year follow-up and 57 have done their 2-year follow-up. For these 57 patients, the participation to this study is terminated.

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 pertaining to outcomes during the follow-up visits has been collected (functional recovery – SCIM; quality of life – SF-36 and WHO-QoL; ASIA).

d) Data analysis

Data analyzed in the last year led to the presentation of five abstracts at the 2016 ASIA Annual Scientific Meeting, as well as to two published manuscripts. Three papers using data collected under this study were produced; one is in press in American Journal of Physical Medicine and Rehabilitation and two are submitted to Journal of Spinal Cord Medicine. The main results obtained so far are presented in the "Publications and conferences" section below.

e) Publications and conferences

We have presented abstracts at the 2016 ASIA Annual Scientific Meeting in Philadephia, PA (April 2016). Two papers were published (1 and 2), one is in press (3), and two are under review (4, 5).

Paper 1: Étienne Bourassa-Moreau, Jean-Marc Mac-Thiong, Ang Li, Debbie Ehrmann Feldman, Dany H. Gagnon, Cynthia Thompson, Stefan Parent. Do patients with complete spinal cord injury benefit from early surgical decompression? Analysis of neurological recovery in a prospective cohort study. ***J Neurotrauma*** **2016; 33(3): 301-6.** *(see Appendix 1)*

The prognosis for neurological improvement (NI) in complete traumatic spinal cord injury is generally poor. It is unknown whether early surgical timing improves NI in the complete traumatic SCI population. The objectives of this study were: 1) to compare the effect of early and late surgical decompression on NI of complete traumatic SCI 2) to assess if surgical timing differently impacts on cervical or thoracolumbar SCI. A prospective cohort study was performed in a single Level 1 trauma center specialized in SCI care. All consecutive cases of traumatic SCI referred between 2010 and 2013 were screened for eligibility. Neurological status was assessed systematically using the ASIA grading system at first arrival to the trauma center and the NI was assessed at rehabilitation discharge. Patients operated within 24h of the trauma were compared with patients operated later than 24h after the trauma. Potential confounders were recorded such as the age, Injury Severity Score (ISS), smoking, body mass index (BMI), the Glascow Coma Scale (GCS) and duration of follow-up.

Fifty-three complete SCI were included in the study with 33 thoracic SCI and 20 cervical SCI. The 38 patients operated <24h were generally younger than the 15 patients operated after 24h although no other potential confounder were statistically different (Table 1). Overall, 28% (15/53) of complete SCI had some NI with 34% (13/38) of patients operated <24h and 13%(2/15) of patients operated ≥24h ($p=0.182$; Figure 1). Sixty-four percent (9/14) of cervical complete SCI operated <24h had some NI whereas none of the 6 complete cervical SCI operated ≥24h improved ($p=0.008$; Figure 2; Table 2). There was no difference in the proportion of patients with a thoracolumbar lesion who had NI based on the surgical delay (Table 2). This study suggests that surgical decompression earlier than 24h in complete SCI may promote improvement in neurological status, especially at the cervical level.

Table 1: Demographic and clinical data of all ASIA A SCI patients

	<24 h *Mean ± SD*	*≥24 h* *Mean ± SD*	*Total* *Mean ± SD*	p *value*
N	38	15	53	
Age (years)	39.6 ± 16.6	49.6 ± 15.4	42.4 ± 16.8	0.049
Sex (female)	11% (4/38)	27% (4/15)	15% (8/53)	0.202
BMI (kg/m^2)	26.3 ± 3.9	26.0 ± 4.0	26.2 ± 3.9	0.953
Comorbidity	26% (10/38)	40% (6/15)	30% (16/53)	0.342
Nonsmoker	76% (29/38)	67% (10/15)	74% (39/53)	0.729
GCS	13.8 ± 2.5	13.7 ± 2.4	13.8 ± 2.4	0.770
ISS	32.1 ± 10.8	34.4 ± 14.1	32.8 ± 11.7	0.252
Surgical timing (h)	16.1 ± 4.9	39.1 ± 16.3	22.6 ± 14.1	<0.001
Follow-up (days)	150.6 ± 39.7	156.9 ± 31.2	152.4 ± 37.3	0.580

SD, standard deviation; BMI, body mass index; GCS, Glasgow Coma Scale; ISS, Injury Severity Score.

Figure 1: The percentage of ASIA grade at last follow-up of all patients with an initial complete SCI. Patients operated <24h post-trauma (38 patients) are compared to patients with operated ≥24h post-trauma (15 patients).

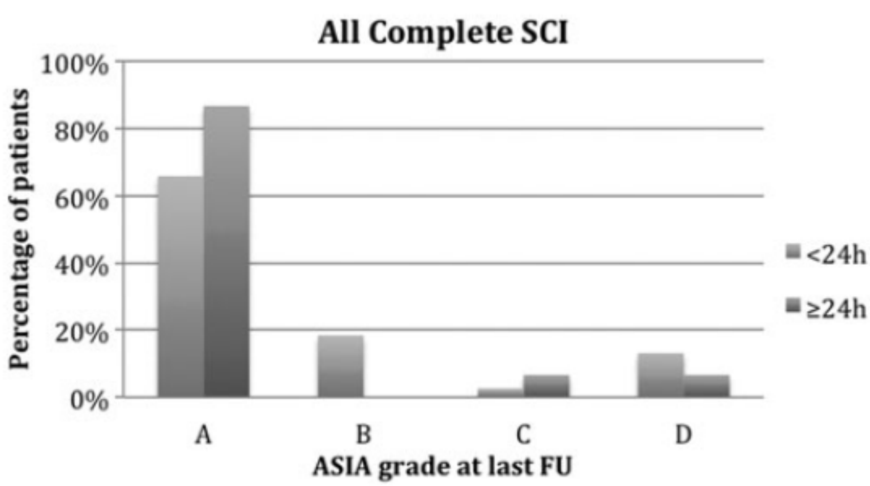

Figure 2: The percentage of ASIA grade at last follow-up of initially complete cervical SCI. Patients operated <24h post-trauma <24h (14 patients) is compared to patients operated ≥24h post-trauma (6 patients).

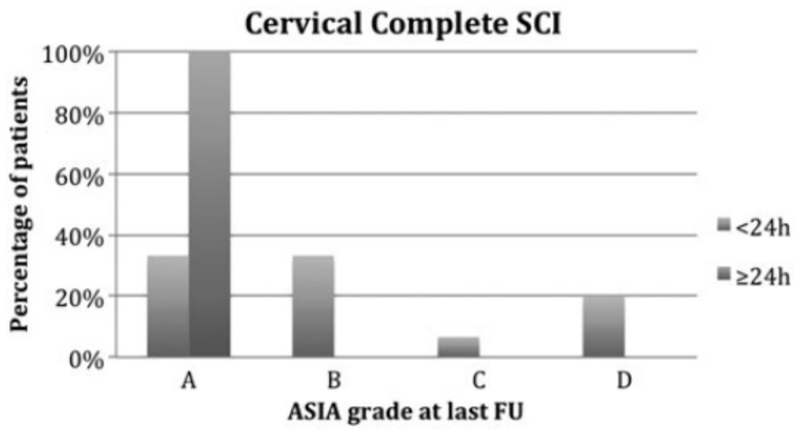

Table 2: Conversion of ASIA grade in complete SCI operated <24h and ≥ 24h

	<24 h	*≥24 h*	*Total*	p *value**
All patients	34% (13/38)	13% (2/15)	28% (15/53)	0.182
Stratification for lesion level				
Thoracolumbar SCI	17% (4/20)	22% (2/9)	18% (6/33)	0.999
Cervical SCI	64% (9/14)	0% (0/6)	45% (9/20)	0.008
Stratification for age				
Age <40	36% (8/22)¶	33% (1/3)*	36% (9/25)	0.999
Age ≥40	31% (5/16)¶	8% (1/12)*	21% (6/28)	0.196

SCI, spinal cord injury.

Improvement rate was not statistically different between the two age groups (¶, $p=0.9999$; *, $p=0.370$).

Paper 2:_ Cynthia Thompson, Debbie E. Feldman, Jean-Marc Mac-Thiong. Surgical management of patients following traumatic spinal cord injury: identifying barriers to early surgery in specialized SCI care centers . *J Spinal Cord Me*d 2016; Apr 8: 1-7.
(see Appendix 2)

Background: Early surgery in individuals with traumatic spinal cord injury (T-SCI) can improve neurological recovery and reduce complications, costs and hospitalization. Non-modifiable patient-related and modifiable healthcare-related factors could influence surgical delay. This study aimed at determining factors contributing to surgical delay in individuals with T-SCI.

Methods: Socio-demographic and clinic-administrative data were collected during the pre-operative period among a prospective cohort including 144 consecutive, eligible individuals with T-SCI admitted in a single Level I trauma centre. The cohort was stratified in two subgroups: early (<24h; N=93) and late (≥24h; N=51) surgery. A multivariate logistic regression analysis using patient- and healthcare-related factors was carried out to identify the main predictors of surgical delay.

Results: The early surgical subgroup underwent surgery 15.6±4.7h post-trauma, which is roughly 32h earlier than the late surgery subgroup (46.9±30.9h; $p<10^{-3}$; Table 3). For the early surgical subgroup, the transfer delay from trauma site to the SCI Level I trauma center was on average 8h shorter (5.0±3.0h vs 13.6±17.0; $p<10^{-3}$) and the surgical team finalized the surgical plan 17h faster (6.0±4.0h vs 23.3±23.6h; $p<10^{-3}$) than the late surgery subgroup (Figure 3). The occurrence of late surgery was predicted by three modifiable factors, mostly the transfer delay to the SCI-center, the delay before surgical plan completion, and the waiting time for the operating room after surgical plan completion. A one-hour increase in one of these factors doubles the odds of patients undergoing late surgery (Table 4). No patient-related factors predicted surgical delay.

Conclusions: A dedicated team for surgical treatment of individuals with T-SCI, involving direct transfer to the SCI-center and faster surgery planning and prompter access to the operating in hospitals dealing with emergencies from all subspecialties could greatly improve surgical delay and increase the rate of patients undergoing early surgery.

Table 3: Average delays (±SD) encountered by patients operated within 24h post-trauma (early surgery) and 24h or more following the trauma (late surgery).

Time interval (h)	ES (<24 h)	LS (≥24 h)	P
Trauma—Arrival SCI center	5.0 ± 3.0	13.6 ± 17.0	$<10^{-3}$
Trauma—Arrival other CH	1.2 ± 1.1	3.3 ± 4.9	0.002
Arrival at other CH—Arrival SCI center	3.8 ± 2.7	10.3 ± 15.6	$<10^{-3}$
Arrival SCI center—Surgery	10.6 ± 4.3	33.3 ± 26.5	$<10^{-3}$
Arrival SCI center—First assessment by MD	2.0 ± 1.6	3.1 ± 3.8	0.18
First assessment by MD—Surgical plan completion	6.0 ± 4.0	23.3 ± 23.6	$<10^{-3}$
Surgical plan completion—Surgery	2.6 ± 2.2	7.0 ± 12.4	0.31
Trauma—Surgery	15.6 ± 4.7	46.9 ± 30.9	$<10^{-3}$

ES: early surgery; LS: late surgery

Table 4: Factors from a multiple logistic regression analysis predicting late surgery

	B	SE-B	Wald	P	Odds (95% CI)
Delay of transfer from CH to SCI center	0.907	0.264	11.770	0.001	2.476 (1.475–4.157)
Delay surgical plan completion—surgery	0.906	0.279	10.541	0.001	2.474 (1.432–4.275)
Delay first medical assessment—surgical plan completion	1.036	0.275	14.242	0.000	2.819 (1.646–4.829)

Paper 3: Andréane Richard-Denis, Cynthia Thompson, Jean-Marc Mac-Thiong. 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 transfer to specialized acute SCI center. *Am J Phys Med Rehabil* 2016; *in press* (also presented in abstract form at the 2016 ASIA Annual Scientific Meeting, April 2016; see appendix 3).

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 SCI-center. Design: A retrospective cohort study involving 116 individuals was conducted. Group 1 (N=87) were managed in a SCI-center promptly after the trauma, whereas Group (N=29) was transfer to 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: LOS was significantly longer for Group 2 (median of 93,0 days) as compared to Group 1 (median of 40,0 days, p<10-3), and average costs ($CAN) were also higher (median of 17 920$ vs 10 560$; 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 SCI-center was associated with shorter LOS and lower costs for patients sustaining tetraplegia. Early referral to a SCI-center before surgery could lower the financial costs for the healthcare system.

Table 5: Demographic and clinical characteristics of patients early and lately transferred to a SCI-center following a motor-complete cervical SCI.

		Early transfer (SCI center-Group 1)	Late transfer (NS center-Group 2)	p-value
N	---	*87*	*29*	---
1. Age	Median (IQR)	46.0 (28.6-62.0)	48.0 (23.5-64.5)	0.97
2. Gender	% Male	78.2	82.8	0.60
3. ISS	% ≥*29*	39.1	58.6	0.053
4. ASIA grade	% A	65.5	82.8	0.08
	% B	34.5	17.2	
5. Neurological level	% C1-C4	51.7	62.1	0.33
6. Traumatic brain injury	% TBI	51.3	27.6	0.02*
7. In-hospital death	% deceased	9.2	6.9	0.70
8. Surgical delay	% >24h post injury	54.0	51.7	0.83
9. Respiratory complications	%	54.0	51.7	0.83
10. Pneumonia	%	47.1	41.4	0.67
11. Pressure ulcer	%	36.8	34.5	1.00
12. Urinary tract infection	%	20.7	31.0	0.31
13. At least one complication (one or more)	%	71.3	72.1	1.00
14. Multiple complications (two and more)	%	44.8	37.9	0.67

ISS: Injury severity score

Table 6: Hospitalization length of stay (LOS) in patients with a motor-complete cervical spine injury early and lately transferred to the SCI-center (Group 1 and Group 2)

Hospitalization stay (in days)			Early transfer (SCI-center-Group 1)	Late transfer (NS center-Group 2)	p-value
Prior to SCI-center admission	Regional center (NS center)	Median (Interquartile range)	0.2 (0.1-0.3)	18.8 (8.2-36.3)	<0.001*
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*
	In the ward	Median (Interquartile range)	40.0 (24.0-67.0)	68.0 (35.5-119.0)	<0.001*
Total acute care hospitalization		Median (Interquartile range)	40.0 (24.0-67.0)	93.0 (61.0-149.0)	<0.001*

Table 7: 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 (CAD$)		**Timing of admission to SCI-center**		**p-value**
		Early transfer (SCI center-Group 1)	**Late transfer (NS center-Group 2)**	
Total	Median (IQR)	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 (IQR)	10 521.6 (6 840.2-18 895.5)	17 920.0 (11 159.3-24 500.4)	0.004*

Paper 4: Andréane Richard-Denis, Debbie E. Feldman, Cynthia Thompson, Jean-Marc Mac-Thiong. Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization. Submitted to *J Spinal Cord Injury*. May 5, 2016. *(see Appendix 4)*

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 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.

Table 8: Socio-demographic and clinical characteristics at hospital admission for individuals with tetraplegia and paraplegia (total cohort N=88)

Characteristics	*Tetraplegia N=43*	*Paraplegia N=45*	*p-value*
ASIA grade			
AIS-A,B	65.1%	82.2%	0.09
AIS-C,D	34.9%	17.8%	
Neurologic level			
High tetraplegia (C1-C4)	39.5%	---	
Low tetraplegia (C5-T1)	60.5%	---	0.11
High paraplegia (T2-T7)	--	22.2%	
Low paraplegia (T8-L1)	--	77.8%	
ASIA motor score *(mean +/-SD)*	38.1 (30.1)	59.0 (16.7)	$<10^{-3}$
Age *(mean +/-SD)*	44.3 (17.2)	40.0 (15.6)	0.40
Sex *(% Male)*	74.4%	86.7%	0,18
ISS *(mean +/-SD)*	25.7 (14.1)	27.2 (7.7)	0.08
BMI *(mean +/-SD)*	27.4 (10.2)	25.5 (4.0)	0.16
Presence of TBI	53.5%	37.8%	0.20
Presence of moderate or severe TBI	2.3%	6.7%	0.33
Early surgery *(<24h post-trauma)*	97.7%	97.8%	1.00
Acute care LOS *(in days) (mean +/-SD)*	32.7 (26.0)	27.9 (16.8)	0.15
Presence of medical complications	58.5%	40.0%	0.10
Presence of multiple complications	23.3%	15.6%	0.26
Presence of early spasticity	74.4%	48.9%	0.02*
Smoking status *(% active smoker)*	25.6%	31.1%	0.63
High-velocity trauma mechanism	41.9%	33.3%	0.27

Table 9: Factors associated with the total SCIM score six-months post injury for patients with acute traumatic tetraplegia (N=43)

	Total SCIM score		
Predictive variable	*β coefficient*	*95%CI*	*P-value*
ASIA grade			
AIS A-B	-27.3	(-42.9;-11.8)	$<10^{-3}$*
AIS C-D	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 10 : Factors associated with the total SCIM score six-months post-injury for patients with acute traumatic paraplegia (N=45)

	Total SCIM score		
Predictive variable	*β coefficient*	*95%CI*	*P-value*
ASIA grade			
AIS A-B	-19.1	(-31.3;-6.9)	$<10^{-3}$*
AIS C-D	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 5: Andréane Richard-Denis, Debbie E. Feldman, Cynthia Thompson, 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. Submitted to *J Spinal Cord Injury*. May 17, 2016. *(see Appendix 5)*

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=0.004). High cervical injuries (C1-C4) showed an important tendency to increase the likelihood of developing a complication, while high cervical injuries and increased trauma severity increased the odds of developing respiratory complications.
Conclusion: Management in a SCI-center even at a later stage during the acute hospitalization will limit the rate of complications to a level similar to that observed in patients managed exclusively in a SCI-center, but at the expense of a longer LOS. Prompt transfer to a SCI-center for complete perioperative management is recommended for motor-complete cervical SCI.

Table 11: 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
N	---	*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

Table 12: Comparison of medical complications and length of stay according to the type of perioperative acute care facility following a motor-complete cervical traumatic SCI

Occurrence of complications		**Type of perioperative acute care facility** Group 1 (SCI-center)	Group 2 (NS-center)	**p-value**
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*

Table 13: Factors associated with the occurrence of medical complications during the acute care hospitalization using multivariate logistic regression analyses

Variable	**Odd ratio**	**95%CI**	**p-value**
Type of perioperative acute care management			
Group 1 (SCI-center)	1 [d]	--	
Group 2 (NS-center)	1.1	(0.4 ; 2,9)	0.87
Neurologic level of injury			
C1-C4	2.2	(0.9 ; 5.1)	0.07*
C5-C8	1 [d]	--	
ISS			
<26	1 [d]	--	
≥26	2.0	(0.84 ; 4.5)	0.12

Table 14: Factors associated with the occurrence of respiratory complications during the acute care hospitalization using multivariate logistic regression analyses

Variable	**Odd ratio**	**95%CI**	**p-value**
Type of perioperative acute care management			
Group 1 (SCI-center)	1[d]	--	
Group 2 (NS-center)	0.7	(0.3 ; 1.8)	0.50
Neurologic level of injury			
C1-C4	3.3	(1.5 ; 7.4)	<0.01*
C5-C8	1[d]	--	
Age	0.99	(0.9 ; 1.0)	0.60
ISS			
<26	1[d]	--	
≥26	2.6	(1.2 ; 5.8)	0.02*

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

Nothing to report

How were the results disseminated to communities of interest?

Nothing to report for this period

What do you plan to do during the next reporting period to accomplish the goals?

We plan on analyzing data related to the impact of surgical delay on functional outcomes and quality of life. The results should be submitted in abstract form to upcoming international conferences interested in spinal cord injuries. We also intend to submit manuscripts derived from the abstracts and presentations to peer-reviewed journals in the field of neurotrauma and SCI.

4. IMPACT

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

Results from paper #1 emphasize the importance of performing early surgery even in SCI patients with a complete injury, in whom the potential for recovery is usually thought to be very poor.

Results from paper #2 show that the delay between trauma and surgery does not depend on the patient's health status but on logistical factors that could potentially be modified to decrease that delay.

Results from papers #3 and #5 show that early referral to a specialized SCI-center for perioperative management following a traumatic SCI is beneficial in reducing hospitalization duration and costs on the healthcare system (paper #3) as well as by requiring less resources for preventing / managing medical complications (paper #5).

Results from paper #4 show that clinical factors related to the acute hospitalization period are associated with the chronic functional outcome in tetraplegic and paraplegic patients. Some factors are non-modifiable but other could be modified by optimizing the acute care following a traumatic spinal cord injury.

What was the impact on other disciplines?

Nothing to report

What was the impact on technology transfer?
Nothing to report

What was the impact on society beyond science and technology?
Nothing to report

5. CHANGES / PROBLEMS

Changes in approach and reasons for change
Nothing to report

Actual or anticipated problems or delays and actions or plans to resolve them
The main issue in this study was with respect to the compliance of patients to come to their follow-up appointments. We do not anticipate problems or delays in the next year.

Changes that had a significant impact on expenditures
Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and / or select agents
Nothing to report

Significant changes in use or care of human subjects
Nothing to report

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

Étienne Bourassa-Moreau, Jean-Marc Mac-Thiong, Ang Li, Debbie Ehrmann Feldman, Dany H. Gagnon, Cynthia Thompson, Stefan Parent. Do patients with complete spinal cord injury benefit from early surgical decompression? Analysis of neurological recovery in a prospective cohort study. *J Neurotrauma* 2016; 33(3): 301-6. *(see Appendix 1)*

Cynthia Thompson, Debbie E. Feldman, Jean-Marc Mac-Thiong. Surgical management of patients following traumatic spinal cord injury: identifying barriers to early surgery in specialized SCI care centers . *J Spinal Cord Me*d 2016; Apr 8: 1-7. *(see Appendix 2)*

Andréane Richard-Denis, Cynthia Thompson, Jean-Marc Mac-Thiong. 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 transfer to specialized acute SCI center. *Am J Phys Med Rehabil* 2016; *in press (see Appendix 3)*

Andréane Richard-Denis, Debbie E. Feldman, Cynthia Thompson, Jean-Marc Mac-Thiong. Prediction of functional recovery six months following traumatic spinal cord injury during acute care hospitalization. Submitted to *J Spinal Cord Injury*. May 5, 2016. *(see Appendix 4)*

Andréane Richard-Denis, Debbie E. Feldman, Cynthia Thompson, 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. Submitted to *J Spinal Cord Injury*. May 17, 2016. *(see Appendix 5)*

Conference papers and presentations

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 conférence; 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 conférence; 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 présentation at the 2016 ASIA Annual Scientific Meeting (international conférence; Philadelphia, April 2016)

Website(s) or other Internet site(s)

Nothing to report

Technologies or techniques

Nothing to report

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	Cynthia Thompson Research assistant N/A 5 Data collection, reduction and analysis; communication with USAMRMC 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 Funding support	Louisane Dupré (until December 23, 2015) Research nurse N/A 2 Follow-up of patients, data collection No funding other than USAMRMC
Name Project role Researcher identifier Nearest person month worked Contribution to project Funding support	Sophie Bruneau (since December 23, 2015) Research nurse N/A 2 Follow-up of patients, data collection No funding other than USAMRMC
Name Project role Researcher identifier Nearest person month worked Contribution to project Funding support	Nathalie Ouellet Medical archivist N/A 1 Data collection No funding other than USAMRMC

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 Neurotrauma

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Do Patients with Complete Spinal Cord Injury Benefit from Early Surgical Decompression? Analysis of Neurological Improvement in a Prospective Cohort Study

Étienne Bourassa-Moreau,[1,2] Jean-Marc Mac-Thiong,[1–3] Ang Li,[1,2] Debbie Ehrmann Feldman,[1]
Dany H. Gagnon,[1] Cynthia Thompson,[2] and Stefan Parent[1–3]

Abstract

The prognosis for patients with a complete traumatic spinal cord injury (SCI) is generally poor. It is unclear whether some subgroups of patients with a complete traumatic SCI could benefit from early surgical decompression of the spinal cord. The objectives of this study were: (1) to compare the effect of early and late surgical decompression on neurological recovery in complete traumatic SCI and (2) to assess whether the impact of surgical timing is different in patients with cervical or thoracolumbar SCI. A prospective cohort study was followed in a single Level 1 Trauma Center specializing in SCI care. All consecutive patients who sustained a traumatic SCI and were referred between 2010 and 2013 were screened for eligibility. Neurological status was assessed systematically using the American Spinal Injury Association impairment scale (AIS) at arrival to the trauma center and at rehabilitation discharge. Patients operated within 24 h of the trauma were compared with patients operated later than 24 h after the trauma. Potential confounders such as age, Injury Severity Score (ISS), smoking history, body mass index (BMI), Glasgow Coma Scale (GCS) score, and duration of follow-up were recorded. Fifty-three patients with complete SCI were included in the study: 33 thoracolumbar and 20 cervical SCIs. The 38 patients operated <24 h were generally younger than the 15 patients operated ≥24 h ($p = 0.049$). Overall, 28% (15/53) of complete SCI had improvement in AIS: 34% (13/38) who were operated <24 h and 13% (2/15) who were operated ≥24 h ($p = 0.182$). Sixty-four percent (9/14) of cervical complete SCI operated <24 h had improvement in AIS as opposed to none in the subgroup of six complete cervical SCI operated ≥24 h ($p = 0.008$). Surgical decompression within 24 h in complete SCI may optimize neurological recovery, especially in patients with cervical SCI.

Key words: ASIA impairment scale; fracture; spinal cord; spinal cord injury; spine; surgery; surgical timing; trauma

Introduction

The effect of surgical timing on neurological recovery after a traumatic spinal cord injury (SCI) has been extensively studied in the last few decades. Studies have shown that early surgery is usually associated with improved neurological recovery.[1–8] The effect of early surgery for complete traumatic SCI (i.e., where no motor or sensory function is preserved at the most caudal level below the lesion) is generally believed to be poor, however. Animal studies suggest that more severe SCI responds poorly to surgical decompression even if surgery is performed within hours of the trauma.[9–11]

A recent survey of spine surgeons showed a trend toward delaying surgical decompression in complete SCI compared with incomplete SCI.[12] Moreover, the clinical decision-making tool, Thoracolumbar Injury Classifications and Severity System, minimizes the importance of surgery for complete SCI comparatively to incomplete SCI.[13] Some authors even suggest that surgical decompression in complete SCI is futile.[1] The review of Fawcett and associates,[14] however, on the natural history of traumatic SCI shows that 80% of complete American Spinal Injury Association (ASIA) impairment scale (AIS) A remains AIS A, 10% regaining to some sensory function (AIS B and about 10% of the initial AIS A patients regaining some motor function (AIS C).

Whether cervical and thoracolumbar patients classified as having an AIS A SCI carry the same prognosis for neurological recovery remains unclear. Local anatomical factors render the thoracic area more susceptible to severe traumatic SCI compared with the cervical area.[15] The thoracic spinal cord is well protected by the rib cage, which leads to a much higher amount of energy

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necessary to traumatize the spinal cord than in the cervical region. The thoracic spinal cord has limited vascularity and a smaller vertebral canal compared with the cervical spinal cord. Therefore, it may be important to distinguish between thoracic and cervical SCI, when referring to the prognosis for recovery.

So far, no prospective studies compared the neurological recovery in complete traumatic SCI in patients who underwent early and late surgical timing.

The objectives of this study were:

1. To evaluate the impact of early surgical decompression on neurological recovery in complete SCI.
2. To compare the neurological recovery between thoracolumbar and cervical complete SCI.

We hypothesized that the subgroup of cervical complete SCI would respond better to early surgical decompression than thoracolumbar SCI in terms of neurological recovery.

Methods

A prospective cohort study was performed in a Level I Trauma Center specializing in SCI care. All consecutive patients admitted with a traumatic SCI from April 2010 to April 2013 were screened for eligibility.

Inclusion criteria were:

- Minimal age of 16
- AIS A traumatic SCI at initial presentation before surgery
- Vertebral fracture and/or luxation from C1 to L2

Exclusion criteria were:

- Neurological or cognitive impairment precluding reliable neurological evaluation
- Surgical intervention performed >3 days after the trauma
- Surgical decompression and fusion performed in another center

The study protocol was approved by the Institutional Review Board, and all patients signed informed consent for their participation in the study.

Management of SCI

Immediately after arriving at the hospital, all patients were evaluated by the emergency specialist, the trauma team, and the spine surgeon. If no other neurological or medical condition precluded neurological evaluation, the first AIS assessment was made at that time point. Complete radiological evaluation including standard radiographs, computed tomography, and/or magnetic resonance imaging were performed to assess the compression and injury to the spinal cord.

Cervical traction was applied in the presence of cervical dislocation or significant cervical misalignment causing spinal cord compression. Cervical traction was not used if neurological evaluation was unreliable or if surgery was to be performed within 1 h of the diagnosis. Administration of high dose corticosteroids was not used in our institution during the study period.

The surgical approach and the indication for decompression were selected by the spine surgeon according to the neurological and radiological evaluations. After the acute hospitalization phase, all patients were transferred to a SCI intensive specialized inpatient rehabilitation program at a rehabilitation facility where they stayed until their physical and functional status reached a plateau in AIS.

Independent variable. Surgical timing (in hours) was defined as the time elapsed between the trauma and the surgical incision and constitutes the independent variable for the study. Various points of discrimination for early surgical timing are used in the literature ranging from 8 h to 4 days.[5–8,12,16] A 24 h cutoff was selected, however, because it is often recognized as the most realistic timing for early surgery that is achievable in the clinical setting and consistent with the biology of secondary injury in SCI.[12]

Dependent variable. The neurological recovery consisting of improvement in the AIS between the preoperative state and discharge from the rehabilitation center was defined as the dependent variable for this study. ASIA assessment was performed preoperatively by a physician member of the surgical team and at rehabilitation discharge by a physician specialized in SCI rehabilitation.

Confounding variables studied. Possible prognostic factors for neurological recovery were recorded: severity of traumatic injuries assessed by Injury Severity Score (ISS), age, pre-existing comorbidities, smoking, body mass index (BMI), Glasgow Coma Scale (GCS) score, and duration of follow-up. The level of neurological lesion was divided into cervical (C1–T1) and thoracolumbar (T2–L5) lesions.

Statistics

All statistical analyses were performed using the IBM SPSS Statistics 19 (Chicago, IL). The chi-square test was used for categorical variables. For continuous variables, either Student *t* tests (if Kolmogorov-Smirnov test confirmed a normal distribution of the variable), or Mann-Whitney *U* tests were used. The level of statistical significance was selected to be alpha = 0.05.

Descriptive statistics and bivariate analyses were used to characterize our cohort and to compare those who were operated within 24 h to those operated ≥24 h. We constructed a regression model to assess whether time of surgery was associated with the outcomes, adjusting for potential confounders. To address our second objective, we compared the proportions of neurological recovery (improvement in AIS) between thoracolumbar and cervical complete SCI.

Results

Fifty-five consecutive patients with a complete SCI (AIS A) injury were included in our study. Two patients, however, were excluded, because they had surgery performed >3 days after the trauma, leaving 53 patients for statistical analyses. There were 33 thoracolumbar and 20 cervical cases with complete SCI.

Seventy-two percent of patients (38/53 patients) were operated <24 h post-trauma whereas 28% (15/53) were operated ≥24 h post-trauma. Patients operated within 24 h were on average 10 years younger ($p = 0.049$). The proportion of females and patients who had comorbidities tended to be smaller in the early surgery group, although the differences were not statistically significant. The two groups were not different in terms of ISS, BMI, smoking status, and GCS score (Table 1).

Cervical traction was used in 7 (35%) of the 20 cases of cervical trauma. Six (86%) of these patients were operated within 24 h. Four (57%) of these seven patients had some neurological recovery. Figure 1 depicts the percentage of patients with their AIS at last follow-up in groups having surgery <24 h and ≥24 h for all patients.

Altogether, 15/53 patients with complete SCI improved neurologically after surgery (28% of sample). At last follow-up, six patients improved to AIS B, three to AIS C, and six to AIS D (Fig. 1). A greater proportion of patients who had surgery within the first 24 h post-trauma had some neurological improvement at discharge from rehabilitation compared with patients operated later. Indeed, 34% (13/38) of patients in the early surgery group improved from a complete (AIS A) to an incomplete spine injury (AIS B, C, or D),

Table 1. Demographic and Clinical Data of All 53 American Spinal Injury Association Impairment Scale A Spinal Cord Injury

	<24 h *Mean ± SD*	*≥24 h* *Mean ± SD*	*Total* *Mean ± SD*	p *value*
N	38	15	53	
Age (years)	39.6 ± 16.6	49.6 ± 15.4	42.4 ± 16.8	0.049
Sex (female)	11% (4/38)	27% (4/15)	15% (8/53)	0.202
BMI (kg/m^2)	26.3 ± 3.9	26.0 ± 4.0	26.2 ± 3.9	0.953
Comorbidity	26% (10/38)	40% (6/15)	30% (16/53)	0.342
Nonsmoker	76% (29/38)	67% (10/15)	74% (39/53)	0.729
GCS	13.8 ± 2.5	13.7 ± 2.4	13.8 ± 2.4	0.770
ISS	32.1 ± 10.8	34.4 ± 14.1	32.8 ± 11.7	0.252
Surgical timing (h)	16.1 ± 4.9	39.1 ± 16.3	22.6 ± 14.1	<0.001
Follow-up (days)	150.6 ± 39.7	156.9 ± 31.2	152.4 ± 37.3	0.580

SD, standard deviation; BMI, body mass index; GCS, Glasgow Coma Scale; ISS, Injury Severity Score.

Table 2. Demographic and Clinical Data of 33 Patients with American Spinal Injury Association Impairment Scale A Thoracolumbar Lesions

Thoracolumbar complete SCI	*<24 h* *Mean ± SD*	*≥24 h* *Mean ± SD*	*Total* *Mean ± SD*	p *value*
N	24	9	33	
Age (years)	40.9 ± 18.7	51.2 ± 16.5	43.7 ± 18.5	0.091
Sex (female)	8% (2/24)	11% (1/9)	9% (3/33)	0.999
BMI (kg/m^2)	25.8 ± 3.6	26.5 ± 3.8	26.0 ± 3.6	0.239
Comorbidity	25% (6/24)	22% (2/9)	24% (8/33)	0.999
Nonsmoker	83% (20/24)	67% (6/9)	79% (26/33)	0.625
GCS	14.7 ± 0.9	14.3 ± 1.3	14.6 ± 1.0	0.993
ISS	30.9 ± 7.1	33.3 ± 3.3	31.5 ± 6.3	0.381
Surgical timing (h)	16.9 ± 4.5	40.1 ± 19.7	23.2 ± 14.9	<0.001
Follow-up (days)	139.1 ± 40.5	163.6 ± 20.9	145.8 ± 37.6	0.166

SD, standard deviation; BMI, body mass index; GCS, Glasgow Coma Scale; ISS, Injury Severity Score.

compared with only 13% of patients operated more than 24 h after trauma. This difference in favor of early surgery did not reach statistical significance ($p = 0.18$).

Analysis of cervical and thoracolumbar complete SCI

Patients with a complete SCI were separated based on the level of their injury. Table 2 presents demographic and clinical data of patients with SCI with a complete injury at the thoracolumbar level, and Table 3 shows the characteristics of patients with a complete cervical injury.

There were no statistically significant differences in the clinical and demographic characteristics in patients with a thoracolumbar injury who had early or late surgery, although they tended to be 10 years younger ($p = 0.09$). The follow-up duration was longer in patients operated more than 24 h post-trauma (163.6 days vs. 139.1 days), but this difference was not statistically significant. Similar results were obtained for patients with a cervical lesion (Table 3), where patients operated within 24 h post-trauma were a decade younger, although this difference was not significant ($p = 0.20$). The follow-up delay tended to be longer for patients who had early surgery (170 vs. 147 days), but once again, this did not reach statistical significance.

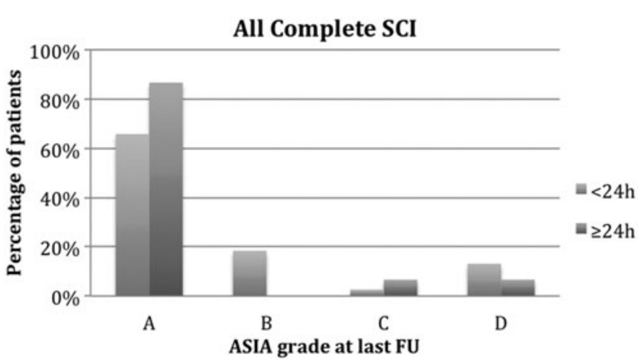

FIG. 1. The percentage of American Spinal Injury Association (ASIA) grade at last follow-up (FU) of all initially complete spinal cord injury (SCI). Patients with surgical timing <24 h (38 patients) are compared with patients with surgical timing ≥24 h (15 patients).

A total of six (18%) patients with a thoracolumbar injury had some neurological improvement at discharge from rehabilitation. The surgical delay did not impact on the proportion of patients who improved on the AIS, where 4/24 (17%) had early surgery and 2/9 (22%) were operated later (Table 4) ($p = 0.99$). Of the four patients who improved in the early surgery thoracolumbar group, two improved to AIS B and two improved to AIS D at rehabilitation discharge. One thoracolumbar patient operated later than 24 h improved to AIS C while the other improved to an AIS D level (Fig. 2).

Contrary to patients with a thoracolumbar injury, whose recovery was not linked to the surgical delay, Table 4 shows that 9/14 (64%) patients with cervical SCI operated within 24 h showed AIS improvement whereas none of the six patients with cervical SCI operated ≥24 h improved ($p = 0.008$). Five patients improved from AIS A to AIS B, one recovered to AIS C, and the remaining three patients were graded AIS D at discharge from rehabilitation (Fig. 3).

In an effort to detect the presence of bias, we stratified our analysis of neurological recovery with possible confounding factors. Our population was stratified in thoracic (T2–T9) and

Table 3. Demographic and Clinical Data of 20 Patients with American Spinal Injury Association Impairment Scale A Cervical Lesions

Cervical complete SCI	*<24 h* *Mean ± SD*	*≥24 h* *Mean ± SD*	*Total* *Mean ± SD*	p *value*
N	14	6	20	
Age (years)	37.3 ± 12.5	47.1 ± 14.7	40.3 ± 13.6	0.199
Sex (female)	14% (2/14)	50% (3/6)	25% (5/20)	0.131
BMI (kg/m^2)	27.1 ± 4.4	25.2 ± 4.4	26.6 ± 4.4	0.739
Comorbidity	29% (4/14)	67% (4/6)	40% (8/20)	0.161
Nonsmoker	64% (9/14)	67% (4/6)	65% (11/20)	0.999
GCS	12.3 ± 3.5	12.8 ± 3.4	12.5 ± 3.3	0.998
ISS	34.6 ± 16.0	36.0 ± 22.2	35.1 ± 17.7	0.999
Surgical timing (h)	14.8 ± 5.5	37.5 ± 10.9	21.7 ± 12.8	
Follow-up (days)	170.1 ± 30.3	147.0 ± 42.7	163.2 ± 35.1	0.353

SD, standard deviation; BMI, body mass index; GCS, Glasgow Coma Scale; ISS, Injury Severity Score.

Table 4. Conversion of American Spinal Injury Association Grade in Complete Spinal Cord Injury Operated <24 h and ≥24 h

	<24 h	*≥24 h*	*Total*	*p value**
All patients	34% (13/38)	13% (2/15)	28% (15/53)	0.182
Stratification for lesion level				
Thoracolumbar SCI	17% (4/20)	22% (2/9)	18% (6/33)	0.999
Cervical SCI	64% (9/14)	0% (0/6)	45% (9/20)	0.008
Stratification for age				
Age <40	36% (8/22)¶	33% (1/3)*	36% (9/25)	0.999
Age ≥40	31% (5/16)¶	8% (1/12)*	21% (6/28)	0.196

SCI, spinal cord injury.
Improvement rate was not statistically different between the two age groups (¶, $p=0.9999$; *, $p=0.370$).

thoracolumbar lesions (T10–L2), age >40 years, and ISS >30. Our cohort comprised 17 patients with thoracic neurological lesion and 16 patients with thoracolumbar lesions. Two of 17 patients with thoracic lesions improved their AIS whereas 4 of 16 with thoracolumbar lesions improved their AIS ($p=0.593$).

Stratification analysis for age was performed to assess the effect of younger age in the early surgery group. Patients <40 and ≥40 years old had similar recovery rate when operated <24 h (Table 4). ISS >30 was also studied as stratification analysis and was not associated with worse neurological prognosis ($p=0.999$).

Discussion

This study suggests that surgical decompression and stabilization earlier than 24 h after a traumatic complete SCI may improve neurological recovery and particularly for those with cervical lesions. Previous retrospective cohort studies that examined patients with incomplete and complete SCI suggested a potential for neurological recovery with early surgical intervention.[17–19] This is the first study examine this hypothesis in a population of solely complete SCI.

The neurological benefit of early surgery in complete cervical lesions is in agreement with the observations from the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS) project conducted recently.[8] The STASCIS showed a conversion rate of

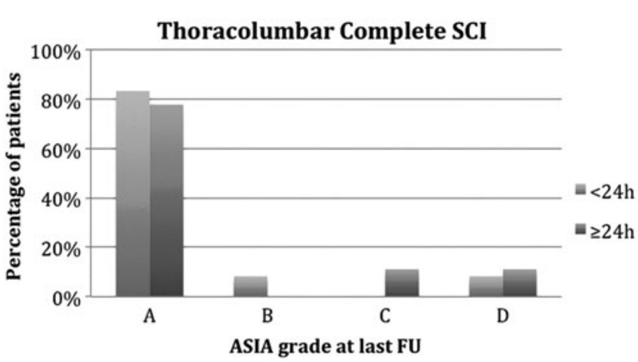

FIG. 2. The percentage of American Spinal Injury Association (ASIA) grade at last follow-up (FU) of initially complete cervical SCI. Patients with surgical timing <24 h (14 patients) are compared with patients with surgical timing ≥24 h (6 patients).

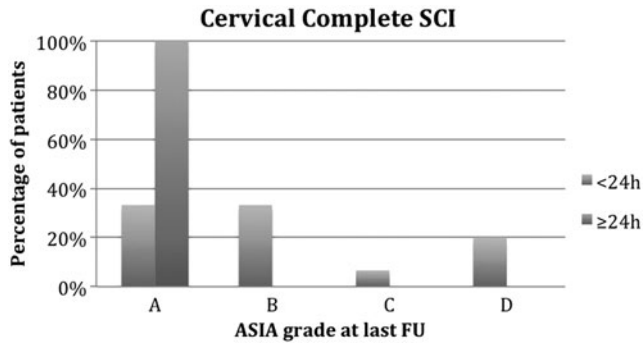

FIG. 3. The percentage of American Spinal Injury Association (ASIA) grade at last follow-up (FU) of all initially complete thoracolumbar SCI. Patients with surgical timing <24 h (24 patients) are compared with patients with surgical timing ≥24 h (9 patients).

43% (19 of 44 patients) in the early surgery group (<24 h) compared with 37% (10 of 17 patients) in the late surgery group (≥24 h).

Cengiz and colleagues[7] suggest a tendency toward better neurological improvement in patients having surgery within 8 h after an acute thoracolumbar SCI. It is possible that a very short surgical delay such as that proposed by Cenzig and colleagues[7] (<8 h vs. >72 h) is necessary to obtain a significant improvement in neurological recovery in patients with thoracolumbar injuries.

We did not find improvement in patients with thoracolumbar SCI who underwent surgery <24 h compared with the later group. The average surgical timing in our early and late surgery groups, however, were, respectively, 16.9 and 40.1 h. While the level of the lesions included in the study from Cenzig and colleagues[7] is predominantly at the thoracolumbar junction, it is also possible that our results differ because of the higher proportion of high- or midthoracic SCI in our cohort. Subanalysis of our cohort showed no statistical difference between thoracic and thoracolumbar neurological improvement.

Wilson and coworkers[20] analyzed the effect of surgical timing in a prospective cohort of traumatic SCI. A multivariate analysis on predictors of ASIA motor score (AMS) at rehabilitation discharge was performed with the data of 55 patients with SCI with ASIA A to D impairment. Similar to the findings of our study, early surgical decompression, incomplete SCI, and cervical trauma (rather than thoracic or thoracolumbar) were associated with AMS improvement at rehabilitation discharge.

Fractures at high- or midthoracic levels (T2–T9) may behave differently compared with thoracolumbar lesions because of poorer vascularity, smaller vertebral canal, and the higher energy needed to cause a vertebral trauma associated with SCI. Accordingly, Zariffa and associates[21] reported that the AIS conversion rate in patients with lower (T10–T12) complete thoracic lesions were more likely to improve their motor score compared with those with higher T6–T9 and T2–T5 lesions. This may support the opinion of Petitjean and coworkers[1] that there is no indication for early surgical decompression in complete thoracic SCI. Although our stratified analysis revealed a similar trend toward better neurological recovery for thoracolumbar compete SCI, it did not show any significant difference.

Study limitations

The small size of our cohort is a limitation of this study; however, to our knowledge, this is the first study to assess this question in persons with complete SCI. It also must be noted that complete SCI represents only 45–50% of the total SCI population.[22–24] This study focused on a specific subgroup of complete SCI that were further subdivided in thoracolumbar and cervical lesions. Our cohort of cervical SCI comprised 20 cervical SCI and 33 thoracolumbar SCI recruited over a 2-year period. The STASCIS study recruited 71 patients with complete cervical SCI over 5 years in six centers.[8] Because our study was a single center study and recruitment occurred over a shorter period, this may reduce the impact of variability in management associated with different centers and in different periods.

Another limitation relates to the varying and relatively short duration of follow-up to assess the neurological recovery. The time elapsed between trauma and discharge from rehabilitation varied from 74 days to 208 days. The duration of follow-up, however, was similar between the cohorts having early versus late surgery, as well as for cervical and thoracolumbar lesions taken separately. In addition, previous data suggest that 80% of conversion of AIS happens within the first 98 days after SCI, and only five patients in our cohort had a follow-up less than 98 days.

Although precise timing data for surgical decompression was collected, timing of utilization of cervical traction and of neurological evaluation were not prospectively collected. These two factors may impact on the measured neurological recovery. Timing of neurological assessment very early after trauma may render harder the detection of subtle incomplete neurological injury because of the clinical setting. This phenomenon may create bias toward the hypothesis of our study. Less reliable early neurological assessment, however, is an unavoidable issue in acute care of patients with traumatic SCI. The exclusion criteria of patients with unreliable neurological assessment may limit the impact of this bias in this study.

In the case of cervical traction, its early use may improve neurological recovery. Its use in the late surgery group may be a bias against our main hypothesis. Only one of the seven patients with cervical traction, however, had surgical decompression >4 h. Because patients who had decompression with cervical traction were mostly operated early anyway, this bias may have very limited impact on the measured outcome.

A fourth limitation relates to our study design, which was observational. In a modern healthcare setting, it is considered unethical to randomize surgical timing in SCI. Therefore the variation in surgical timing is the result of time needed for patient transfer, radiological assessment, delays related to stabilization of a medical condition and associated injuries, and restricted access to the operating room. This may introduce a healthcare access bias, because older and severely injured patients with more comorbidities tend to have their surgery delayed.

Conclusions and Recommendations

Some may consider complete SCI with fatalism, because it carries a poor neurological prognosis. Neurological improvement, however, is proven possible in this population. The findings of this study suggests that early surgical intervention within 24 h after a traumatic complete SCI may promote neurological recovery, especially for those with cervical level lesions. Therefore, we recommend keeping surgical timing at least lower than 24 h to promote neurological recovery.

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Author Disclosure Statement

No competing financial interests exist.

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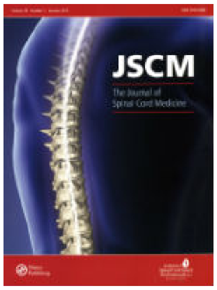
10. Appendix 2: Manuscript published in Journal of Spinal Cord Medicine



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Surgical management of patients following traumatic spinal cord injury: identifying barriers to early surgery in a specialized spinal cord injury center

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Research article

Surgical management of patients following traumatic spinal cord injury: identifying barriers to early surgery in a specialized spinal cord injury center

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Context/Objective: Early surgery in individuals with traumatic spinal cord injury (T-SCI) can improve neurological recovery and reduce complications, costs and hospitalization. Patient-related and healthcare-related factors could influence surgical delay. This study aimed at determining factors contributing to surgical delay in individuals with T-SCI.

Design: Prospective cohort study.

Setting: Single Level I trauma center in Québec, Canada.

Participants: One hundred and forty-four patients who sustained a T-SCI.

Interventions: None.

Outcome measures: Socio-demographic and clinical administrative data were collected during the pre-operative period. The cohort was stratified in early surgery, or ES (<24 hours post-trauma) and late surgery, or LS (≥ 24 hours post-trauma) groups. A multivariate logistic regression analysis using patient- and healthcare-related factors was carried out to identify the main predictors of LS.

Results: 93 patients had ES (15.6 ± 4.7 hours post-trauma), which is 31 hours earlier than the 51 patients in the LS group (46.9 ± 30.9 hours; $P < 10^{-3}$). The transfer delay from trauma site to the SCI center was 8 hours shorter (5.0 ± 3.0 hours vs 13.6 ± 17.0; $P < 10^{-3}$) for the ES group, and the surgical plan was completed 17 hours faster (6.0 ± 4.0 hours vs 23.3 ± 23.6 hours; $P < 10^{-3}$) than for the LS group. The occurrence of LS was predicted by modifiable factors, such as the transfer delay to the SCI center, the delay before surgical plan completion, and the waiting time for the operating room.

Conclusions: A dedicated team for surgical treatment of individuals with T-SCI, involving direct transfer to the SCI center, faster surgery planning and access to the operating room in hospitals dealing with emergencies from all subspecialties could improve surgical delay and increase the rate of patients undergoing ES.

Keywords: Delay, Pre-operative management, Prospective study, Spinal cord injury, Surgery

Introduction

Although relatively rare, traumatic spinal cord injuries (T-SCI) have a devastating impact on the physical and psychological status of patients by decreasing quality of life, social participation and productivity.[1,2] The worldwide estimated incidence of T-SCI varies from 10.4 to 83 cases per million[3] due to several regional differences[4] and trends over time. In Canada, the age-adjusted incidence of T-SCI is 51.4 cases per million in persons older than 64 years and 42.4 cases per million among those 15–64 years of age.[5]

T-SCI involve a significant financial burden on patients and the healthcare system. Costs of T-SCI to society were estimated in 2006 at 9.7 billion USD per year in the United States,[9] In Canada, costs in the first year after T-SCI were estimated between 43 400 and 122 900 Canadian Dollars (CAD) (in 2002; 27,637–78,262 USD) depending on the severity of the neurological deficit.[10]

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While the majority of patients with an acute T-SCI will undergo surgery for stabilization and/or decompression of the spine, recent studies suggest performing early surgery, ideally within 24 hours of the injury.[11–16] Early surgery reduces costs and length of hospital stay[11] and decreases complication rate.[12,13] Santos *et al.*[14] developed a simulation model in a Canadian SCI center showing that surgery within 24 hours post-trauma has indirect benefits on quality of life, life expectancy, neurological recovery and occurrence of complications in patients with tetraplegia. Our team showed that early surgery is associated with better neurological status and improvement in AIS grade among patients admitted for a complete cervical T-SCI.[15] Early surgery may be considered as best practice for cervical T-SCI.[16]

Many factors can contribute to the surgical delay once the patient is admitted to a specialized SCI center. These include patient-related factors such as a contraindication to early surgery due to, among other reasons, severe traumatic brain injury with intracranial hypertension or concomitant life-threatening injury requiring emergent intervention prior to spine surgery (e.g. severe intra-abdominal or pelvic bleeding, aortic or cardiac injury), as well as healthcare-related factors due to the limited access to the operating room because of a high load of emergent cases. Potentially modifiable factors are transportation delays from the site of trauma, evaluation by the emergency trauma and spine teams, and availability of the operating room. Accordingly, Furlan *et al.*[17] have shown that extrinsic factors, unrelated to the patient's health status, are mostly accountable for the delay between trauma and surgery. However, their study was conducted with a small sample of 63 patients and only cervical T-SCI, and did not account for other possible factors that could influence and delay surgery. Therefore, the objective of this study is to determine the factors contributing to surgical delay in individuals with T-SCI in a single Level-I trauma center specialized in the care of SCI. A secondary objective was to verify if the time intervals were different based on the severity of the neurological deficit of patients with T-SCI.

Materials and methods

Patients

A prospective cohort of 175 consecutive patients with a T-SCI admitted to a single Level I SCI-specialized trauma center between April 2010 and May 2015 was included in this study (138 males and 37 females; 46.4 ± 19.7 years old). Patients entered the cohort at the time of admission and were followed until discharge from the acute care center. They were included if they sustained a spine trauma that involved a SCI and had surgery performed in our institution. Patients were excluded if the spine injury was below the L1–L2 intervertebral disc or if they were diagnosed with a pre-existing spinal stenosis without overt spine instability. The study was approved by the institutional review board and all patients were enrolled on a voluntary basis.

In the presence of a T-SCI associated with overt spinal instability and/or spinal cord compression, surgeons at our institution will usually proceed with surgery in an attempt to limit the secondary injury to the spinal cord, unless there is a medical contraindication to surgery. A multidisciplinary team composed of the trauma, spine surgery, and physical medicine and rehabilitation teams ensures the acute care of the patient. When the diagnosis is established and surgical treatment is indicated, the surgical unit is informed and the patient is placed on the waiting list, which also includes all surgical emergencies from other subspecialties. Prioritization of all surgical emergencies is under the responsibility of a coordinator.

Data collection and outcomes

Socio-demographic, clinical and administrative data pertaining to the pre-operative period were collected on a daily basis through a prospective database (Quebec Trauma Registry) for all patients admitted at our institution following a traumatic event.

The main healthcare related factor was delay to surgery which was broken down into specific intervals:

I. Only for patients transferred to a community hospital (CH) prior to arrival at SCI center:
   a. Delay between trauma and arrival at the CH;
   b. Delay between arrival at the CH and the emergency room of SCI center;

II. For all patients:
   c. Delay between trauma and arrival at the emergency room of SCI center (corresponds to the sum of delays a. and b. for patients transferred from a CH);
   d. Delay between arrival at SCI center and first medical assessment in the emergency room (ER);
   e. Delay between first medical assessment in the ER and finalization of surgical plan, corresponding to the moment when the surgical request form is received by the operating room;
   f. Delay between finalization of surgical plan and beginning of surgery;
   g. Overall time spent in the emergency room.

Other healthcare-related factors were collected, such as the day patients were transferred to the SCI center, the day for finalization of surgical plan, the subspecialty of the physician performing the first assessment in the

ER of the SCI center, and the distance between the CH and the SCI center for patients not directly admitted to the SCI center.

Patient-related factors consisted of socio-demographic (age, sex) and clinical data: level of spine injury (cervical or thoracolumbar), severity of trauma as measured by the Injury Severity Score (ISS), the Charlson comorbidity index (CCI) providing a weighted score of patients comorbidities, and pre-operative severity of neurological deficit assessed from the American Spinal Injury Association scale (complete – ASIA A vs incomplete – ASIA B, C or D).

Data analysis

We stratified our cohort into two subgroups based on the surgical delay, i.e. time elapsed between the trauma and surgical incision. The early surgery (ES) subgroup included patients who had spine surgery within 24 hours post-trauma, and the late surgery (LS) group had surgery 24 hours or more post-trauma. Continuous data were compared between subgroups using Mann-Whitney U tests, while categorical data were compared using χ^2 tests. Continuous data were reported as means ± one standard deviation, and categorical data were reported as proportions and percentages.

We determined predictors of having LS rather than ES, by investigating 16 factors in a multivariate logistic regression. The patient-related factors were: 1) age; 2) sex; 3) pre-operative severity of neurological deficit (complete – ASIA A vs incomplete – ASIA B, C or D); 4) injury level (cervical vs thoracolumbar); 5) ISS; 6) CCI. The healthcare-related factors were: 7) transfer to a CH or direct admission to the SCI center; 8) delay in arrival at the CH; 9) delay of transfer from CH to SCI center; 10) distance between CH and SCI center; 11) time in the ER of the SCI center; 12) delay in arrival at SCI center/first medical assessment; 13) subspecialty of physician performing first medical assessment in SCI center; 14) delay between first medical assessment and finalization of surgical plan; 15) delay between finalization of surgical plan and beginning of surgery; 16) day of the week (weekday or weekend day) surgical plan is completed and surgical request form is received by the operating room. All statistical analyses were performed using the IBM SPSS Statistics 21 software (IBM Corp, Armonk, NY, USA).

Results

Among the 175 patients who agreed to participate in the study, 15 were directly admitted from a CH to the specialized spine center without going through the ER, and 16 had surgery more than 7 days post-injury. These 31 patients were excluded from the analysis (leaving 144 patients) because of the potential bias due to the injury occurring outside the province of Quebec and urgent medical conditions that needed to be treated prior to the spine injury. Table 1 details the demographic and clinical characteristics of the 93 patients in the ES and 51 in the LS subgroups. Patients in the ES group were on average 8 years younger than those in the LS group (P = 0.02) and had a complete T-SCI in a greater proportion than the LS group (P = 0.01), which is consistent with epidemiological studies reporting a greater proportion of incomplete lesions in older patients.[2,8] The proportion of males and females was the same in both groups, as well as the severity of trauma (ISS) and the comorbidity level (CCI).

Table 1 Demographic and clinical characteristics of patients with T-SCI operated within 24 hours and 24 hours or more post-trauma

	ES (<24 h)	LS (≥24 h)	P
N	93	51	
Surgical delay (mean ± SD)	15.6 ± 4.7	46.9 ± 30.9	*$<10^{-3}$*
Age (mean ± SD)	41.2 ± 18.5	48.9 ± 20.1	*0.02*
Sex			
Male	78.5%	84.3%	0.40
Female	21.5%	15.7%	
CCI (mean ± SD)	0.25 ± 0.69	0.25 ± 0.64	0.82
ISS (mean ± SD)	27.1 ± 9.7	25.8 ± 12.4	0.14
Level of injury			
Cervical	46.2%	60.8%	0.10
Thoracolumbar	53.8%	39.2%	
Severity of neurological deficit			
Complete (ASIA A)	64.1%	42.0%	*0.01*
Incomplete (ASIA B-C-D)	35.9%	58.0%	

ES: early surgery; LS: late surgery; SD: standard deviation; ISS: Injury Severity Score; CCI: Charlson Comorbidity Index

Table 2 Average delays (±SD) encountered by patients operated within 24 hours post-trauma (early surgery) and 24 hours or more following trauma (late surgery)

Time interval (h)	ES (<24 h)	LS (≥24 h)	P
Trauma—Arrival SCI center	5.0 ± 3.0	13.6 ± 17.0	*$< 10^{-3}$*
Trauma—Arrival other CH	1.2 ± 1.1	3.3 ± 4.9	*0.002*
Arrival at other CH—Arrival SCI center	3.8 ± 2.7	10.3 ± 15.6	*$< 10^{-3}$*
Arrival SCI center—Surgery	10.6 ± 4.3	33.3 ± 26.5	*$< 10^{-3}$*
Arrival SCI center—First assessment by MD	2.0 ± 1.6	3.1 ± 3.8	0.18
First assessment by MD—Surgical plan completion	6.0 ± 4.0	23.3 ± 23.6	*$< 10^{-3}$*
Surgical plan completion—Surgery	2.6 ± 2.2	7.0 ± 12.4	0.31
Trauma—Surgery	15.6 ± 4.7	46.9 ± 30.9	*$< 10^{-3}$*

ES: early surgery; LS: late surgery

Comparison between early and late surgery subgroups

Interval between occurrence of trauma and arrival at SCI center

A minority of patients with T-SCI (14/144 or 9.7%) was directly transported from the site of trauma to the SCI center without prior transfer in a CH. This proportion was similar between the ES and LS subgroups (χ^2 test: 11% vs 8% of patients with T-SCI, respectively; P = 0.57). Not surprisingly, persons who had shorter times from trauma to SCI center were more likely to have ES ($P < 10^{-3}$; Table 2). The delay between trauma and arrival at the SCI center was longer for patients transported to a CH prior to the SCI center (CH: 8.6 hours ± 11.3 hours; SCI center: 2.4 hours ± 6.4 hours; $P < 10^{-3}$), which affected the total delay between trauma and surgery, although not significantly (CH: 27.3 hours ± 24.5 hours; SCI center: 21.0 hours ± 17.4 hours; P = 0.09). The distance between the CH and the SCI center was not different between patients who had ES or LS (ES: 83 ± 98 km; LS: 128 ± 159 km; P = 0.26). Only 6 patients (3 ES, 3 LS) were transferred to the SCI center by air transportation, from a distance ranging between 503 km and 647 km. All other patients were transferred by road transportation (ambulance, private vehicles, etc.).

The interval between trauma and arrival at the SCI center differed based on the severity of the neurological deficit (Table 3). Patients with a complete T-SCI were transferred 4 hours faster to the SCI center ($P < 10^{-3}$), which was however not related to whether patients transit to a CH or are directly admitted to the SCI center. There were no differences in the transfer delay from the site of trauma to the SCI center whether patients had a cervical or thoracic/thoracolumbar lesion.

Intervals between arrival at SCI center and beginning of surgery

The delay between arrival at the SCI center and beginning of surgery was three times longer for T-SCI patients who had LS ($P < 10^{-3}$). It can be broken down into three major phases: delay between arrival at SCI center and first medical assessment in the ER; delay between the first medical assessment in the ER and surgical plan completion; and delay between surgical plan completion and beginning of surgery (Table 2). The only significant difference between ES and LS subgroups was for the time between the first medical assessment and completion of surgical plan, which was 4 times shorter and represented 56% of the waiting time for the ES group as compared to 70% of the waiting delay for the LS group ($P < 10^{-3}$; Table 2). There was no significant difference in the time waiting for the first medical assessment and in the delay between surgical plan completion and beginning of surgery between

Table 3 Average delays (±SD) encountered by patients with a complete SCI and an incomplete SCI

Time interval (h)	Complete SCI	Incomplete SCI	P
Trauma—Arrival SCI center	6.4 ± 12.0	10.2 ± 9.7	*$< 10^{-3}$*
Trauma—Arrival other CH	1.6 ± 2.8	2.4 ± 3.7	*0.006*
Arrival at other CH—Arrival SCI center	4.8 ± 10.8	7.8 ± 8.8	*0.001*
Arrival SCI center—Surgery	16.2 ± 17.9	21.7 ± 21.1	*0.049*
Arrival SCI center—First assessment by MD	2.0 ± 2.2	2.8 ± 3.1	*0.021*
First assessment by MD—Surgical plan completion	11.6 ± 17.2	13.0 ± 16.0	0.56
Surgical plan completion—Surgery	2.6 ± 2.7	5.9 ± 11.1	0.28
Trauma—Surgery	22.6 ± 22.6	31.9 ± 25.0	*$< 10^{-3}$*

Table 4 Logistic regression models for prediction of late surgery (≥ 24 hours post-trauma)

	B	SE-B	Wald	P	Odds (95% CI)
Delay of transfer from CH to SCI center	0.907	0.264	11.770	0.001	2.476 (1.475–4.157)
Delay surgical plan completion—surgery	0.906	0.279	10.541	0.001	2.474 (1.432–4.275)
Delay first medical assessment—surgical plan completion	1.036	0.275	14.242	0.000	2.819 (1.646–4.829)

the ES and LS subgroups. Only one patient was operated for another medical emergency before undergoing spine surgery. This patient required the placement of a cerebral shunt, which resulted in a delayed spine surgery that finally took place 96 hours post-trauma.

Seventy-four percent of patients with a complete T-SCI had ES, as compared to 53% of patients with an incomplete T-SCI ($\chi^2 = 6.450$; $P = 0.011$). The waiting time upon arrival at the SCI center was 5 hours shorter for patients with a complete T-SCI ($P = 0.049$) which contributed, along with the prompter transfer from the site of trauma to the SCI center, to the 9-hour shorter delay trauma-surgery as compared to incomplete patients with T-SCI ($P < 10^{-3}$; Table 3). There were no differences in the duration of each step of patient management once admitted at the SCI center based on the level of injury (cervical or thoracic/thoracolumbar).

Other healthcare-related factors affecting surgical delay

The proportion of patients who had ES or LS was different depending on the day of surgical plan completion and reception of the request form by the OR ($\chi^2 = 4.916$; $P = 0.027$), but not on the day patients with T-SCI were transferred to the SCI center. When the surgical plan was completed and the request form sent to the OR at the end of the week, i.e. between Friday and Sunday, 75% of patients underwent ES. This proportion dropped to 50% when decisions were made during weekdays, i.e. between Monday and Thursday.

There was also a relationship, although not significant, between the subspecialty of the first physician assessing patients upon arrival at the SCI center ER and whether patients were operated within 24 hours or later. Fifty-nine percent of patients who were examined by a spine surgeon had ES, whereas this proportion reached 81% when first assessed by the trauma team ($\chi^2 = 5.197$; $P = 0.07$). There was no relationship between the number of medical assessments received at the ER of the SCI center and the delay between trauma and surgery.

Using a multivariate logistic regression model, we determined that only healthcare-related factors were associated with being in the LS group. These factors were: transfer time between the community hospital and the SCI center, time between first medical assessment and surgical plan completion, and time between surgical plan completion and actual surgery (Table 4).

Discussion

The results of this study show that healthcare-related, modifiable factors are mainly responsible for the delay between trauma and surgery. The most important contributors are the time of transfer from the site of trauma to the SCI center, the interval between the first medical assessment and surgical plan completion, and the delay between surgical plan completion and beginning of surgery. Interestingly, no patient-related factors such as severity of trauma, severity of injury or age were related to surgical delay. This goes along the same lines as what Furlan *et al.*[17] reported, while Samuel *et al*.[18] observed that injury characteristics and pre-existing comorbidities were associated with longer surgical delays in patients with cervical T-SCI.

Our center is a Level-I trauma center serving as the tertiary referral center for T-SCI in western Quebec and as the single referral center for all ventilation-assisted T-SCI in Quebec. Therefore, patients with a T-SCI should systematically be transferred at our center for acute care management. However, our results showed that only 10% of them were directly transferred from the site of trauma to our SCI center. This might be due to the long distance between the trauma site and the SCI center in some patients, considering that hemodynamic instability can occur frequently and would be difficult to manage during transportation on long distances. Nevertheless, patients started being managed by the SCI specialized team within less than 2.5 hours post-trauma, which was 6 hours faster than for patients transported to another CH. Our 2.5-hour delay was also well below what was observed by Harrop *et al.*,[19] where patients sustaining a T-SCI were transported to a Level I or II hospital within 5.2

hours in Pennsylvania. Finally, whether patients were transferred from a CH located at a long distance from the SCI center by air or road transportation did not seem to affect the surgical delay, since 3 out of the 6 patients transferred by air transport had LS surgery, with delays ranging between 28 hours and 96 hours. This goes along the same lines as what was reported by Harrop *et al.*,[19] where long delays from trauma to arrival at the trauma center were observed in patients transferred by helicopter transportation.

The other step in management resulting in the greatest delay was the time between first medical assessment in the ER and surgical plan completion, which is consistent with what was already reported.[17,18] It was unlikely related to the severity of trauma, since the ISS was similar between ES and LS patients. This interval was 4 times larger for patients who had LS, and was also one of the main predictors of undergoing LS. It represented 56% of the total waiting time for the ES group and 70% for the LS group. This is a smaller proportion of time than what was reported by Samuel *et al.*,[18] where the inpatient waiting time represented approximately 90% of the total surgical delay. As well, Furlan *et al.*[17] reported a 14-hour interval waiting for surgical decision in patients who had LS. This is more than 9 hours shorter than in our study, where patients who had LS waited approximately 23 hours between the first medical assessment and surgical plan completion. Need for medical stabilisation and treatment of more urgent injuries could have an impact on this delay, although the ISS was similar in both groups. This highlights the importance of the dedicated trauma team composed of general surgeons also trained in intensive care, which tend to decrease the waiting time for surgery.

Difficulty in access to specialized imaging (especially MRI) could also be involved, as well as the fact that most of the late surgeries were performed during weekdays. Indeed, it is possible that on some occasions, management of trauma patients arriving during weekdays and requiring surgery will depend upon the availability of the operating rooms and of the spine surgeons, considering the high number of elective cases being performed simultaneously. Also, some patients can be assessed more than once by doctors from different subspecialties while in the ER, such as neurosurgeons, intensivists, trauma specialists, etc., before the spine surgeon who will be establishing the surgical treatment plan. Although our analyses did not show differences in the proportion of ES and LS patients who had multiple medical assessments, this is a factor that most likely affects the time interval before surgical plan completion.

Samuel *et al.*[18] have shown that only 44% of patients with a cervical T-SCI had surgery within 24 hours post-trauma, despite the growing body of evidence supporting the benefits of ES. This rate is below what was obtained in our study, where 64% of patients had ES. They also reported that the majority of patients with a complete cervical T-SCI, i.e. 57%, had ES, as compared to 49% of patients with an incomplete injury. This is consistent with our data, where the proportion of patients with a complete T-SCI undergoing ES was much larger than the proportion of patients with an incomplete T-SCI (74% vs 53%). Shorter waiting time in all steps of management was responsible for the smaller surgical delay for patients with a complete T-SCI.

Could the rate of patients operated within 24 hours post-injury be increased?

In our study, 64% of patients with T-SCI had ES while the remaining 36% had LS, with an average delay of nearly 46 hours. Based on the Canadian studies by Noonan *et al.*[20] and Furlan *et al.*,[19] we calculated the number of patients enrolled in our study that could have been operated within 24 hours, had our delays been the same as reported in those studies. We considered the time of transfer from the CH to the SCI center, the delay between the first medical assessment and surgical plan completion, and the delay waiting for the operating room, which were the three main predictors of having LS.

Noonan *et al.*[20] demonstrated that direct transport of patients with T-SCI injured within a 20-minute drive of a SCI center significantly increases the number of patients directly admitted to the SCI center. Among patients previously transported to a CH in our study, 54 went to a CH located within 40 km of the SCI center. We can assume that these patients were most likely injured within a 20- to 30-minute drive from our SCI center. Had they been directly admitted to the SCI center, this would have resulted in a 42% rate of direct admissions, most likely resulting in a reduced surgical delay. If we consider that direct admission to the SCI center results in a 4-hour decrease in surgical delay,[20] 5 patients transported to a CH within 40 km of the SCI center would have been operated within 24 hours, which represents a 4% increase in ES rate.

With regards to the time waiting for surgical plan completion, Furlan *et al.*[17] reported delays of 4 hours for patients who had ES and 14 hours for those operated later. This is much shorter than the delays obtained in our study, which were 6 hours and 23 hours for the ES and LS groups, respectively. Had this delay been 9 hours shorter for our LS patients, to be consistent with

Furlan's data, 17 additional patients would have had surgery within 24 hours post-trauma, resulting in a 12% increased ES rate. Finally, the other main predictor of LS was the delay between surgical plan completion and beginning of surgery, which was 4 hours longer for patients who had LS. This variable was not considered by Furlan *et al.*[17] and Samuel *et al.*[18] However, if we hypothesize that the average delay between surgical plan completion and beginning of surgery in the LS group was the same as the ES group, i.e. approximately 3 hours, there are 4 patients that would have ended up being operated within 24 hours post-injury.

Based on the growing clinical evidence that prompt surgery in patients with T-SCI is beneficial and favours better outcomes,[12,13,15,16] changes in logistics to prioritize spine surgeries for T-SCI should be made. The time interval between T-SCI and beginning of surgery could further be reduced by avoiding transporting the patients to a CH when the trauma occurs in a short distance from a specialized SCI center, and by decreasing the waiting time for a surgical decision and the time for access to the operating room. Although this study was conducted in a single SCI center, results could certainly be generalized to other centers. Considering that the care delivery model used at our facility is comparable to what is observed in Canada, where SCI centers are high-volume patient flow Level I trauma centers in nearly all cases (14/15 acute centers; Noonan *et al.* 2012), the main challenge for providing timely care to patients with SCI resides in optimizing the transition delays between and within different phases of patient with SCI management, especially the pre-hospital and SCI center acute care phases. Instituting policies to ensure swift transfer and surgery post-injury for those with T-SCI can ultimately improve outcomes for these patients.

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Disclaimer statements

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11. Appendix 3: Manuscript accepted in American Journal of Physical Medicine and Rehabilitation

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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 transfer to specialized acute SCI center

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Abstract:	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 SCI-center. Design: A retrospective 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) was transfer to 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: LOS was significantly longer for Group 2 (median of 93,0 days) as compared to Group 1 (median of 40,0 days, p<10-3), and average costs ($CAN) were also higher (median of 17 920.0$ vs. 10 52,6$, 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 SCI-center was associated with shorter LOS and lower costs for patients sustaining tetraplegia. Early referral to a SCI-center before surgery could lower the financial burden for the healthcare system.

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ABSTRACT

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 SCI-center.

Design: A retrospective 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) was transfer to 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: LOS was significantly longer for Group 2 (median of 93,0 days) as compared to Group 1 (median of 40,0 days, $p<10^{-3}$), and average costs ($CAN) were also higher (median of 17 920.0$ vs. 10 52,6$, 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 SCI-center was associated with shorter LOS and lower costs for patients sustaining tetraplegia. Early referral to a SCI-center before surgery could lower the financial burden for the healthcare system.

Key words: spinal cord injury; length of stay; specialized centers; costs.

INTRODUCTION

The incidence of traumatic spinal cord injuries (SCI) 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 to other musculoskeletal traumatic injuries, a SCI is associated with extensive economic costs, mostly due to substantial health care burden[2, 3]. This is particularly true for individuals that are more severely affected. Motor-complete cervical SCI requires additional load of care, as this condition is associated with severe respiratory and cardio-vascular 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 1,124$ (CAD), and the annual economic burden associated with new cases of traumatic SCI was estimated as 2.67 billion$ (CAD) in 2011[7]. Thereby, improving the efficiency and the use of optimal resources is necessary.

Managing motor-complete cervical SCI remain a clinical challenge and require the integration skills of many specialists and urgent medical stabilization care[8]. Once medical stabilization is reached, prompt transfer to SCI-center is recommended[9, 10]. In Canada, specialized acute care centers are tertiary care designated centers developed to help patients suffering from acute SCI and were showed to improve recovery, decrease the occurrence of complications[10-12]. In this way, early transfer is recommended (<48 hours) but this recommendation rely 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 non-specialized (NS) regional center or direct transfer to the SCI-center should be prioritized. So, optimal timing for transfer to SCI-center should also be established with respect to the spinal surgical procedure and on 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 peri-operative 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 peri-operatively at a NS vs. SCI-center following a traumatic motor-complete cervical SCI.

MATERIAL AND METHODS

Patients

We conducted a retrospective cohort study of prospectively collected data including 116 consecutive adult patients (92 males; 24 females) aged 46.0±19.3 years old admitted to a single Level I SCI-specialized trauma center between April 2008 and November 2014 for a motor-complete cervical traumatic SCI. 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 non-surgically or sustaining a cervical SCI with milder neurological deficits (AIS-C or 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 two groups based on the timing of admission to the specialized center. Group 1 included 87 individuals “early” transferred to the SCI-center, while Group 2 included 29 patients “lately” 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 received complete peri-operative management by a specialized multidisciplinary team, while Group 2 consisted of 29 patients transferred to the SCI center *for postoperative management only*. More clearly, patients from Group 2 received pre-operative, surgical and immediate post-operative management in a NS center before being transferred to the SCI-center. Patients from Group 1 could also be first transported to a NS center after their trauma, but were all surgically managed in the SCI-center. The term “peri-operative period” refers in the present work to three phases: 1) the pre-operative period (period between the trauma and surgical management); 2) surgical procedure; 3) post-operative 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 other. In Quebec, Canada, all patients sustaining a traumatic spinal cord injury should be directed to one of the two designated acute care centers (SCI-center) according to its location: one center serving the eastern, while the other serves the western part of the province. This system was established in the late 70's in order to allowed 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 non-specialized centers following their SCI in order to stabilized patients and confirm the diagnosis of a SCI. Even if our provincial government strongly encourage prompt transfer to the SCI-center in the pre-operative phase, some non-specialized centers may choose to transfer patients only after surgical management. It is important to note that all patients were transported by ambulance. No helijet or else were used. The Level-1 trauma center involved in this study was designated in 1977 as one of the two acute care specialized SCI reference centers of our province [19, 20]. Since this designation, our hospital center has managed 70 to 100 patients with traumatic SCI per year[20]. It comprises a multidisciplinary healthcare professionals 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 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. When their condition was judged stable by the intensive care team, patients were transferred to the ward while continuing rehabilitation therapies. The peri-operative 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, contractures, malnourishment, aspiration and improve cardiovascular and respiratory outcomes. Cardiovascular and respiratory management were individualized based on the clinical judgement 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

Socio-demographic 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 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, gender and trauma severity as measured by the Injury Severity Score (ISS). The ISS score was dichotomized according to Bull's method[21] using the LD_{50}, meaning the ISS score representing a "lethal dose of injuries" for 50% of the patients injured. The suggested LD_{50} score was 40 for individuals 15-44 years old and 29 for ages 45-64. Since the median age of our two groups was 46 and 48 years old, we dichotomized the ISS into <29 and ≥29. 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 was reported using the AIS grades 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 two 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 two categories (<24h or ≥24h post-trauma). Finally, the following complications were considered: 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[22]. 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[23]. Finally, the presence of PU was diagnosed based on the clinical guidelines defined by the National Pressure Ulcer Advisory Panel (NPUAP)[24]. 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. The same was performed for the occurrence of multiple complications, where we considered patients having experienced more than one complication (two and more complications) during the SCI-center stay.

The main outcome variables were hospital length of stay (LOS) and costs related to hospitalization in the SCI center ($CAD). Details are provided below.

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 two 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. LOS in a 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. LOS in the intensive care unit (ICU) of the SCI center was also collected for both groups.

In our system of care, urgent and acute care such as that required for traumatic SCI, is covered by our universal healthcare 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, since the spine surgery and, on some occasions, the tracheostomy were performed in the NS center for individuals lately 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 depends on the distance and time required for transfer since it is provided by the public healthcare 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 pre- or postoperatively.

Statistical Methods

In order to compare the two groups, we first used non-parametrical analyses (Mann-Whitney tests for continuous variables and chi-square tests for categorical variables). We used IBM SPSS Statistics Version 21 software 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) gender; c) ISS (*<29 and ≥29)*; d) surgical delay (<24h or ≥24h post-trauma); e) ASIA grade (A or B); f) neurologic 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 urinary tract infection; l) occurrence of at least one complication; m) occurrence of multiple complications (two and more).

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 and trauma severity as measured by the ISS, but there was a tendency towards 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%) while two 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 patients out of 87) 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 of 0.2 days) (Table 2). On the other hand, patients in Group 2 spent more than two weeks (median of 18.8 days, p<0,001) in a 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 to Group

1(Table 2). Table 3 show that results were similar when matching individuals according to their trauma severity (ISS <29 vs. ≥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).

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 6000 $ (costs in Canadian dollars) lower for Group 1 than 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 two factors: late transfer to the SCI-center (Group 2) and the occurrence of respiratory complications (Table 6)

DISCUSSION

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

Determining factors specific to SCI-centers that may influence the LOS and costs of care is however complex. In theory, there are three aspects of patient care that differ between the two 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 two groups. In a specialized SCI center like 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, and 5) increase function and promote neurological recovery, 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 peri-surgical 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 a SCI center only after surgery. This is supported by previous studies that have suggested that prompt transfer to SCI-center optimize outcomes following SCI [10, 12]. Since 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 propose 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 SCI-center later and therefore explain results of this study. However, this hypothesis is somehow counterintuitive and is not supported by the following observations. First, as NS centers typically do not involve healthcare providers specialized in the management of traumatic SCI 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 traumatic SCI, we can also add that in our public system, there is no incentive whatsoever for NS centers to treat more complex patients with traumatic SCI, since it will increased 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 B represent a relatively homogenous group of patients with regard to the acute management, since both cervical AIS A and 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 show 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 two levels of severity on acute care outcomes. But against, when looking at the total acute care LOS, individuals from Group 2 may have had a significant longer period of time to recover (Table 2), particularly knowing that the neurological recovery is more rapid within the first three months post injury[18].

Table 1 also shows a tendency towards higher trauma severity in Group 2 (NS center). However, outcome comparison after matching the participants according to their trauma severity (ISS) still showed a significant longer LOS and a tendency towards 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 results of this study.

Regarding results of the regression analysis, two 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 urinary tract infection (UTI), pressure ulcers and pneumonia were demonstrated to increase costs of acute care hospitalization in SCI patients[11], 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 increased the risk of complication occurrence, which may put them at higher vulnerability following a SCI[31, 32]. Although, according to the results of this study (beta coefficient), the age does not seems 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 SCI[38], 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 a

SCI may be needed, and/or most importantly, early medical stabilization. This study does not intend to question the importance of medical stabilization following a 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 peri-operative management upon medical stabilization following a traumatic SCI may decrease costs of care. In the context where the NIRRU index considered in this study did not include physician fees or transportation fees that could highly vary from one healthcare system to another, costs evaluated essentially reflect inpatient acute care stay, which may be directly proportional to the acute care LOS. Therefore, since all patients sustaining a TSCI will require hospitalization in an acute care setting, this study could apply elsewhere. In fact, every healthcare system treating patients with acute TSCI should aim to decrease resources 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 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. 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 a 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 two groups. Consequently, it is assumed that the costs of intensive functional rehabilitation would be similar between the two 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 towards higher severity of complete SCI in Group 2. Although this difference was not significant, additional comparative non-parametrical sub-analyses showed that the LOS and costs of care were similar for patients with AIS grade A and B in each group. Moreover, considering that multivariate also take into account this potential cofounding variable; it is unlikely that this issue had influenced 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 helijet or other expensive mean 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 is likely to be similar between the two groups. However, if other means of transport are used in a healthcare 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 neurologic and functional outcomes), economic impact and resources 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 peri-operative care following a motor-complete cervical SCI. Furthermore, length of stay 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 a SCI-center following a TSCI, but may also add that transfer prior to surgical management is beneficial on acute care resources utilization, even if medical stabilization was first performed in a regional non-specialized center. Many factors could be beneficial to 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 healthcare system, results still can be applied elsewhere. In fact, the present study has mainly evaluated costs of care based on the length of stay (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 a SCI-center prior to surgical management may by an efficient way, applicable to any healthcare system, to decrease resources utilization that may be an important issue worldwide.

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Authors Disclosure Statement

No competing financial interests exist.

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Table 1

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

		Early transfer (SCI center-Group 1)	Late transfer (NS center-Group 2)	p-value
N	---	*87*	*29*	---
1. Age	Median (IQR)	46.0 (28.6-62.0)	48.0 (23.5-64.5)	0.97
2. Gender	% Male	78.2	82.8	0.60
3. ISS	% *≥29*	39.1	58.6	0.053
4. ASIA grade	% A	65.5	82.8	0.08
	% B	34.5	17.2	
5. Neurological level	% C1-C4	51.7	62.1	0.33
6. Traumatic brain injury	% TBI	51.3	27.6	0.02*
7. In-hospital death	% deceased	9.2	6.9	0.70
8. Surgical delay	% >24h post injury	54.0	51.7	0.83
9. Respiratory complications	%	54.0	51.7	0.83
10. Pneumonia	%	47.1	41.4	0.67
11. Pressure ulcer	%	36.8	34.5	1.00
12. Urinary tract infection	%	20.7	31.0	0.31
13. At least one complication (one or more)	%	71.3	72.1	1.00
14. Multiple complications (two and more)	%	44.8	37.9	0.67

ISS: Injury severity score

Table 2

Hospitalization length of stay (LOS) in patients with a motor-complete cervical spine injury early and lately transferred to the SCI-center (Group1 and 2).

Hospitalization stay (in days)			**Early transfer (SCI-center-Group 1)**	**Late transfer (NS center-Group 2)**	**p-value**
Prior to SCI-center admission	Regional center (NS center)	Median (Interquartile range)	0.2 (0.1-0.3)	18.8 (8.2-36.3)	<0.001*
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*
	In the ward	Median (Interquartile range)	40.0 (24.0-67.0)	68.0 (35.5-119.0)	<0.001*
Total acute care hospitalization		Median (Interquartile range)	40.0 (24.0-67.0)	93.0 (61.0-149.0)	<0.001*

ICU: Intensive care unit

Table 3

Comparison of length of stay 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-value
		ISS ≥29		
N	---	*34*	*17*	---
Length of stay	Median (Interquartile range)	57.0 (32.3-101.3)	107.0 (65.5-149.0)	0.007*
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	
Length of stay	Median (Interquartile range)	32.0 (23.5-55.5)	86.0 (60.0-149.55)	<0.001*
Costs of care	Median (Interquartile range)	10144.2 (6478.5-17332.7)	17028.3 (8523.1-20776.3)	0.13

N: number of patients; NS center: non-specialized center

Table 4

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

Factors associated with hospital LOS in the SCI-center		
	Beta coefficient (95% CI)	*p-value*
Timing of SCI-center admission (Group 2-NS center vs. Group 1-SCI)	50.5 (30.8- 70.2)	<0.001*
Occurrence of multiple complications	50.2 (33.0- 67.4)	<0.001*
Age	0.6 (0.1-1.0)	0.014*

R-squared= 0,358 (percentage of the response variable variation that is explained by our linear model); 95% CI, Confidence Interval

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 (CAD$)		Timing of admission to SCI-center		p-value
		Early transfer (SCI center-Group 1)	Late transfer (NS center-Group 2)	
Total	Median (IQR)	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 (IQR)	10 521.6 (6 840.2-18 895.5)	17 920.0 (11 159.3-24 500.4)	0.004*

Table 6

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

Factors associated with higher hospitalization costs (CAN$)		
	Beta coefficient (95% CI)	*p-value*
Timing of SCI-center admission (Group 2-NS center vs. Group 1-SCI)	7070.4 (1589.8-12551.0)	0.013*
Respiratory complications	5796.0 (125.8-11466.2)	0.045*

R^2= 0.186

95%CI, Confidence Interval

12. Appendix 4: Manuscript submitted to Journal of Spinal Cord Medicine

The Journal of Spinal Cord Medicine

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

--Manuscript Draft--

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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.

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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 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.

Keywords

Spinal cord injuries; prediction; function; acute; trauma

Abbreviations

T-SCI, traumatic spinal cord injury

ASIA, American Spinal Injury Association

AIS, ASIA Impairment Scale

LOS, Length of stay

Introduction

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

Previous studies agree that the severity of the T-SCI at initial presentation is the main factor associated with neurologic and functional outcomes, with complete SCI predicting worse outcome.[1-5] The impact of other clinical and socio-demographic characteristics, such as the level of the SCI or age, is debated.[1, 2, 5, 6] While most predictive factors of functional recovery following SCI are non-modifiable, potential modifiable predictors, such as clinical events occurring during the course of the acute care hospitalization may be of importance. In addition, the surgical planning,[7-11] the development of early spasticity,[12, 13] the occurrence of medical complications and the acute care length of stay (LOS) [14] were suggested to influence the rehabilitation process and/or the neurological recovery. However, there is no study to date that has considered factors related to the acute care hospitalization process in a prediction model of functional outcome.

Previous studies predicting functional recovery are based on general functional outcome scales, such as the Functional Independence Measure (FIM) or the Glasgow Outcome Scale (GOS).[1, 4, 15,

[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

Our analyses were based on a prospective cohort including 159 adult patients with acute T-SCI from C1 to L1 consecutively admitted to a single Level I trauma center specialized in SCI between January 2010 and February 2015 (126 males and 33 females; 46.2±20.0 years old). 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, sex, body mass index (BMI), trauma severity measured by the Injury Severity Score (ISS), presence of a high velocity trauma, 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 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 ASIA impairment scale (AIS) 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 AIS motor score was also noted, with a higher score designating higher motor strength.[18]

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-SCI. [10] Pneumonia was diagnosed using clinical features and 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[20]; and PU were diagnosed using clinical guidelines defined by the National Pressure Ulcer Advisory Panel (NPUAP). [21] 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, [22, 23] 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 (≥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 ± standard deviation for continuous variables, and proportions or percentages for categorical variables.

All analyses were performed separately for individuals sustaining tetraplegia and paraplegia. 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. The association between the independent variables (Table 1) 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 (Fig. 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 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 decrease 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 the absence of motor-sacral sparing following SCI predicts limited neurological recovery, [24] 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. It is recognized that the occurrence these complications in chronic SCI may interfere with the physical and social well-being. [25] 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 occurrence, [26] particularly given that it also predisposes individuals with SCI at higher risk of chronic relapses. [27] 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 paraplegia, [28-31] which could further limit their functional recovery. However, although severity of complications was not assessed in this study, there was no significant difference between the two groups in terms of number of complications (Table 2). 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,[32, 33] 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 complications, [34] 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 LOS. [35-37] 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.[34, 38]

While it is assumed that spasticity can alter functional outcome, it remains unproven.[13] 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 (Tables 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 syndrome,[39] 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, baseline characteristics of patients lost to follow-up were similar to those completing the study, except for age (Table 3). 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 tetraplegia[3] and generally reaches a plateau around six months post-injury to slow down thereafter[2, 3, 40] and subsequently, the intensive functional rehabilitation is generally advanced or completed at this time.[41] 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[22, 42] and the importance of patient's perception, [23] strong validation studies are still lacking. Finally, 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.

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 (ASIA 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.

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

Potential predictive variable	*Input variable for multivariate analysis*		*Coding*
	Tetraplegia	*Paraplegia*	
1. Surgical delay			<24h post-trauma >24h post-trauma
2. Early spasticity	x	x	Presence or not
3. Sex			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 *Tetraplegia: C1 to C4* *Paraplegia: T2 to T7* Low level *Tetraplegia: C4 to T1* *Paraplegia: T8 to L1*
16. Injury severity score (ISS)		x	Continuous data

ASIA, American Spinal Injury Association

TBI, Traumatic brain injury

LOS, Length of stay

Table 2: Socio-demographic and clinical characteristics at hospital admission for individuals with tetraplegia and paraplegia (total cohort N=91)

Characteristics	*Tetraplegia N=43*	*Paraplegia N=45*	*p-value*
ASIA grade			
AIS-A,B	65.1%	82.2%	0.09
AIS-C,D	34.9%	17.8%	
Neurologic level			
High tetraplegia (C1-C4)	39.5%	---	
Low tetraplegia (C5-T1)	60.5%	---	0.11
High paraplegia (T2-T7)	--	22.2%	
Low paraplegia (T8-L1)	--	77.8%	
ASIA motor score *(mean +/-SD)*	38.1 (30.1)	59.0 (16.7)	$<10^{-3}$
Age *(mean +/-SD)*	44.3 (17.2)	40.0 (15.6)	0.40
Sex *(% Male)*	74.4%	86.7%	0,18
ISS *(mean +/-SD)*	25.7 (14.1)	27.2 (7.7)	0.08
BMI *(mean +/-SD)*	27.4 (10.2)	25.5 (4.0)	0.16
Presence of TBI	53.5%	37.8%	0.20
Presence of moderate or severe TBI	2.3%	6.7%	0.33
Early surgery *(<24h post-trauma)*	97.7%	97.8%	1.00
Acute care LOS *(in days) (mean +/-SD)*	32.7 (26.0)	27.9 (16.8)	0.15
Presence of medical complications	58.5%	40.0%	0.10
Presence of multiple complications	23.3%	15.6%	0.26
Presence of early spasticity	74.4%	48.9%	0.02*
Smoking status *(% active smoker)*	25.6%	31.1%	0.63
High-velocity trauma mechanism	41.9%	33.3%	0.27

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).

Characteristics	*Patients with 6 months FU N=88*	*Patients excluded N=71*	*p-value*
ASIA grade			
AIS-A,B	73.9%	61.4%	0.12
AIS-C,D	26.1%	38.6%	
Neurologic level			
High tetraplegia (C1-C4)	19.3%	26.8%	0.34
Low tetraplegia (C5-T1)	29.5%	31.0%	0.86
High paraplegia (T2-T7)	11.4%	9.9%	0.80
Low paraplegia (T8-L1)	39.8%	32.4%	0.41
ASIA motor score *(mean +/-SD)*	49.2 (26.0)	51.1 (26.0)	0.99
Age *(mean +/-SD)*	42.1 (16.5)	51.2 (22.7)	$<10^{-3}$*
Sex *(% Male)*	80.7%	77.5%	0.70
ISS *(mean +/-SD)*	26.5 (11.1)	26.3 (10.7)	0.83
BMI *(mean +/-SD)*	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 *(in days) (mean +/-SD)*	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)

	Total SCIM score		
Predictive variable	β *coefficient*	*95%CI*	*P-value*
ASIA grade			
AIS A-B	-27.3	(-42.9;-11.8)	$<10^{-3}$*
AIS C-D	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)

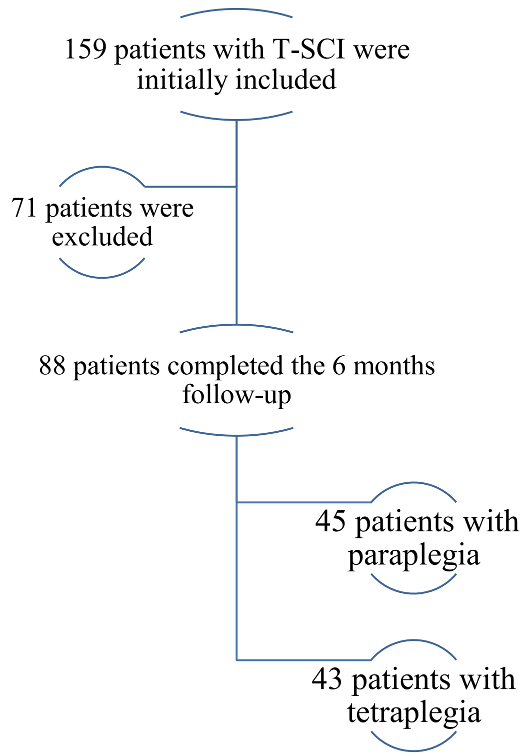
	Total SCIM score		
Predictive variable	β *coefficient*	*95%CI*	*P-value*
ASIA grade			
AIS A-B	-19.1	(-31.3;-6.9)	$<10^{-3}$*
AIS C-D	0^d		
BMI	-1.3	(-2.3;-0.4)	$<10^{-3}$*
ISS	-0.8	(-1.4; -0.2)	0.01*
Presence of early spasticity	-6.3	(-13.9;1.4)	0.11
	R^2= 0.548		

0^d Reference category

ASIA, American Spinal Injury Association

BMI, Body Mass Index

Figure 1: Description of the inclusion process of patients in this prospective study.



Figure

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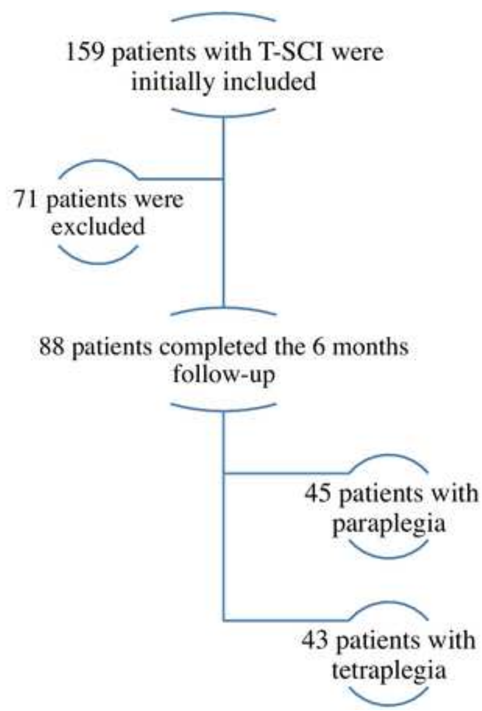

13. Appendix 5: Manuscript submitted to Journal of Spinal Cord Medicine

The Journal of Spinal Cord Medicine

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

--Manuscript Draft--

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Abstract:	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=0.004). High cervical injuries (C1-C4) showed an important tendency to increase the likelihood of developing a complication, while high cervical injuries and increased trauma severity increased the odds of developing respiratory complications. Conclusion: Management in a SCI-center even at a later stage during the acute hospitalization will limit the rate of complications to a level similar to that observed in patients managed exclusively in a SCI-center, but at the expense of a longer LOS.

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	Prompt transfer to a SCI-center for complete perioperative management is recommended for motor-complete cervical SCI.

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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

ABSTRACT

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=0.004). High cervical injuries (C1-C4) showed an important tendency to increase the likelihood of developing a complication, while high cervical injuries and increased trauma severity increased the odds of developing respiratory complications.

Conclusion: Management in a SCI-center even at a later stage during the acute hospitalization will limit the rate of complications to a level similar to that observed in patients managed

exclusively in a SCI-center, but at the expense of a longer LOS. Prompt transfer to a SCI-center for complete perioperative management is recommended for motor-complete cervical SCI.

Key words*:* spinal cord injury, complications, specialized centers, tetraplegia, acute care.

Abbreviations: SCI, Spinal Cord Injury; LOS, Length of stay; NS center, Non-Specialized center

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The authors report no declarations of interest.

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 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 restriction. This is particularly true during the acute care hospitalization, as the neurologic deficit is at its peak and associated traumatic injuries requiring additional surgical procedures may be present. As a result, the rehabilitation process may be delayed and individuals may be prone to developing complications.

The occurrence of complications following SCI is associated with increased hospital length of stay (LOS), costs of care and mortality rate,[2, 3] and may also impact neurological and functional outcomes.[4, 5] While the occurrence of acute complications remains frequent,[6] studies geared 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 neurological and functional outcomes as well as promoting social reintegration.[7, 8] SCI-centers have demonstrated their effectiveness by decreasing hospital resource utilization and overall mortality rate.[3, 7-10]

Recommendations for early transfer to SCI-centers are however based on poor evidence (Level V - panel opinion).[8] 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[11-13] and decrease risks of complications,[14, 15] 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.[16]

Although some studies have addressed the impact of specialized acute SCI-centers on the occurrence of complications[2, 17, 18], these studies either compared individuals managed in a NS or a SCI-center for the entire acute care hospitalization, or by comparing individuals transferred at some point to the SCI-center, regardless of the time spent in the NS center. In addition, patients sustaining severe tetraplegia were not specifically examined. Thus, the hypothesis underlying the current study is that complete perioperative and surgical management in a specialized SCI-center will decrease the occurrence of complications. Accordingly, the purpose of this study was to compare the occurrence of complications between patients surgically and preoperatively managed in a non-specialized center (NS) before being transferred to the SCI-center versus individuals promptly transferred to a SCI-center for complete surgical and perioperative 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. The institutional review board approved this study. The severity of the injury was assessed using the ASIA (American Spinal Injury Association) International Standards for neurological classification of SCI. All subjects included in this study sustained a motor-complete cervical traumatic SCI, which was defined as a grade A or B severity on the ASIA impairment scale (AIS), consisting of no preserved motor function through sacral segments.[19] 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 perioperative 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 in 29 patients acutely managed in one of ten non-specialized (NS) acute care centers for perioperative and surgical management 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 SCI 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 SCI team provided 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. Patients were transferred to the ward after their condition was deemed stable by the medical team. Rehabilitation therapies were provided continuously throughout the hospitalization. Perioperative care in the specialized SCI-center follows evidence-based recommendations for the acute care of SCI patients.[8] 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 directed the acute rehabilitation process, applying interventions to promote functional and neurological recovery and coordinating the transfer to a functional rehabilitation facility once the patient’s condition does not require additional active medical or surgical intervention.

Data collection and outcomes

All data pertaining to the hospitalization at the Level I SCI-specialized acute center was prospectively collected by research assistants. For patients in Group 2, chart review was required to collect information pertaining to the presence of complications upon admission to the SCI-center.

An independent medical archivist performed the retrospective data collection for the following variables: age, gender, body mass index (BMI) and trauma severity as measured by the Injury Severity Score (ISS).[20] The ISS was dichotomized into high (≥ 26) and low trauma severity (<26), based on the observed median value of 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 AIS. 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 <24h or ≥24h post-trauma.

Non-neurologic complications

The main outcome (main dependent variable) was the occurrence of non-neurological medical complications during the hospitalization at the SCI-center. A non-neurological complication is defined as a secondary condition developing and diagnosed after the initial trauma, as opposed to a condition directly due to the trauma. Since information regarding the occurrence of complications during the hospitalization in the NS center (prior to transfer to the SCI-center) was generally absent in the transfer records of patients for both groups, this information could not be collected in the present study. However, complications developed previously in the NS center but still present at admission to the SCI-center were noted for both groups.

The following complications were considered: 1) overall respiratory complications, 2) pneumonia, 3) urinary tract infections (UTI), and 4) pressure ulcers (PU). These complications were shown to be the most frequent in acute care hospitalization following SCI.[14] Overall respiratory complications included pneumonia, acute respiratory distress syndrome, pulmonary embolism, bronchitis, atelectasis, pulmonary oedema, and pneumothorax. Since the incidence of pneumonia is high in patients with acute tetraplegia, pneumonia was also analyzed independently.[8, 21] Respiratory complications were diagnosed using clinical features and were confirmed by a radiologist using chest X-rays.[22] UTI were diagnosed using criteria from the 2006 Consortium for Spinal Cord Medicine Guidelines, based on the presence of 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 or more of the above-mentioned complications during their stay at the specialized SCI center, and was expressed as a percentage.

Analysis

T- tests and chi-square tests were first used to compare baseline characteristics between the two groups (Table 1). Normality of the distribution was assessed using the Kolmogorov-Smirnov test with a significance level set at 0.05. Comparison of the occurrence of medical complications between the two groups was also done using Chi-square tests .

Then, in order to account for discrepancies in clinical and socio-demographic characteristics, a multivariate logistic regression model was used to determine the impact of the type of perioperative acute care facility (Group 1-SCI center, or Group 2-NS center) on the occurrence of medical complications. As a first step, bivariate analyses (chi-square and t-tests for categorical and continuous variables respectively) were used to determine the strength of association between each independent variable and the occurrence of complications (outcome). We retained those variables that were associated with the outcome with a p-value of 0.2 for the multivariate regression model. The same procedure was done to identify variables associated with the occurrence of respiratory complications in a separate model.

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. IBM SPSS Statistics Version 21 software package was used for all statistical analyses.

RESULTS

Patient characteristics

The entire cohort for our study consisted in 116 subjects who sustained a traumatic motor-complete cervical SCI. There were 87 patients in Group 1 (SCI-center), while 29 (NS center) were in Group 2. Individuals from Group 2 were hospitalized for a median of 18.8 (IQR8.2-36.3) days in a NS center before their transfer to the SCI center.

Socio-demographic and clinical characteristics are shown in Table 1. There were no significant differences between the two groups in terms of age, gender, severity of the SCI (AIS grade), neurologic level of injury, 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 hospital stay at the SCI-center, which was similar for both groups (Table 2). When looking at individual types of complications, there were no differences between the two groups with respect to respiratory complications, pneumonia, UTI and PU (Table 2).

Patients who were preoperatively managed in the SCI-center (Group 1) were sent sooner to the intensive rehabilitation facility as compared to patients of Group 2 (NS center) (Table 2). Indeed, following their stay in the NS center (of nearly 30 days), patients from Group 2 were hospitalized in the SCI-center for an additional 20-day period on average (mean of 77.3 and 56.6 days, for Groups 2 and 1 respectively). It is important to note that the surgical delay was similar for both groups (SCI vs. NS center) (Table 1).

Three variables were associated with the overall occurrence of medical complications following bivariate analyses (Table 3) and were then included as potential predictive factors of the occurrence of complications in the multivariate logistic regression model: 1) the type of perioperative acute care facility (Group 1 or 2), 2) neurologic level of injury, and 3) trauma severity (ISS). A higher level of cervical injury (C1 to C4) showed a tendency towards increased likelihood of developing a medical complication, with an odd ratio of 2.2 (p=0.07) (Table 4).

Finally, four variables were associated with the occurrence of respiratory complications following bivariate analyses (Table 3) and were subsequently included as potential predictive factors of the occurrence of respiratory complications in the multivariate logistic regression model: 1) the type of perioperative acute care facility (Group 1 or 2), 2) neurologic level of injury, 3) age, and 4) trauma severity (ISS). Higher level of cervical injury (C1 to C4) and higher trauma severity were significantly associated with the occurrence of respiratory complications, with odd ratios of 3.3 and 2.6 respectively (Table 5).

DISCUSSION

This study is the first to assess the occurrence of complications during the acute hospitalization phase with respect to the type of perioperative acute care facility following a motor-complete cervical SCI. Results of this study indicate that the rate of medical complications during the SCI-center stay was similar for individuals preoperatively managed in a SCI vs. NS center (Group 1 or 2). However, results also suggest that individuals preoperatively managed in a NS center were transferred significantly later to functional rehabilitation facility (they had a longer LOS in acute care).

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 84% worldwide.[6, 25-27] This great variability may be attributed to the different methods and definitions employed. Data on complications in this study were collected prospectively, similar to Grossman et al.[27] who also used a prospective data collection and reported a rate of 84% in patients with complete SCI. Others used a retrospective data collection and may have not had a complete picture of all the medical complications.[6, 25, 26]

Specialized acute care SCI-centers improve outcomes and decrease the occurrence of complications following a SCI.[7, 10] Surprisingly, results of this study did not confirm the initial hypothesis of this study of a lower occurrence of medical complications in Group 1, since the complication rate was similar between the two groups. Moreover, the type of perioperative acute care facility was not predictive of the occurrence of complications in our regression models. It is however important to underline that complications developing in the NS center and resolved at the time of admission in the SCI-center were not included in the current study. It is thus possible that the number of complications was underestimated in Group 2, considering that the average stay in the NS center prior to transfer was considerable (27.4±26.5 days), ample time to develop a complication and for it to resolve. On the other hand, the rate of medical complications for Group 1 might have been overestimated since this Group had a higher proportion of persons with concomitant TBI than Group 2. The occurrence of concomitant TBI is a risk factor for complications following SCI.[28, 29]

Considering that complete acute care management in a NS center was previously shown to be associated with a higher complication rate,[7, 10, 17] referral to a SCI-center following surgery seems beneficial in order to prevent the expected increase in complication rate for patients managed exclusively in a NS center. Lowering the complication rate following surgery in a NS center to a level similar to that achieved with complete management in a SCI-center could require additional efforts and resources, as suggested by the longer LOS in the SCI-center for Group 2 despite a mean of 27 days already spent in the NS center. Moreover, 10.3% of patients in Group 2 were admitted to the SCI-center with existing complications developed during their stay at the NS-center, which would require additional care from the SCI-center team in order to promote the healing process but also to prevent recurrence.[30]

The occurrence of medical complications during the SCI-center stay was associated with a high level of cervical SCI. Motor-complete SCI is recognized as the main predictor of worst neurological and functional outcomes[16, 31] and is a predictive factor for the occurrence of acute complications.[6] Since only motor-complete tetraplegia was included in this study, the level of injury was expected to be a significant predictor of complication occurrence. Indeed, individuals sustaining higher level of cervical SCI may suffer from severe respiratory and cardiovascular dysfunction[21] as well as severe mobility restriction, dependency for activities of daily living, bed mobility and transfers,[32, 33] which may ultimately lead to medical complications.

The occurrence of respiratory complications was associated with the level of cervical injury and higher trauma severity. High cervical motor-complete SCI is typically associated with severe respiratory, cardiovascular and mobility dysfunction.[21] 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.[34] Moreover, dysphagia is also frequently diagnosed in the acute and subacute periods following the injury.[35] As a result, these individuals are particularly prone to respiratory infections and complications; they also may require mechanical ventilation assistance and prolonged intensive care stay.[36]

Finally, the LOS in the SCI-center was significantly longer for individuals transferred after surgery in a NS center. Many factors could influence the acute care LOS, including early admission to specialized SCI-center.[7, 37] Indeed, early management by a specialized multidisciplinary team may help to optimize the use of hospital resources and facilitate eventual transfer to the functional rehabilitation center.[2, 3] SCI-centers deal with a larger population of patients with SCI, and may therefore be better at early recognition and prevention of risk factors contributing to common complications.

Study limitations

The main limitation of this study is the small number of patients, particularly for Group 2, limiting the statistical power of this study. A prospective study including more patients should be performed. Also, since patients in Group 2 came from different hospital centers, patient management may vary in the different centers, which may have influenced our results.

Data pertaining to the surgical intervention was not collected in this study. However, since the surgical delay was similar and the purpose of spinal surgery following an acute cervical SCI remains realignment and decompression of the spinal canal for both groups, it is unlikely that differences in the surgical procedure influenced the results of this study.

CONCLUSIONS

This study suggests that the complication rate is similar for patients with tetraplegia who are operated in a nonspecialized center and transferred to a SCI-center for post surgical management as for those patients managed in a SCI-center for complete perioperative and surgical care. However, patients who were transferred from the NS post-surgery had a longer LOS in the SCI-center contributing to an increased delay before initiating intensive functional rehabilitation. Prompt transfer to a SCI-center before surgery for motor-complete cervical SCI may optimize the care trajectory by favouring earlier transfer to rehabilitation.

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
N	---	*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

N, number of subjects
ISS, Injury severity score
TBI, Traumatic brain injury

Table 2

Comparison of medical complications and length of stay according the type of perioperative acute care facility following a motor-complete cervical traumatic SCI.

Occurrence of complications		**Type of perioperative acute care facility**		**p-value**
		Group 1 (SCI-center)	**Group 2 (NS-center)**	
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 3: Factors associated with medical complications and with respiratory complications: Bivariate analysis

	Medical complications	P	Respiratory complications	P
SCI-center NS center	71.3% 72.4%	1.00	54.0% 51.7%	0.83
Male Female	72.8% 66.7%	0.61	55.4% 45.8%	0.50
ISS<26 ISS≥26	63.6% 78.7%	0.10	40.0% 65.6%	0.01*
AIS-A AIS-B	72.8% 68.6%	0.66	56.8% 45.7%	0.31
Level C1-4 Level C5-8	79.4% 62.3%	0.06*	66.7% 37.7%	0.03*
TBI No TBI	66.7% 75.8%	0.31	56.5% 50.0%	0.58
Surgical Delay <24h ≥24h	 71.4% 71.6%	1.00	 51.0% 55.2%	0.71
Smoker Non-smoker	70.4% 72.6%	0.84	55.6% 51.6%	0.71
Age	44.8±18.5 (complications) 49.1±21.1 (no complications)	0.28	45.2±17.5 (complications) 47,0±21.3 (no complications)	0.03*

SCI, Spinal cord injury
NS, Non-specialized
ISS, Injury severity score
AIS, ASIA impairment scale
TBI, Traumatic brain injury

Table 4

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

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Variable	Odd ratio	95%CI	p-value
Type of perioperative acute care management			
Group 1 (SCI-center)	1 [d]	--	
Group 2 (NS-center)	1.1	(0.4 ; 2,9)	0.87
Neurologic level of injury			
C1-C4	2.2	(0.9 ; 5.1)	0.07*
C5-C8	1 [d]	--	
ISS			
<26	1 [d]	--	
≥26	2.0	(0.84 ; 4.5)	0.12

1 [d], reference category

ISS, Injury severity score

Table 5

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

Variable	**Odd ratio**	**95%CI**	**p-value**
Type of perioperative acute care management			
Group 1 (SCI-center)	1[d]	--	
Group 2 (NS-center)	0.7	(0.3 ; 1.8)	0.50
Neurologic level of injury			
C1-C4	3.3	(1.5 ; 7.4)	<0.01*
C5-C8	1[d]	--	
Age	0.99	(0.9 ; 1.0)	0.60
ISS			
<26	1[d]	--	
≥26	2.6	(1.2 ; 5.8)	0.02*

1 [d], reference category

ISS, Injury severity score

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