Outcomes Following Ischemic Myelopathies and Traumatic Spinal Injury

Jacopo Bonavita,¹ Monica Torre,^{2,3} Rita Capirossi,¹ Ilaria Baroncini,¹ Elisa Brunelli,¹
Giorgia Chiarottini,⁴ Elisa Maietti,⁵ Silvia Olivi,¹ Marco Molinari,² and Giorgio Scivoletto^{2,3}

¹Spinal Unit, Montecatone Rehabilitation Institute, Imola, Italy; ²Spinal Unit, IRCCS Fondazione S. Lucia, Rome, Italy; ³Spinal Rehabilitation (SpiRe) Lab, IRCCS Fondazione S. Lucia, Rome, Italy; ⁴Specialization School in Physical Medicine and Rehabilitation, Tor Vergata University, Rome, Italy; ⁵Center for Clinical Epidemiology of the School of Medicine, University of Ferrara, Ferrara, Italy

Background: As the general population ages, the rising prevalence of vascular lesions of the spinal cord will become significant. **Purpose:** 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). **Methods:** We conducted a retrospective study in a spinal cord unit of 2 rehabilitation hospitals. We studied 168 patients with a TSCI and 72 with an ISCI. At admission and discharge, patients were evaluated by American Spinal Injury Association Impairment Scale (AIS) standards and Spinal Cord Independence Measure (SCIM). Length of stay, occurrence of complications, and discharge dispositions were also recorded. Linear and logistic regression models were used to analyze the effects of the etiology of the lesion, AIS level at admission, and level of the lesion. **Results:** Patients with an ISCI were older and experienced fewer cervical lesions and fewer complete lesions than patients with TSCI. By linear and logistic regression, etiology was a predictor (together with lesion features) of functional (SCIM improvement and SCIM at discharge) outcome, with traumatic patients having better outcome than ischemic ones. Age, AIS level, and lesion level were the chief predictors of length of stay, occurrence of complications, and discharge dispositions. **Conclusions:** A diagnosis of ischemia and trauma could be a determinant of functional recovery in SCI patients. **Key words:** functional outcome, neurological outcome, outcome assessment, rehabilitation, spinal cord ischemia

The majority of studies reporting on incidence, epidemiology, clinical pictures, and functional outcome of individuals with spinal cord injury have focused on traumatic spinal cord injury (TSCI), rather than non-traumatic etiology.

In recent years, there has been a significant increase in the number of people with non-traumatic SCI. The few epidemiological studies do not allow an accurate estimation of the actual incidence and prevalence, which are probably underestimated.¹ Some studies report that the incidence of non-traumatic injuries is high and has a variability between 25% and 80% of the total number of patients admitted to spinal units.² Ditunno³ highlighted the importance of studying different outcomes in these 2 groups of patients, even considering the increase in the average age of the population and the consequent increase in the incidence of non-traumatic SCI. He also specified the need not to generalize the results of the studies

on a specific non-traumatic etiology to other etiologies, because different pathologies may result in different prognoses.⁴

Literature currently shows a great variability in the distribution of non-traumatic spinal cord lesions. The pathogenesis includes different etiologies such as degenerative (vertebral spondylosis with spinal stenosis), inflammatory, neoplastic, vascular ischemia, congenital disease, and others.⁵

Studies concerning ischemic SCI (ISCI) are relatively few and involve a small number of patients.⁶⁻¹⁶ The exact incidence of spinal cord ischemia is unknown. Some authors¹⁷ consider an impact of 1.2% of patients admitted to a neurological or a rehabilitation setting with vascular diseases.⁹ Others report that the acute spinal cord ischemia syndrome probably accounts for 5% to 8% of all acute myelopathies.¹¹ According to other authors, the percentage of patients with spinal cord ischemia admitted to spinal rehabilitation units is between 1% and 11%.¹⁸

Corresponding author: Giorgio Scivoletto, MD, Spinal Unit, IRCCS Fondazione S. Lucia, via Ardeatina 306, 00179, Rome, Italy; e-mail: g.scivoletto@hsantalucia.it

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The possible causes of ISCI are several and include complications following cardiac or vascular surgery (usually on the descending thoracic or thoraco-abdominal aorta).¹⁶ Moreover, an aging population means an increase in the prevalence of patients with vascular diseases and possibly with vascular myelopathies. In this group of patients, the study of outcomes and of specific patient characteristics is significant. It is possible that ISCI patients reach different neurological and functional outcomes compared to the TSCI group.

The aim of this study was to compare the neurological and functional outcomes of a relevant group of patients with ISCI with another group of TSCI patients. In particular, the purpose was to compare neurological and functional changes between admission and discharge in the 2 patient groups. Our intention was to define whether the different etiology is a strong predictor of different outcomes (length of stay, complications before and during hospitalization, functional gain, neurological changes, and destination after discharge).

Methods

This multicentric retrospective study involved 2 spinal cord units in 2 rehabilitation hospitals in Italy.

Patients

We retrospectively compared 240 patients with SCI: 168 with traumatic injury (TSCI) and 72 with ischemic injury (ISCI). The distinction between the 2 groups was made in a dichotomous way, without specifying any etiological subcategories. All patients were enrolled in 1 of the 2 centers involved in the study, for their first rehabilitation hospitalization after acute injury, at some point over 5 years.

In the ISCI group, we included the following subcategories: idiopathic ischemia, ischemia secondary to atherosclerosis (patients with a family history and/or clinical data indicating a cerebral artery occlusive disease, coronary or peripheral vessel disease, or, alternatively, the presence of more than 2 risk factors, such as hypertension, diabetes mellitus, hyperlipidemia, smoking),

lesions secondary to surgery for vascular diseases (aneurysm repair, embolization of vascular malformations, arteriovenous fistula, aortic dissection), and barotrauma.^{6,16}

Both neuroimaging and anamnestic history were used to diagnose spinal cord ischemia, even if the diagnosis was sometimes based on exclusion criteria, such as the clinical history and the presence of associated vascular factors; in particular, the diagnosis of exclusion of idiopathic ischemia was made when it was not possible to identify the diagnostic criteria for the atherosclerosis group and when it was not simultaneously possible to recognize another cause of myelopathy.¹³

Procedure

All patients were evaluated at admission and discharge according to the American Spinal Injury Association (ASIA) International Standards for Neurological Classification of Spinal Cord Injury (neurological level and ASIA Impairment Scale [AIS] for the complete/incomplete status)¹⁹ and to the Spinal Cord Independence Measure (SCIM version III) for the evaluation of independence in daily living activities.²⁰ SCIM was used because it is mandatory for reimbursement in Italy and because it is the most sensitive and specific scale to measure independence in spinal lesions, differently from the Functional Independence Measure (FIM), which is more generic and not specific for SCI. Both ischemic and traumatic patients were classified according to the AIS in complete (AIS A) and incomplete (AIS B, C and D) lesions. We also divided the patients into 3 groups according to the neurological level: cervical, thoracic, and lumbar-sacral. Since different levels can have different functional outcomes, these factors were considered relevant for the prognosis in patients with SCI.

For all patients, descriptive statistics were also used for age, gender, lesion to admission time (LTA; elapsed time from the onset of trauma to admission, calculated in days), length of stay (LOS; calculated in months), occurrence of complications before and during hospitalization (calculated in a dichotomous way, presence/absence), and discharge destination (returning home or transfer to another facility) to provide general information of the population studied.

The main complications found were pressure ulcers, deep venous thrombosis, pulmonary embolism, heterotopic ossification, infections, urological complications, and pain. Clinical assessments were conducted by certified rehabilitation physicians with at least 1 year's experience in examining patients with SCI.

Statistical analysis

Descriptive statistics were reported as means and standard deviations for numerical variables or as frequencies and percentage for categorical variables. The association between etiology and other variables was examined using *t* test on means or Pearson's chi-square test on frequencies.

A multivariate analysis was performed to test whether the association between outcomes and etiology persists after accounting for possible confounders, using linear regression models for continuous outcomes (LOS and SCIM gain) and logistic regression models for dichotomous variables (AIS improvement, returning home, and complications).

Analysis was run using R 3.1.2 statistical program, and results were considered significant at the 0.05 level.

Results

Two hundred forty patients were involved in the study: 168 TSCI (age 20-86 years) and 72 ISCI (age

15-86 years). The association between confounders (age, LTA, gender, lesion level, AIS on admission) and etiology highlighted that all variables except LTA (time between event and hospitalization) were significantly different in the 2 groups. Patients with ISCI were older, with a smaller percentage of males, and experienced fewer cervical lesions and fewer complete lesions than patients with TSCI (**Table 1**).

The analysis of association with the outcomes showed that etiology was not associated with AIS improvement and complications both on admission and during hospitalization. On the contrary, ischemic etiology had significantly lower SCIM gain, shorter LOS, and a higher percentage of patients who returned home at discharge (**Table 2**).

Multivariate analysis

Linear regression models

LOS. According to linear analysis, etiology, if adjusted for the effect of confounding factors, is not a significant predictor of LOS. LOS was significantly affected by gender, lesion level, and AIS on admission. On average, males were hospitalized a month longer than females; patients with cervical lesion had a higher LOS, almost 2 months longer than those with thoracic or lower levels; and complete patients (AIS A) had a

Table 1. Association between confounders and etiology

Confounders	Total (n=240)	Ischemia (n= 72)	Trauma (n= 168)	<i>p</i>
Age, years	46.7±18.2	59.3±15.5	41.3±16.6	<.001
LTA, days	43.8± 37.2	49.5±42.9	41.3±34.2	.153
Gender				
Female	42 (17.5%)	23 (31.9%)	19 (11.3%)	<.001
Male	198 (82.5%)	49 (68.1%)	149 (88.7%)	
Lesion level				
Cervical	84 (35.0%)	16 (22.2%)	68 (40.5%)	.024
Thoracic	116 (48.3%)	41 (57.0%)	75 (44.6%)	
Lumbar-sacral	40 (16.7%)	15 (20.8%)	25 (14.9%)	
AIS grad at admission				
A	92 (38.3%)	17 (23.6%)	75 (44.6%)	.009
B	26 (10.8%)	9 (12.5%)	17 (10.1%)	
C	41 (17.1%)	12 (16.7%)	29 (17.3%)	
D	81 (33.8%)	34 (47.2%)	47 (28.0%)	

Note: Bold *p* values indicate significance. AIS = American Spinal Injury Association Impairment Scale; LTA = lesion to admission time.

Table 2. Association between outcomes and etiology

Outcomes	Total (n=240)	Ischemia (n= 72)	Trauma (n=168)	p
LOS, months	5.5±3.4	4.4±2.4	5.9±3.7	<.001
SCIM admission	23.6±19.2	27.2±19.8	22.0±18.8	.060
SCIM discharge	57.9±25.5	51.3±28.6	60.8±23.6	.015
SCIM gain	34.4±21.1	24.1±20.3	38.8±20.0	<.001
AIS grade improvement				
No	195 (81.2%)	63 (87.5%)	132 (78.6%)	.149
Yes	45 (18.8%)	9 (12.5%)	36 (21.4%)	
Complications at admission				
No	150 (62.5%)	46 (63.9%)	104 (61.9%)	.884
Yes	90 (37.5%)	26 (36.1%)	64 (38.1%)	
Complications during stay				
No	135 (56.2%)	44 (61.1%)	91 (54.2%)	.394
Yes	105 (43.8%)	28 (38.9%)	77 (45.8%)	
Return home				
No	26 (10.8%)	2 (2.8%)	24 (14.3%)	.016
Yes	214 (89.2%)	70 (97.2%)	144 (85.7%)	

Note: Bold *p* values indicate significance. AIS = American Spinal Injury Association Impairment Scale; LOS = length of stay; SCIM = Spinal Cord Independence Measure.

4-month longer hospitalization than those with an AIS grade D (**Table 3**).

SCIM gain. Etiology, if adjusted for the effect of confounding factors, appeared to be a significant predictor of SCIM gain (difference between SCIM score at discharge and admission) (**Table 3**). Traumatic patients had a higher SCIM gain than ischemic patients (by about 11 points). Etiology, age, LTA, lesion level, and AIS on admission were found to be significant predictors of SCIM gain. The SCIM gain decreases with the increase of age and LTA. Patients with thoracic level had a higher SCIM gain than those with cervical level, whereas the difference of SCIM gain between patients with lumbar level and patients with cervical level was not statistically significant. The SCIM gain increased by about 9 points, going from AIS A to AIS C and D (**Table 3**).

Logistic regression models

AIS improvement. According to logistic regression models, AIS categories on admission were the only predictive factors of neurological improvement resulting in a gain in AIS. AIS B and C patients had odds of improvement 30 times greater than that of AIS A patients (**Table 4**). AIS D patients, however,

were not likely to show a significantly greater improvement than AIS A patients (**Table 4**).

Destination at discharge. Using logistic regression models, the analysis showed that etiology was not a significant predictor of returning home or transfer to another facility, as well as age, gender, and LTA. The only significant predictor of discharge destination was the AIS on admission and the lesion level. Patients with thoracic level had odds of returning home 3.9 times higher than patients with cervical level (**Table 4**). Patients with AIS D on admission presented odds of returning home 25 times greater than AIS A patients (**Table 4**).

Complications on admission. Using logistic regression model analysis, etiology did not appear to be a significant predictor of complications on admission, as well as age, gender, and lesion level. The outcome was instead significantly affected by LTA and AIS on admission. The odds ratio of having complications on admission increased with increasing LTA and was significantly smaller in AIS C and D patients when compared with AIS A patients (**Table 5**).

Complications during hospitalization. Using logistic regression model analysis, etiology did not appear to be a significant predictor of

Table 3. Linear regression models: LOS and SCIM gain

	LOS (months)		SCIM gain	
	Coef (95% CI)	<i>p</i>	Coef (95% CI)	<i>p</i>
Etiology				
Ischemia	—		—	<.001
Trauma	0.21 (-0.72; 1.14)	.661	11.1 (5.1; 17.2)	
Age (every 5 years)	0.04 (0.01; 0.06)	.518	-1.5 (-1.6; -1.3)	<.001
Gender				
Female	—		—	
Male	1.25 (0.26; 2.24)	.013	0.8 (-5.64; 7.3)	.802
Lesion level				
Cervical	—		—	
Thoracic	-1.73 (-2.59; -0.87)	<.001	7.2 (1.6; 12.8)	.033
Lumbar-sacral	-1.89 (-2.97; -0.80)		6.1 (-1.0; 13.3)	
AIS grade at admission				
D	—		—	
C	2.30 (1.20; 3.41)	<.001	1.10 (-6.12; 8.33)	.012
B	3.75 (2.44; 5.05)		-2.09 (-10.62; 6.44)	
A	4.35 (3.40; 5.30)		-8.81 (-15.02; -2.60)	
LTA (every week)	0.01 (0.00; 0.02)	.709	-1.0 (-1.1; -0.9)	<.001

Note: Bold *p* values indicate significance. AIS = American Spinal Injury Association Impairment Scale; LOS = length of stay; LTA = lesion to admission time; SCIM = Spinal Cord Independence Measure.

Table 4. Logistic regression models: AIS improvement and discharge home

	AIS grade improvement		Discharge home	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Etiology				
Ischemia	—		—	
Trauma	2.64 (0.83; 8.34)	.099	0.35 (0.07; 1.79)	.207
Age (every 5 years)	0.99 (0.96; 1.02)	.887	0.98 (0.20; 4.85)	.760
Gender				
Female	—		—	
Male	0.76 (0.24; 2.41)	.635	0.69 (0.14; 3.44)	.648
Lesion level				
Cervical	—		—	
Thoracic	1.22 (0.45; 3.30)	.785	3.91 (1.43; 10.68)	.018
Lumbar-sacral	0.75 (0.17; 3.26)		3.65 (0.71; 18.90)	
AIS grade at admission				
D	—		—	
C	135.89 (16.35; 1129.37)	<.001	0.05 (0.01; 0.48)	<.001
B	112.85 (12.77; 997.45)		0.27 (0.02; 4.77)	
A	3.62 (0.39; 33.38)		0.04 (0.01; 0.36)	
LTA (every week)	0.94 (0.93; 0.95)	.176	0.99 (0.98; 1.00)	.808

Note: Bold *p* values indicate significance. AIS = American Spinal Injury Association Impairment Scale; LTA = lesion to admission time; OR = odds ratio.

Table 5. Logistic regression models: Complications on admission and during hospitalization

	Complications on admission		Complications during hospitalization	
	OR (95%CI)	<i>p</i> value	OR (95%CI)	<i>p</i> value
Etiology				
Ischemia	—		—	
Trauma	0.80 (0.35; 1.85)	.607	0.97 (0.46; 2.07)	.941
Age (every 5 years)	1.09 (1.07; 1.12)	.090	1.14 (1.12; 1.16)	.010
Gender				
Female	—		—	
Male	1.90 (0.76; 4.72)	.169	2.32 (1.00; 5.43)	.051
Lesion level				
Cervical	—		—	
Thoracic	1.14 (0.55; 2.38)	.624	0.39 (0.19; 0.82)	.036
Lumbar-sacral	0.70 (0.24; 2.03)		0.69 (0.27; 1.74)	
AIS grade at admission				
D	—		—	
C	6.41 (2.13; 19.32)	<.001	4.5 (1.80; 11.25)	<.001
B	9.75 (2.86; 33.23)		6.97 (2.38; 20.39)	
A	22.57 (7.97; 63.91)		16.40 (6.72; 40.06)	
LTA (every week)	1.09 (1.08; 1.10)	.005	1.02 (1.01; 1.03)	.437

Note: AIS = American Spinal Injury Association Impairment Scale; LTA = lesion to admission time; OR = odds ratio.

complications during hospitalization. The only significant predictors of complications during hospitalization were age, lesion level, and AIS on admission. The odds ratio of developing complications during hospitalization increased with age; it was smaller in thoracic patients than in patients with cervical level and decreased with AIS improvement (**Table 5**).

Discussion

Non-traumatic SCI represents a significant portion of the population with SCI. In recent years, its incidence in rehabilitation settings has progressively increased. On average, non-traumatic SCI patients are older than traumatic ones. Moreover, they have complex and specific needs and have different rehabilitation possibilities. All these factors make it difficult to predict outcomes.²¹

Despite the increase of non-traumatic SCI over the last years, the majority of clinical studies in literature are still focused on traumatic SCI. With regard to ischemic spinal cord lesions, there are a number of studies evaluating this kind of lesion.⁶⁻¹⁶ However, most of these studies are from single centers, with a limited number of cases

(with one exception [ref. 16]) and with outcome assessment based mainly on neurological status, ambulatory capacity, and bladder control.^{6,7,10,11,15,16} Furthermore, only few of these studies compared patients with ischemic spinal cord lesions to those with TSCI and will be discussed below.

The purpose of our study was to compare the functional and neurological outcomes in a group of patients with spinal cord ischemia with those of a group of TSCI patients. Our study highlighted several significant differences in demographic factors and lesion characteristics between ISCI and TSCI groups. The ISCI group included older individuals with a smaller percentage of males and had more incomplete lesions and less cervical lesions. These features can be considered key factors in determining the outcomes of patients with SCI. Therefore, at a first analysis, the outcomes of the 2 groups were significantly different, in particular with regard to LOS, SCIM at discharge, SCIM gain, and percentage of patients returning home after rehabilitation. Therefore, we adopted a statistical procedure to control for the confounding effects of these factors.

Once the confounding factors have been eliminated by means of statistics, etiology remains a

determinant only for SCIM gain. ISCI patients seem to achieve less independence in daily living activities at the end of rehabilitation, with an 11-point lower SCIM gain than TSCI patients. As stated above, this is one of the few studies that compared ISCI and TSCI patients and the one with the higher number of subjects. Previously only 4 studies performed the same comparison. Iseli⁸ compared the ambulation capacity and neurological status of ISCI and TSCI patients and found that the 2 groups achieved comparable improvement. However, they did not assess the functional status of the 2 cohorts. The studies by Scivoletto¹³ and McKinley¹⁴ evaluated the functional improvement of ISCI and TSCI and used a statistical methodology to eliminate the confounding effect of clinical (AIS grade and lesion level) and demographic (age and gender) factors. Contrarily to the results of the present study, in both works the 2 cohorts of subjects showed comparable levels of independence in the activities of daily living. However, these studies^{13,14} used the Barthel Index and the FIM, respectively as outcome measures; whereas in the present one, we used the SCIM III, which is more sensitive to capture the functional status and the improvements of SCI patients. Another study by Pouw¹² showed results comparable to the present one, with TSCI patients achieving higher SCIM scores than ISCI. However, this study is based on a small number of subjects, as the authors examined only 20 ischemic patients with paraplegia. Therefore, our work confirms the validity of Pouw's article and increases its generalizability, as we examined patients with different levels of lesion and AIS grade. In our series, there are other factors influencing SCIM gain (age, lesion level, and completeness). These factors are already well studied and self-explanatory: it is clear that younger age, lower levels of lesion, and more incomplete lesions are associated with a higher level of independence.

For all the other outcomes taken into account, etiology did not prove to be a determining factor. Most of the outcomes are explained by the same factors described above (age, level, and completeness of the lesion), with 2 noticeable exceptions.

Rehabilitation length of stay is explained by lesion level and AIS grade at admission, as well

as gender, which is new data and deserves some discussion. Male gender is more frequent in the traumatic population, and males are more exposed to high-energy accidents. Therefore, they are possibly more affected by associated lesions that, in turn, may slow down the achievement of independence.²

The second new piece of information is the relationship between the presence of complications and long LTA. The longer the LTA time, the higher the risk complications; no difference is seen between traumatic and ischemic etiology. Although this is not the focus of the present work, it deserves some discussion: LTA is the only modifiable factor among those that determine the presence of complications at admission. Although we could not exclude the possibility that a long LTA is the consequence of complications during the acute stay, we believe that the relationship between LTA and complications may be explained by a less than optimal attention to the prevention of complications and a suboptimal nurse-to-patient ratio in the acute wards, especially for patients with more severe lesions.²² Furthermore, LTA is mutually influenced by the level and completeness of the lesion, as patients with high level and complete lesions are those with a high level of immobility and, unfortunately, those who often require a long stay in the acute ward.²³

Limitations

A limit of the present study is attributable to the inclusion of ISCI patients with different etiologies; this creates the risk of having a non-homogeneous population. Another possible limitation is the long LOS of the present study; it is much longer than, for example, the LOS in the United States. Although, it reflects the European reality and is in line with previous studies,¹² this may limit the generalizability of our results to settings different from the European ones.

Another bias could be the fact that a small number of patients could restrict the significance of the results of the study. On the other hand, similar factors can potentially affect the course of the hospitalization of both groups of patients (ISCI and TSCI), such as issues arising from the trauma or

injurious event itself (eg, hemodynamic instability, infection, pain), comorbidity already present on admission, and other clinical complications occurring during hospitalization (eg, deep venous thrombosis, infections, pressure ulcers, pain, heterotopic ossification). Therefore, some of the outcomes that have been measured, such as the length of hospital stay, might be influenced and be similar in both the ISCI and TSCI groups.

Conclusion

The results of our study demonstrate that etiology is a significant predictor only for

functional (SCIM) improvement, with traumatic patients having better outcomes than ischemic ones. AIS grade and lesion level were the chief predictors of LOS, SCIM gain, occurrence of complications, and discharge destination.

Multicentric trials of outcome and survival following spinal cord ischemia should be conducted in order to perform statistical analysis involving a larger sample to better understand the factors that influence the outcomes for this specific group of patients. Furthermore, recognizing the real incidence of ischemic myelopathies, it will be possible to implement prevention programs on risk factors.

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