Neurological recovery after traumatic spinal cord injury: prognostic value of magnetic resonance

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ABSTRACT

STUDY DESIGN: Retrospective observational study.

OBJECTIVES: Assess the relationship between Magnetic Resonance (MR) image patterns and neurological recovery in patients with Traumatic Spinal Cord Injury (TSCI).

SETTING: Spinal cord injury unit in Spain. METHODS: Patients admitted for acute TSCI between January 2010 and December 2018 with a MR exam performed in the acute phase were selected. Five patterns were established: normal, single-level edema, multilevel edema, hemorrhage, and spinal cord transection. Comparisons between the ASIA Injury Severity (AIS) score and Motor Index (MI) at admission and at discharge were made.

RESULTS: Collected 296 patients. Normal and cord transection patterns were excluded due to the low number of cases. Single-level edema pattern was primarily observed in cases with incomplete injuries, hemorrhage pattern in complete injuries, and multilevel edema pattern at similar percentages in complete and incomplete lesions. Improvement of the AIS score was found in 40.9% of singlelevel edema, 20.2% of multilevel edema, and 19.0% of hemorrhage (p=0.042) patterns. By excluding the AIS grade D from the analyses, the figures increased to 70.3%, 52.2%, and 19.4% respectively ($p < 0.001$). This significant relationship was confirmed by multivariate analysis, although it was not as relevant as the examination according to ASIA-ISCoS performed at admission (p=0.005 vs $p < 0.001$). Mean variation of the MI was also significantly different ($p < 0.001$) between the three groups: 22.6 ± 21.4 for single-level edema, 16.9 ± 21.1 for multilevel edema, and 4.5 ± 8.4 for hemorrhage.

CONCLUSION: MR injury patterns observed at the acute phase are associated with the possibility of improvement of the AIS score and MI.

INTRODUCTION

The neurological examination, performed according to the ASIAISCoS International standards Neurological Classification (ISNCSCI), is the safest way to diagnose and classify the level and degree of a Spinal Cord Injury (SCI). This fact does not discard the relevance of imaging techniques in the study of SCI, either as a support method for the diagnosis or for the characterization of potential concomitant injuries. The only routine imaging test that allows to directly assess the parenchyma of the spinal cord is Nuclear Magnetic Resonance (NMR), considered the *gold standard* method and thus, in general, recommended for all patients with SCI [1], as long as there are no contraindications.

Besides its usefulness as a diagnostic tool, some studies have suggested that NMR image injury patterns in T2 sequence may be correlated with patient´s neurological and functional prognosis. This hypothesis was first introduced by Kulkarni et al. in 1988 [2], in which the authors also established the first classification of SCI NMR patterns. In their study, the data showed good progress in patients with no image of injury in NMR, intermediate prognosis in individuals with spinal cord edema, and deficient in cases of hemorrhage. It should be noted that no contrast hypothesis was tested in the study.

The abovementioned classification was modified two years later by the same authors [3] and revised in other works after that. Thus, in 1992, Schaefer [4] observed that the length of the injury was relevant in cases of edema, being worse the prognosis in large injuries. This observation was in line with the results reported later by Flanders [5]. In 2006, with more accurate MRI systems, Boldin highlighted the importance of the hemorrhage size, determining a less negative prognosis than initially considered in cases with small hemorrhages (<4 mm) [6].

Complete transection is another NRM pattern described in few studies, with very low frequency of occurrence and poor prognosis regarding neurological recovery [7].

Gathering all these works, the following NMR injury image patterns may be established (Fig. 1):

Normal

Single-level edema

Multilevel edema

Hemorrhage

Complete transection

Given the interest in the search of prognostic factors in SCIs, the aim of this study was to assess the relationship between NMR parenchymal injury patterns and neurological prognosis.

METHODS

Study setting

The study was carried out at the Spinal Cord Injuries Unit (SCIU) of the *Complexo Hospitalario Universitario de A Coruña*, reference center for the treatment of spinal cord injuries in Galicia (Spain) for a population of around 2,750,000 inhabitants.

Characteristics of the study

Observational, descriptive, and retrospective follow-up study was performed.

Selection of cases

Individuals admitted to the SCIU between January 2010 and December 2018 were selected.

Inclusion criteria: >18 years of age, acute Traumatic Spinal Cord Injury (TSCI), NMR study performed within seven days following the injury.

Exclusion criteria: severe comorbidities that precluded performing a standardized neurological examination and/or assessment of the NMR image; such as symptomatic multiple sclerosis, chronic SCI, neurodegenerative disease, or spinal instrumentation.

The following variables were collected and analyzed: age, sex, NMR image pattern, in-hospital mortality, Motor Index (MI), SCI level, and AIS score at admission and at discharge.

With the collaboration of a neuroradiologist, SCIs were classified into five groups based on the NMR image pattern: normal, single-level edema, multilevel edema, hemorrhage, and spinal cord transection. The distinction between single-level edema and multilevel edema was done by comparing the sagittal length of the injury with the size of an adjacent vertebra.

SCI characteristics were assessed based on the international standards for neurological classification of SCIs following the ASIA scale revised in 2011. Neurological progress was determined by assessing the changes in the AIS score and MI between the initial exam and at discharge. To simplify the analyses, the levels of injury were grouped as tetraplegia and paraplegia.

All patients followed the same protocol at hospital admission and received an equal number of hours of therapy (physiotherapy and occupational therapy).

Statistical analyses

Data were organized and analyzed using IBM® SPSS® Statistics V19 (IBM Corp, 2010, Armonk, NY. USA). Quantitative variables are expressed as median ± standard deviation and qualitative variables as absolute value and percentage (%). Variables were described and compared. Multivariate linear and logistic regression analyses were done to determine which variables were associated with the events of interest.

RESULTS

Seven hundred twenty individuals with acute SCI were admitted during the study period, of which 489 were of traumatic nature and 296 met the inclusion criteria. Mean age was 60.1 ± 19.9 years; 72.6% men and 27.4% women; 68.2% were tetraplegic (21.5% complete injuries) and 31.8% paraplegic (54.2% complete injuries).

At admission, the incidence was, respectively, 32.3%, 10.3%, 26.1%, and 31.3% for AIS grades A, B, C, and D, being at discharge, 22.4%, 7.8%, 12.9%, and 54.5%.

NMR images showed predominance of spinal cord edema patterns, mostly single-level edema (Fig. 2). Few patients showed a normal or cord transection pattern, so they were excluded from the analyses.

No statistically significant differences were seen between the different patterns when analyzed by sex (p = 0.125), contrarily to the significance observed by age (p = 0.001). Thus, individuals with multilevel edema patterns were older (mean age 65.2 ± 18.3), while the group with hemorrhage patterns were younger (mean age (51.5 ± 21.9). Furthermore, the percentage of paraplegics (64.8%) was higher in the group with hemorrhage patterns, followed by single-level edema (28.2%), and multilevel edema (20.0%) ($p < 0.001$). The mortality rate also differed between patterns (p = 0.041): 17.4% in hemorrhage patterns, 15.4% in multilevel edema, and 6.3% in single-level edema.

Regarding the AIS score, predominance of incomplete injuries was seen among single-level edemas, while in the case of hemorrhages most cases were complete injuries. Similar percentages of complete and incomplete injuries were observed in cases with multilevel edemas. All cases showing a spinal cord transection pattern classified as AIS grade A and those with a normal cord pattern as AIS grade D (Fig. 3).

Progress of injury grade based on nuclear magnetic resonance patterns

We compared the neurological exam at admission versus discharge (excluding the patients who died) to determine which of the patterns was associated with greater improvement (Table 1).

Thus, overall, and considering the different grades of injury, higher percentage of improvement of the AIS score was seen in cases with a single-level edema pattern; this percentage was always lower in hemorrhage patterns. It was not possible to contrast our hypothesis due to the low number of cases in each group. In general, 40.9% of the patients with a single-level edema pattern and 40.2% with a multilevel edema pattern showed improvement in their AIS score, while in individuals with a hemorrhage pattern, improvement was seen in 19.0% of the cases. Differences were statistically significant (p=0.042) (Chi-square test).

Due to the uneven inter-group distribution of ASIA D injuries, which may lead to a ceiling effect regarding grade improvement, we repeated the analysis excluding AIS grade D at admission individuals. Under this new condition, percentages in grade improvement increased to 70.3% in patients with single-level edema patterns, 52.2% for multilevel edema patterns, and only 19.4% in cases of spinal cord hemorrhage. A positive relationship ($p < 0.001$) (Chi-square test) was also determined.

Examining the potential confounding variables that might have an effect on neurological progress, AIS score *at admission* was the only one that showed an influence on the possibility of improving the AIS score ($p < 0.001$), with no influence of sex ($p = 0.399$), level of injury ($p < 0.163$), or age ($p = 0.079$).

Given the results obtained with the univariate analysis, we carried out a multivariate analysis to jointly assess the two factors with significant relationship (ASIA *at admission* and the NMR pattern), including also the age.

Both the image pattern and the AIS score *at admission* showed significant relationship with the possibility of improving the AIS score, not observed for the variable age (Table 2). Significant differences in progression were determined in the comparisons of the NMR patterns between hemorrhage and single-level edema; the likelihood of improving the AIS score was 18-times greater in individuals with single-level edema. There were no differences between patients with multilevel or single-level edema.

Progress of the MI score based on nuclear magnetic resonance injury patterns

Significant differences in MI at admission were seen between the three main image patterns ($p < 0.001$); mean MI were 59.8 ± 27.2, 42.5 ± 29, and 41.6 ± 21.7 for single-level edema, multilevel edema, and spinal cord hemorrhage, respectively.

Changes between admission and discharge were calculated globally and as percentage of change to eliminate possible errors due to the uneven figures at admission. Variation was 22.6 ± 21.4 points for the first group, 16.9 ± 21.1 for the second, and 4.5 ± 8.4 for the third (Table 3). On the other hand, differences were wider when presented as percentage of change (53.3 ± 32.9%, 36.6 ± 40.4%, and 9.7 ± 22.4%, respectively). Significant differences were found in all cases ($p < 0.001$) (Kruskall-Wallis test).

Analyses of the possible confounding factors showed significant relationship, overall and in percentage of change, of both the initial AIS score and level of injury with the possibility of improving the MI score ($p < 0.001$).

In this case, the multivariate analyses showed that the factor with the greatest relationship in MI change was, once again, the initial AIS score, and to lesser extent tetraplegia against paraplegia. No association with NMR patterns was seen, although there was a trend towards greater improvement in single-level edema patterns in comparison to hemorrhage patterns (Table 4).

DISCUSSION

Most agreements and articles acknowledge that the main predictive factor for neurological recovery (functional and of acute life-threatening prognosis) in SCIs is the neurological examination according to ASIA-ISCoS ISNCSCI performed in the first 24–72 h post-injury [8, 9]. Estimation of prognosis has great relevance not only to provide diagnostic guidance to the patient and family members but also because of the greater lifethreatening risk in cases of complete and high cervical SCIs, associated with a greater probability of requiring mechanical ventilation and critical care. It is advisable to keep in mind that besides basic knowledge by the specialist, the neurological examination according to ASIA-ISCoS ISNCSCI requires the ability of the patient to collaborate. However, it is not uncommon for patients with TSCI to arrive at the hospital with an altered state of consciousness, without forgetting pediatric patients or people with history of previous cognitive impairment. Thus, it is key to have other methods to allow us to make an assessment during the acute-subacute phase. The aim of this study was to evaluate the relationship between NMR injury patterns in the acute phase of TSCI and neurological prognosis.

The data of this study show clear prevalence of edema over any of the other patterns, with a balance between single-level edemas and edemas that are more extensive. There are only 46 cases with a spinal cord hemorrhage pattern, whilst other patterns are almost anecdotal. A meta-analysis by Bozzo et al. [1] analyzed the frequencies of the distinct injury patterns, although the selected articles are not entirely comparable to ours, as some only analyzed tetraplegia and the periods at which the images were obtained were broader. In these studies, the percentage of hemorrhage patterns was higher in comparison to that of our sample (from 22% to 32%), except for the work by Shimada et al. Likewise, higher percentage of extensive edemas rather than at a single-level were reported in all the studies, contrary to our observations. As pointed out in the article by Leypold et al. [10], this may be explained by the fact that the characteristics of the NMR image vary greatly during the first days after the TSCI, with increase of the size of the edemas and hemorrhages over the first hours. In some older works higher percentages of injuries showing normal patterns were reported [2, 3], although since their publication there has been a technological leap, and most probably small signal changes that can be correctly identified nowadays, were overlooked then.

Sociodemographic differences were noted in the different pattern groups, which may be explained by the epidemiology of the lesions. I.e., mean age of patients with hemorrhage injury patterns was lower and percentage of complete injuries higher. This type of trauma results from high-energy impacts (traffic accidents, falls from a height), which occur more frequently among the younger population, as shown in a study carried out in our center [11]. The cause of the higher percentage of paraplegia in cases with hemorrhage patterns seems to be also associated with the intensity of the impact. Thoracic SCIs are less frequent because of the protection given by the rib cage; higher intensity mechanical forces are needed to cause a lesion at that segment in comparison to the cervical spinal cord, leading to a larger number of complete spinal cord injuries [12], usually associated with hemorrhage patterns.

Despite the years since the publication of the first works suggesting the hypothesis of NMR images as a prognostic factor for SCI, few studies on this topic were performed until the last decade. A review carried out in 2011 [1] analyzed the articles published until then on the subject, and statistical evaluation of the image/neurological prognosis relationship was only done in four of them. Sample size in all these works was small, adding up to 205 patients between all of them, the most recent published in 2005. The conclusions of the 2011 review already pointed to a worse prognosis in cases with hemorrhage and multilevel edema patterns, as has been seen in the present work.

Over the last decade, a larger number of studies assessing this relationship have been published. As already pointed out by other authors [13], the reason for this may be that the quality of the images obtained with the devices has greatly improved over the past years and are now accessible worldwide. Data of our work are in line with most of the published studies, including those from 20 years ago. Thus, although AIS score at admission has shown to be the main prognostic factor, ample evidence demonstrates that the NMR injury pattern is a prognostic factor in AIS score changes.

A recent work by Martineau et al. [14], with an approach similar to that of our study, but collecting only cervical injuries, reported results that are comparable to the ones presented here, with a slightly smaller cohort. Both studies agree that initial AIS score is the best predictor of neurological recovery by assessing improvement in the AIS score and MI. Univariate and multivariate analyses were also performed in their study, showing a negative correlation with the presence of hemorrhage and extension of the edema.

A 2017 systematic review [15] examined the existing evidence on the topic and determined moderate evidence of worse prognosis among patients with large intraparenchymal hemorrhage by assessing the AIS score and its changes. This conclusion was reached thanks to the work by Boldin et al. [6]. Evidence for the rest of the conclusions of this study is of low or very low level, e.g., worse prognosis in cases of more extensive edemas and in hemorrhages in general.

More recently, in 2020, another review was published, although many of the studies included had already been analyzed in the previously mentioned works [16]. The authors of the review concluded that prognosis regarding recovery, assessed through features measured in the neurological examination according to ASIA-ISCoS ISNCSCI, is worse in patients with spinal cord hemorrhage, particularly when they are more extensive, and with larger size edemas. This review was carried out analyzing tetraplegic patients.

Similar conclusions were reached in individual studies, pointing out a worse prognosis in cases of extensive edema [17–19] and hemorrhage patterns [19–22], although the methodology folowed is not entirely comparable to the one used in our work.

A study by Aarabi et al. [23], carried out on patients who underwent spinal cord decompression, reported contrary findings. Statistical analyses showed that the greatest predictor of ASIA variations was the length of sagittal edema, being even more specific than the AIS score at admission.

A peculiarity of our study, and what differentiates it from other similar works, is the shorter period until the NMR is carried out. Most agreements recommend obtaining the images during the acute phase, but avoiding the first hours because the signal of the injury undergoes a dynamic progress over the first days. In a study performed by Leypold et al. [10] with a small number of patients, but with significant results, growth of the edema in acute SCI was seen by repeating the NMR study after a mean of 72 h. Matsushita et al. [24] analyzed this in a larger study, concluding that the tests performed between 24 and 48 h post-injury were more useful than those performed within the first 24 hours. In another work published the same year, Rutges et al. [25] measured the progress of the different patterns, and observed that the injuries increased particularly over the first 48 h and began to decrease from Week 3 (although there showed some variability depending on the AIS score). In hemorrhage cases, growth occurred particularly between Days 2 and 7 and decreased from Week 2 on.

In most works, assessment is carried out with NMR studies performed at 72 h after the injury, while in our service the NMR is requested over the first 24 h because the panel of experts recommends this study to be carried out during the first hours whenever possible [26] as an aid in decision-making. Passed this time, and after the patient has been admitted, it is not always advisable to move the patient to the NMR room. Thus, unless there is an urgent indication (unexplained radiological clinical findings or neurological deterioration), transfer is avoided until the patient is clinically stable.

Even though our work and the ones analyzed assess the changes in the signal on the sagittal axis, other recent studies focus on the axial axis. The BASIC scale developed in 2015 [27] is based on this premise; injuries are categorized (grade 0 to 4) according to the covered surface in the axial axis and the presence of hemorrhage. This scale has proven a significant association with the AIS score at admission and its progress. Subsequent works, in which the BASIC scale was used, have confirmed its prognostic utility [28], showing better results than those of the sagittal axis image [29], although in general it is recommended to use both planes jointly to optimize the prognostic value [30].

Limitations

The neurological examination according to ASIA-ISCoS ISNCSCI allows good follow-up of patient´s progress at motor level, however, the inclusion of certain values of a validated scale of function, e.g., the SCIM-III or the WHOQOL-BREF, might have been of interest. CONCLUSIONS - NMR injury patterns evaluated during the acute phase in individuals with TSCI show good correlation with neurological prognosis, although its superiority as a prognostic factor against initial AIS score has not been demonstrated. However, NMR images provide useful data in cases in which patient's collaboration and/or study data are not optimal.

- TSCIs with NMR hemorrhage patterns have less possibilities of improving their AIS score and their MI in comparison to multilevel edema patterns. Similarly, less improvement is seen in individuals with multilevel edema in comparison to those with a single-level edema pattern.

- Patients with spinal cord hemorrhage patterns are younger in comparison to individuals with edema patterns, presenting higher percentages of complete injuries at thoracic or lumbar levels, which seems to be related to the etiology of the injury, as they are often secondary to high-energy trauma.

- Normal NMR patterns are rare in SCIs and usually correspond to incomplete lesions. Spinal cord transection is also an infrequent pattern, associated to complete injuries.

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AUTHOR CONTRIBUTIONS

RMB: conception and design of the study, analysis of data, drafting of the article. OVM: analysis of MR image and critical revision. SPD: analysis of data and interpretation, critical revision. SSB: data collection and critical revision of the article. MEFV: data collection and critical revision of the article. ARS: data collection and critical revision of the article. RMF: conception and design of the study, final approval of the version to be published. AMM: data collection and interpretation, critical revision of the article.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICAL APPROVAL

Data were collected from the SCIU admissions register and electronic clinical records, and subsequently codified and anonymized in a database. Data were treated following the guidelines of the Galicia Research Ethics Committee (*Consellería de Sanidade de la Xunta de Galicia*) in compliance with the Organic Law 3/2018, of December 5, Protection of Personal Data and Guarantee of Digital Rights, as required in Spain. The Ethics Committee (registration code 2020/370) approved the study.

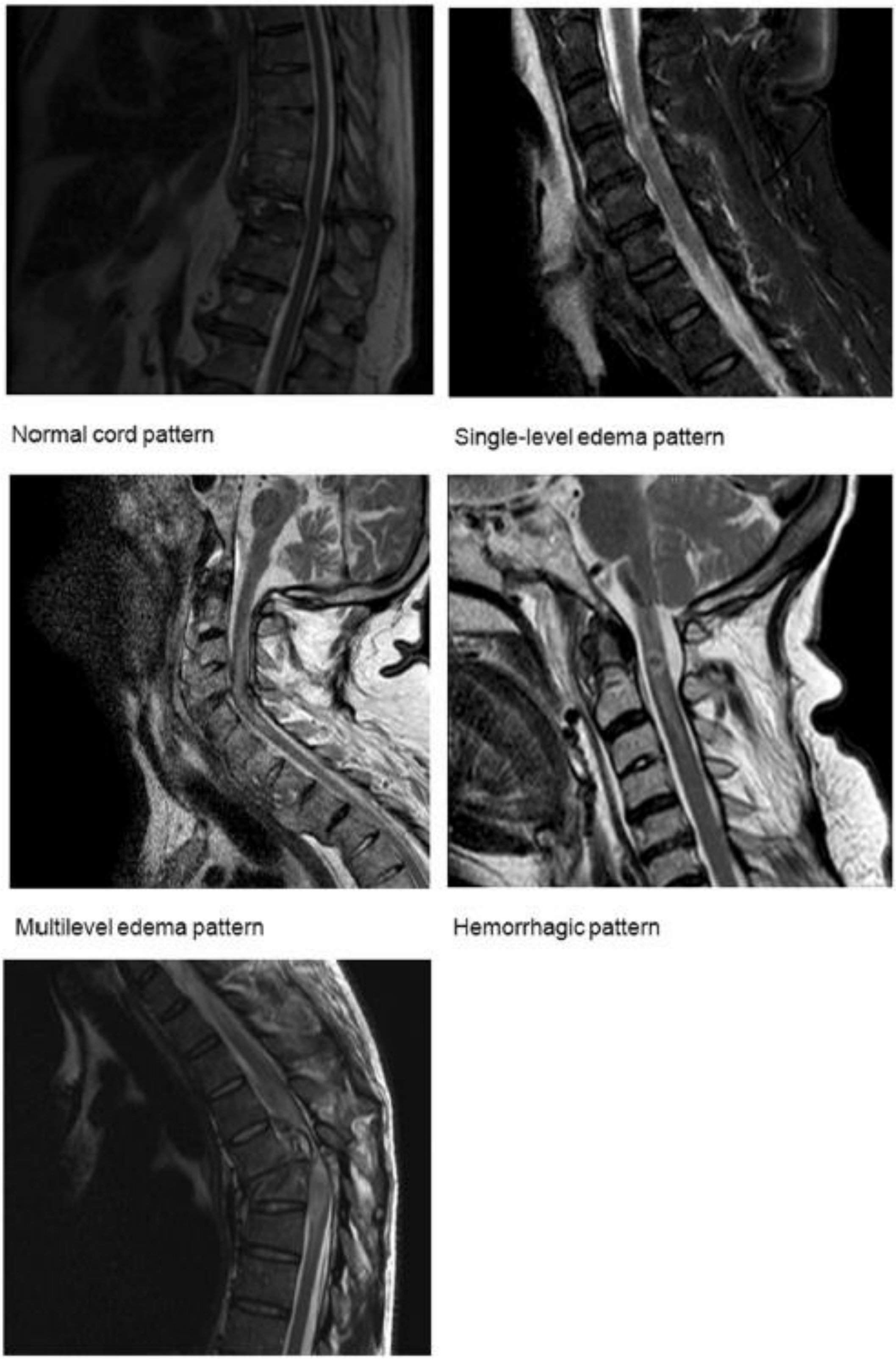

Fig. 1 Spinal cord injury patterns as seen by nuclear magnetic resonance imaging. Case examples corresponding to the five patterns established in the study

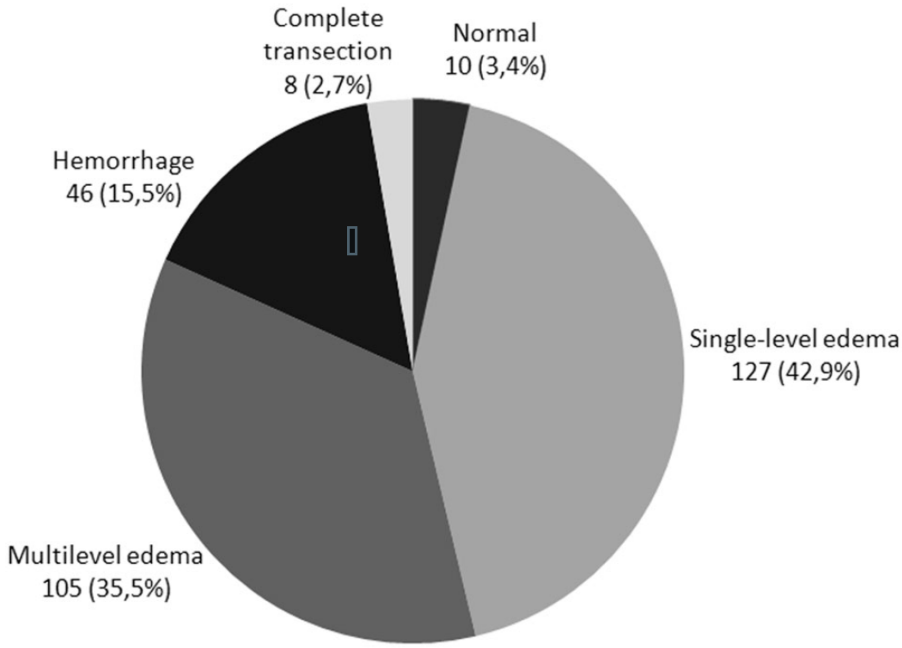

Fig. 2 Epidemiology of the patterns. Distribution of injury patterns based on nuclear magnetic resonance.

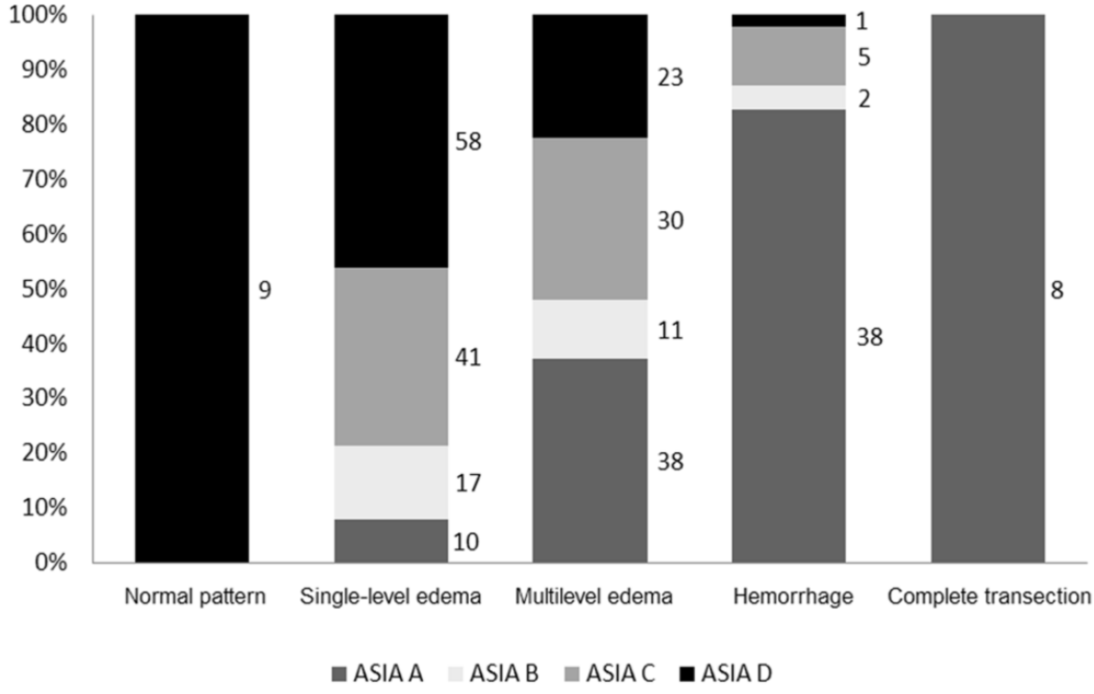

Fig. 3 Distribution of AIS score based on nuclear magnetic resonance injury patterns. Analysis of the frequency of the AIS grades within the established groups according to the magnetic resonance imagen patterns.

Table 1. Progress of AIS score throughout hospitalization based on the different injury patterns.

		Single-level edema	Multilevel edema	Hemorrhage	*p* value
AIS grade A	Improvement	5 (62.5)	10 (33.3)	5 (16.7)	
	No improvement	3 (37.5)	20 (66.7)	25 (83.3)	
AIS grade B	Improvement	11(73.3)	6 (66.7)	0 (0.0)	
	No improvement	4 (26.7)	3 (33.3)	2 (100.0)	
AIS grade C	Improvement	29 (70.1)	20 (66.7)	2 (50.0)	
	No improvement	12 (29.9)	10 (33.3)	2 (50.0)	
AIS grade D	Improvement	4 (7.1)	1 (4.8)	0 (0.0)	
	No improvement	54 (93.1)	22 (65.7)	1 (100.0)	
Global	Improvement	49 (40.9)	37 (40.2)	7 (19.0)	0.042
	No improvement	71 (59.1)	55 (59.8)	30 (89.0)	
Without AIS grade D	Improvement	45 (70.3)	36 (52.2)	7 (19.4)	<0.001
	No improvement	19 (29.7)	33 (47.8)	29 (80.6)	

Table 2. Multivariate analysis of AIS score progress.

	B	Standard error	Wald	gl	*p* value	OR	95% CI for OR	
							Inf	Sup
Age at the time of the injury	−0.24	0.009	6.481	1	0.11	0.977	0.959	0.995
NMR pattern			10.580	2	**0.005**			
Multilevel versus single-level edema	−0.315	0.378	0.694	1	0.405	0.730	0.348	1.531
Hemorrhage vs single-level edema	−1.843	0.574	10.321	1	**0.001**	0.158	0.051	0.487
AIS score at admission			50.386	3	**<0.001**			
AIS Grade B vs A	0.862	0.541	2.540	1	0.111	2.368	0.820	6.834
AIS Grade C vs A	1.340	0.429	9.733	1	**0.002**	3.817	1.645	8.857
AIS Grade D vs A	−2.412	0.600	16.173	1	**<0.001**	0.090	0.028	0.290
Constant	1.211	0.656	3.407	1	0.065	3.356		

Statistically significant results marked in bold.

Table 3. Motor index progress based on image patterns.

	Mean (SD)	Median	*h*	*P* value (Kruskall-Wallis)
Initial motor index				
Single-level edema	59.8 ± 27.2	64.5	43	**<0.001**
Multilevel edema	42.5 ± 29	46	51	
Hemorrhage	41.6 ± 21.7	50	29	
Motor index at discharge				
Single-level edema	80.9 ± 20.3	88	24	**<0.001**
Multilevel edema	59.3 ± 32.4	70	56	
Hemorrhage	48.9 ± 23.5	50	25	
Variation of the motor index				
Single-level edema	22.6 ± 21.4	17	29	**<0.001**
Multilevel edema	16.9 ± 21.1	10	29	
Hemorrhage	4.5 ± 8.4	0	6	
Percentage change of the motor index				
Single-level edema	53.3 ± 32.9	59.7	46.5	**<0.001**
Multilevel edema	36.6 ± 40.4	37.8	73.1	
Hemorrhage	9.7 ± 22.4	0	9.8	

Statistically significant results marked in bold.

Table 4. Multivariate analysis of motor index.

	B	Standard error	*p* value	95% CI	
				Lower limit	Upper limit
Tetraplegia vs paraplegia	−1.141	7.432	0.012	4.264	33.580
Nuclear magnetic resonance patterns					
Hemorrhage vs single level edema	−13.799	8.144	0.092	−29.863	2.264
Multilevel edema vs hemorrhage	−8.021	5.238	0.127	−18.353	2.311
AIS score at admission					
AIS Grade B vs A	25.325	8.400	0.003	8.758	41.893
AIS Grade C vs A	38.296	7.274	**<0.001**	23.949	52.643
AIS Grade D vs A	40.860	7.487	**<0.001**	26.093	55.628

Statistically significant results marked in bold.