

## ORIGINAL ARTICLE

# Recovery following ischemic myelopathies and traumatic spinal cord lesions

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**Background:** As the general population ages, the rising prevalence of vascular lesions of the spinal cord will become significant. The aim of this study was to compare the neurological and functional outcomes of patients with ischemic spinal cord injury (ISCI) and traumatic spinal cord injury (TSCI).

**Setting:** Spinal cord unit of a rehabilitation hospital in Italy.

**Study design:** Retrospective study.

**Patients and methods:** We studied 179 patients with a TSCI and 68 with an ISCI. At admission and discharge, patients were examined by American Spinal Injury Association (ASIA) standards, Barthel Index, Rivermead Mobility Index and Walking Index for Spinal Cord Injury. Bowel and bladder management and discharge destination were recorded at discharge. Analysis of covariance (ANCOVA) and logistic regression models were used to analyze the effects of the etiology of the lesion, AIS level at admission, site of the lesion and the presence of complications on measured outcomes.

**Results:** Patients with an ISCI were older and experienced fewer cervical lesions and complications at admission. By ANCOVA and logistic regression, age, AIS level and lesion level were the chief predictors of neurological and functional outcome, whereas etiology had no effect on outcome.

**Conclusions:** A diagnosis of ischemia and trauma is not a determinant of neurological and functional recovery in spinal cord injury patients. Instead, the outcome of these patients is influenced by age, lesion level and AIS level.

*Spinal Cord* (2011) **49**, 897–902; doi:10.1038/sc.2011.31; published online 5 April 2011

**Keywords:** spinal cord ischemia; spinal cord injuries; neurological outcome; functional outcome

## Introduction

Spinal cord ischemia is a rare disorder, the incidence of which is unknown. Sandson<sup>1</sup> reported that it constitutes ~1.2% of cases that are admitted to a neurological department with vascular pathologies. Spinal cord ischemia usually affects the area of the anterior spinal cord artery and is characterized by sudden and progressive onset, pain, loss of strength and decreased sensation to temperature and pain sensations, and relative preservation of position and vibratory sensations (anterior spinal cord syndrome).<sup>2</sup>

Likely because of its rarity, little data exist on spinal cord ischemia. The largest series<sup>2–8</sup> have been primarily reported on neurological, bladder and walking recovery. Moreover, few studies have compared spinal cord ischemia with traumatic injuries,<sup>4,5</sup> and only two<sup>5,8</sup> have corrected for the

effects of differences between these populations. Patients with traumatic spinal cord injury (TSCI) are typically younger, often present with complete lesions, and have shorter times between the development of the lesion to admission for rehabilitation<sup>9</sup> than those with non-traumatic lesions—these disparities render the two populations incomparable.

The importance of research on outcomes in non-traumatic patients was discussed by Ditunno,<sup>10</sup> who highlighted the little attention that has been paid to non-traumatic spinal cord lesions, which will likely increase in an aging society. Ditunno<sup>10</sup> also emphasized the risks of making generalizations with regard to non-traumatic spinal cord lesions, which include disparate pathologies with varying prognoses. Ditunno also stressed the need for specific statistical methods to avoid biases because of differences between traumatic and non-traumatic populations.

The aim of this study was to compare the functional and neurological outcomes of patients with ischemic spinal cord injury (ISCI) and TSCI.

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Received 21 October 2010; revised 3 March 2011; accepted 6 March 2011; published online 5 April 2011

## Patients and methods

### Patients

We retrospectively compared 68 patients with an ISCI and 179 with a TSCI who were admitted for their first rehabilitation between 1997 and 2008. ISCI is, in part, a diagnosis of exclusion,<sup>3,6</sup> based on the clinical picture, anamnestic records of associated vascular factors and neuroimaging (MRI) and laboratory tests (blood and CSF study).<sup>3,6,7</sup>

Patients with an ISCI were divided into three groups—idiopathic ischemia, surgery for aortic pathologies and arteriosclerosis. As Per Nedeltchev,<sup>7</sup> we diagnosed arteriosclerosis based on a history and findings of cerebral, coronary or peripheral artery disease or the presence of >2 vascular risk factors (hypertension, diabetes mellitus, hyperlipidemia, cigarette smoking and positive personal and family history). Arteriosclerosis of the spinal artery is rarely associated with spinal infarcts; conversely, aortic atherosclerotic lesions correlate well with spinal cord ischemic pathologies.<sup>11–13</sup>

Idiopathic ischemia was diagnosed when subjects did not meet the criteria for atherosclerosis and when other possible causes of myelopathy were ruled out.<sup>1,7</sup> On the basis of a previous study,<sup>14</sup> patients in whom ISCI was associated with vascular malformations, spinal tumors and spinal cord compression were excluded. Patients with other neurological or non-neurological pathologies that did not allow full participation in the rehabilitation were also excluded. Whenever a patient was transferred to a general hospital for more than 3 weeks because of acute pathologies, such as cardiac infarction, which required treatment from a specialist, the re-admission was considered a second admission, and the patient was excluded.

### Measures

For all patients, the following variables were recorded: lesion to admission time (LTA, days); injury-related variables (etiology, medical complications at admission); length of stay (LOS, days); and discharge destination (to the patient's home or an institution). The medical complications were: pressure sores, deep vein thrombosis, pulmonary embolism, heterotopic ossification and urological complications (excluding urinary tract infections).

Neurological examinations were conducted at admission and discharge, as per American Spinal Injury Association (ASIA) standards.<sup>15</sup> Motor scores (MS), neurological level and ASIA Impairment Scale (AIS) grades were evaluated. Sensitive scores were not included in the analysis, because motor evaluation is the best predictor of impairment in patients with an SCI.<sup>16</sup>

On the basis of previous studies,<sup>17</sup> functional status at admission and discharge was assessed by a trained examiner (GS) using:

- Barthel Index (BI): scores from 0 to 100 were assigned, wherein higher scores reflected greater independence in daily activities; BI subitem scores were also recorded to determine upper extremity function.<sup>17</sup>
- Rivermead Mobility Index (RMI): a 15-item mobility scale that assesses bed mobility, transfers and walking; scores range from 0 to 15.<sup>17</sup>
- Walking index for spinal cord injury (WISCI):<sup>18</sup> a new 0–20 scale that evaluates walking based on the need for physical assistance, braces and devices.
- Bladder voiding modalities and autonomy in bowel management were assessed per the Gruppo Italiano Studio Epidemiologico Mielolesioni (GISEM) study.<sup>19</sup> Bladder outcome was categorized into two voiding modalities at discharge:
  - Good bladder control (patients can start and stop micturition at will; residual volume less than 100 ml, not requiring additional bladder emptying; bladder pressure lower than 70–80 cm H<sub>2</sub>O (males) and 40–60 cm H<sub>2</sub>O (females)).<sup>20</sup>
  - Other voiding modalities (indwelling catheter, intermittent catheterization, self-intermittent catheterization and Valsalva maneuver).

We recorded whether patients were independent with regard to bowel management.

### Statistical analysis

All statistical analyses were carried out with SPSS for Windows (version 14.0, Chicago, IL, USA). Descriptive statistics were calculated for all variables. Normality of variables was assessed by Shapiro–Wilk normality test. *T*-test and Mann–Whitney U test were used to analyze independent samples, and Fisher's exact test and Pearson's chi square test were used to evaluate differences between ISCI and TSCI patients. Because these populations differ with regard to elements that affect the recovery from an SCI, the effects of confounding factors were analyzed by analysis of covariance (ANCOVA) and logistic regression.

*Normality of measures.* According to the Shapiro–Wilk test for normality, scores that are related to BI, RMI, WISCI and MS are not distributed normally, thus, for these measures, Mann–Whitney U test was carried out for non-parametric data.

*ANCOVA and logistic regression.* To compare the differences between TSCI and ISCI patients and normalize the effects of confounding factors, BI delta, RMI delta, WISCI delta, MS delta, (calculated as the difference in each score at admission and discharge) and LOS were analyzed by ANCOVA using age, LTA, and BI, RMI, WISCI and MS values at admission as covariates and etiology of lesion (ischemic or traumatic), AIS grade (A, B, C, D and E), lesion level (cervical, lumbar and thoracic) and presence of complications (0 = absence, 1 = presence) as fixed factors. These factors were selected because they are the chief prognostic factors of SCI patients.

The subdivision by neurological level was broad, because within each subdivision, patients with different lesion levels might have disparate functional outcomes.<sup>21</sup> However, the number of patients in our study did not allow us to divide them into more specific groups. Regardless, this division has been demonstrated to be sufficiently precise.<sup>9,17</sup>

Logistic regression analysis was carried out to examine the same (age, LTA, AIS grade and lesion level) variables as predictors of AIS grade improvement (defined as an increase of at least one AIS grade between admission and discharge), bowel management independence, adequate bladder control, discharge destination and BI subitems. For discharge destination, the role of BI at discharge and the absence or presence of pressure sores at discharge were noted. All other variables were considered as independent factors; odds ratios and their 95% confidence intervals (CIs) were also calculated.

In all analyses, a *P*-value of 0.05 indicated significance. For brevity, only significant results are reported; nonsignificant results are discussed when appropriate.

## Results

The study group comprised 67 women and 180 men whose average age was  $43.9 \pm 19.2$  years (range: 13–88 years); 179 presented with TSCI and 68 had an ISCI. The lesion was thoracic in 119 patients, cervical in 66 and lumbar in the remaining 62. No patient was excluded because of concomitant pathologies or transfer to a general hospital. No patient experienced exacerbation of neurological status.

With regard to etiology, 59% of the 69 cases of spinal cord ischemia were due to arteriosclerosis; 10% was due to aortic pathologies and surgery, and 31% was idiopathic.

ISCI patients were significantly older ( $P < 0.001$ ) and had a shorter LOS ( $P < 0.05$ ) than TSCI patients (Table 1). Compared with ischemic patients, traumatic cases were more often male ( $P < 0.001$ ), developed cervical and lumbar lesions more frequently ( $P < 0.001$ ), and experienced more complications at admission ( $P < 0.05$ ); the groups did not differ with regard to AIS grade at admission and discharge or AIS grade improvement (Table 2).

ISCI patients presented with higher BI scores at admission than TSCI subjects ( $24.6 \pm 21.2$  vs  $19.3 \pm 19$ , respectively,  $P < 0.001$  by Mann–Whitney U test) and lower BI delta values, ( $34 \pm 25.5$  vs  $46 \pm 26.4$ , respectively,  $P < 0.05$  by Mann–Whitney U test). BI subitems data were available only for a subset of 133 patients. In this subset, TSCI patients had better outcomes on several BI delta subitems (washing ( $P < 0.05$ ), dressing ( $P < 0.05$ ), and wheelchair transfer ( $P < 0.05$ )) than ISCI subjects (Table 3).

The presence of complications was associated with the level of the lesion ( $P < 0.05$ , Table 2).

**Table 1** Patients' characteristics regarding age, lesion to admission and length of stay, according to etiology of trauma

Variables	ISCI			TSCI			P*
	n	Mean	s.d.	n	Mean	s.d.	
Age	68	57.6	17.2	179	38.7	17.4	<0.001
LTA	68	66.6	100.7	179	56.7	68.2	0.40
Length of stay (LOS)	69	105.8	72	179	133.5	78	0.01

Abbreviations: ISCI, ischemic spinal cord injury; LTA, lesion to admission; LOS, length of stay; TSCI, traumatic spinal cord injury.

\**P*-value refers to *t*-test for independent samples.

## ANCOVA models

Lesion etiology was not a significant predictor of outcome. For BI and RMI, the significant predictors of improvement were age ( $P < 0.001$ ), AIS grade ( $P < 0.001$ ), BI score at admission ( $P < 0.001$ ) and RMI at admission ( $P < 0.001$ ), respectively; furthermore, the relationship between AIS grade and the site of the lesion influenced the mean BI and RMI deltas (ie, the two-way interaction between AIS grade and lesion site was significant,  $P < 0.05$ ).

Age ( $P < 0.01$ ), LTA ( $P < 0.05$ ), WISCI score at admission ( $P < 0.001$ ) and AIS level ( $P < 0.001$ ) were significant predictors of improvement in WISCI score. The mean WISCI delta was lower for AIS level A and higher with better AIS levels.

The ANCOVA model implicated age ( $P < 0.001$ ) and AIS level ( $P < 0.001$ ) as significant predictors for MS delta. The mean MS delta was lower for AIS level A and higher at better AIS levels.

None of the variables in the ANCOVA model (age, LTA, lesion etiology, site of lesion, AIS level and presence of complications) was a significant predictor of LOS.

## Logistic regression models

**AIS level improvement.** Age ( $P < 0.01$ ) was the only significant predictor of AIS level improvement (OR 0.974); the probability of improvement in AIS level was higher in younger patients.

**Bowel management independence.** Age ( $P < 0.01$ ), lesion level ( $P < 0.01$ ), and AIS level ( $P < 0.01$ ) were the only significant predictors of bowel management independence. The odds ratio for age was 0.976, indicating that the probability of achieving bowel management independence was higher in younger patients. The odds ratios for patients with thoracic

**Table 2** Patients characteristics regarding gender, site of lesion, AIS at admission and complications according to etiology of trauma

Variables	ISCI (n = 68)	TSCI (n = 179)	Total (n = 247)	P*
<b>Sex</b>				
Female	32 (47%)	35 (20%)	67 (27%)	<0.001
Male	36 (53%)	144 (80%)	180 (63%)	
<b>Site of lesion</b>				
Cervical	9 (13%)	57 (32%)	66 (27%)	<0.001
Thoracic	48 (70%)	71 (40%)	119 (48%)	
Lumbar	11 (17%)	51 (38%)	62 (25%)	
<b>AIS (at admission)</b>				
A	23 (34%)	89 (50%)	112 (45%)	0.176
B	5 (7%)	14 (8%)	19 (8%)	
C	23 (34%)	48 (27%)	71 (29%)	
D	17 (25%)	28 (15%)	45 (18%)	
<b>Complications</b>				
Absence	50 (73%)	109 (61%)	159 (64%)	0.041
Presence	18 (27%)	70 (39%)	88 (36%)	

Abbreviations: AIS, ASIA impairment scale; ISCI, ischemic spinal cord injury; TSCI, traumatic spinal cord injury.

\**P*-value refers to Fisher's Exact Test for 2 by 2 tables and to Pearson's Chi Square Test otherwise. Column percentages are given in brackets.

**Table 3** Deltas score for each Barthel Index subitems (deltas are calculated as the difference between the score at discharge and the score at admission) according to lesion etiology

Deltas score	ISCI (n = 33)	TSCI (n = 100)	Total (n = 133)	P*
<b>Feeding</b>				
0	27 (82%)	73 (73%)	100 (75%)	0.589
5	4 (12%)	17 (17%)	21 (16%)	
10	2 (6%)	10 (10%)	12 (9%)	
<b>Washing</b>				
0	29 (88%)	64 (64%)	93 (70%)	0.009
5	4 (12%)	36 (36%)	40 (30%)	
<b>Self-care</b>				
0	23 (70%)	59 (59%)	82 (62%)	0.308
5	10 (30%)	41 (41%)	51 (38%)	
<b>Bladder management</b>				
0	16 (49%)	39 (39%)	55 (41%)	0.439
5	3 (9%)	6 (6%)	9 (7%)	
10	14 (42%)	55 (55%)	69 (52%)	
<b>Bowel management</b>				
0	19 (58%)	41 (41%)	60 (45%)	0.250
5	1 (3%)	5 (5%)	6 (5%)	
10	13 (39%)	54 (54%)	67 (50%)	
<b>Wheelchair transfers</b>				
0	8 (24%)	10 (10%)	18 (14%)	0.007
5	17 (52%)	33 (33%)	50 (37%)	
10	7 (21%)	40 (40%)	47 (35%)	
15	1 (3%)	17 (17%)	18 (14%)	
<b>Locomotion</b>				
0	11 (33%)	15 (15%)	26 (20%)	0.079
5	16 (49%)	54 (54%)	70 (52%)	
10	4 (12%)	13 (13%)	17 (13%)	
15	2 (6%)	18 (18%)	20 (15%)	
<b>Stairs management</b>				
0	24 (73%)	69 (69%)	93 (70%)	0.103
5	8 (24%)	15 (15%)	23 (17%)	
10	1 (3%)	16 (16%)	17 (13%)	
<b>Dressing management</b>				
0	20 (61%)	31 (31%)	51 (38%)	0.004
5	8 (24%)	27 (27%)	35 (26%)	
10	5 (15%)	42 (32%)	47 (36%)	

Abbreviations: ISCI, ischemic spinal cord injury; TSCI, traumatic spinal cord injury.

\*P-value refers to Fisher's Exact Test for 2 by 2 tables and to Pearson's Chi Square Test otherwise. Column percentages are given in brackets.

and lumbar lesions were 5.4 and 3.8 times higher, respectively, than that of patients with cervical lesions. The odds ratios for patients with AIS levels C and D were 2.9 and 47 times higher, respectively, than that of patients with AIS level A.

**Good bladder control.** AIS level ( $P < 0.01$ ) was the only significant predictor of good bladder control. The odds ratios for AIS B, C and D patients were 37, 58 and 630 times higher, respectively, than that of patients with AIS level A.

**Discharge disposition.** BI score at discharge ( $P < 0.01$ ) and the presence of sores ( $P < 0.01$ ) were significant predictors

of discharge destination. Odds ratios were computed for patients who returned home versus those who were admitted to other wards or institutionalized. The odds ratio for the presence of sores was  $\sim 4.5$ . The probability of returning home after discharge for patients without sores was  $\sim 4.5$  times higher than for patients with sores; this probability rose with increasing BI scores at discharge.

**BI subitems.** By logistic regression of BI subitems, there were no significant predictors of improvement in self-care or feeding. Age, lesion level and AIS level were the chief predictors of most BI subitems. In contrast, there were no significant effects of etiology on BI subitems by logistic regression analysis, with the exception of improvement in dressing, for which AIS level ( $P < 0.01$ ), lesion level ( $P < 0.01$ ) and etiology ( $P < 0.05$ ) were significant predictors. The odds ratio of dressing management independence for patients with a traumatic etiology was 7.7 times higher compared with patients with vascular etiologies.

## Discussion

This series is the largest comparison of neurological and functional outcomes between ISCI and TSCI patients. On the basis of a simple comparison of these patients (Tables 1 and 2), ISCI patients seem to have better neurological and functional outcomes than TSCI subjects. However, the two populations differ with regard to several prognostic factors (age, gender, lesion to admission time and level of lesion), rendering them incomparable. However, the ANCOVA analysis clearly demonstrated that etiology (traumatic or vascular) was not a predictor of neurological or functional outcome. In both populations, the outcome was determined by the above-mentioned prognostic factors (age, lesion level and AIS grade).

The neurological improvement (in terms of AIS grade conversion and motor score improvement) that we observed in the two populations is consistent with previous studies.<sup>3-5,8</sup> Our statistical analysis clearly demonstrates that neurological recovery is not influenced by lesion etiology. By logistic regression, AIS grade conversion depended primarily on age. In the ANCOVA model, age, AIS level and lesion level were the chief predictors of MS.

Although neurological improvement has been correlated with lesion level and AIS grade,<sup>17,21,22</sup> its relationship with age remains unsubstantiated. Recently Pouw *et al.*<sup>8</sup> observed that neurological recovery was the same in paraplegic TSCI and ISCI patients; further, because ISCI patients were older than the traumatic population, the authors concluded that neurological recovery was independent of age. Similarly, Furlan *et al.*<sup>23</sup> did not observe a correlation between age and neurological recovery in patients with TSCI. Thus, this issue deserves further examination, because Scivoletto *et al.*<sup>17,24</sup> noted that in a mixed sample of traumatic and non-traumatic SCI patients, younger patients had a higher rate of AIS grade conversion.

Our ANCOVA models demonstrate that etiology does not predict functional outcomes in SCI patients. In our model,

age, AIS level at admission and lesion level were the major predictors of BI improvement, consistent with previous studies. Recently, Pouw *et al.*<sup>8</sup> found that etiology (traumatic or ischemic) is not a significant predictor of functional outcome, as evaluated using the Spinal Cord Independence Measure. In their prediction model, lesion completeness, age and gender were the only significant determinants of functional outcome, consistent with our data.

The effect of age on independence in performing daily activities has been demonstrated in several studies, in which younger patients have had better outcomes than older subjects.<sup>17</sup> The effects of lesion level and completeness are self-evident and have been examined in several reports.<sup>21,22</sup> Further, by logistic regression, age, lesion level and AIS level at admission were the chief predictors for most BI subitems, which has not been demonstrated in the literature. Lesion etiology was a predictor only for improvement in dressing, for which traumatic patients had a higher probability of improvement.

We assessed outcomes with regard to mobility and walking using specific instruments. By ANCOVA, etiology did not predict RMI or WISCI improvement in SCI patients. In our model, age, AIS level at admission and lesion level were the major predictors of mobility and walking improvement, consistent with previous results. Iseli *et al.*<sup>4</sup> observed comparable walking-recovery rates in traumatic and ischemic patients and concluded that lesion completeness at admission was a principal determinant of walking recovery. In non-traumatic patients with mixed etiologies, Scivoletto<sup>17</sup> showed that mobility and walking recovery was better in younger patients.

We performed a novel analysis of the likelihood of bladder function recovery in the two populations. By logistic regression, etiology was not a determinant of improved bladder control. AIS level at admission was the chief predictor of good bladder control at discharge; these findings are consistent with other studies—Scivoletto<sup>25</sup> found that patients with AIS D grade and, in particular, those with Brown-Sequard and central cord syndromes experience the greatest recovery in bladder function.

The two populations had comparable discharge destination rates, with ~80% of patients returning home. BI score at discharge and the presence of pressure sores were the main predictors of discharge destination, whereas etiology was not a determinant; higher BI scores were associated with a greater probability of returning home at discharge, and the presence of pressure sores was associated with a higher likelihood of being institutionalized. These data support those of previous reports, in which discharge disposition has depended primarily on the level of independence in daily activities.<sup>26</sup> The association between pressure sores and the risk of institutionalization was demonstrated in the GISEM study.<sup>19</sup>

This study has certain limitations. In the general population and for longer periods of observation, the outcomes of patients with spinal cord infarction can be influenced by concomitant pathologies (particularly cardiac or cerebral vascular disease). In our study, the statistical methods, which were corrected for the covariant effects of age, prevented

us from analyzing the effects of concurrent pathologies on rehabilitation outcomes.

Another limitation is the timing of the examinations. The mean post-injury interval (combining LTA with LOS) of all patients was ~6 months (Table 1). As 12-months post-injury is considered the cutoff for the chronic phase in most SCI patients, patients of both population could have further improvement between 6 and 12 months. This issue should be addressed in a dedicated study with a longer follow-up.

It has been suggested that patients with ischemic lesions of idiopathic origin have more favorable outcomes.<sup>7</sup> However, comparing ischemic lesions was not an aim of this study and should be addressed in a separate report with a larger study group.

## Conclusions

Patients with traumatic or ischemic SCIs experience the same neurological and functional outcomes.

## Conflict of interest

The authors declare no conflict of interest.

## Acknowledgements

This work was supported in part by Italian Ministry of Health grants to GS and MM. We thank Blue Pencil Science for editing this manuscript.

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