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Diaphragm Pacing in Patients with Spinal Cord Injury: A European Experience

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Keywords
Spinal cord injury · Diaphragm pacing · Mechanical ventilation · Weaning

Abstract
Background: Patients with high spinal cord injury (SCI) are unable to breathe on their own and require mechanical ventilation (MV). The long-term use of MV is associated with increased morbidity and mortality. In patients with intact phrenic nerve function, patients can be partially or completely removed from MV by directly stimulating the diaphragm motor points with a diaphragm pacing system (DPS). ***Objectives:*** We describe our multicenter European experience using DPS in SCI patients who required MV. ***Methods:*** We conducted a retrospective study of patients who were evaluated for the implantation of DPS. Patients evaluated for DPS who met the prospectively defined criteria of being at least 1 year of age, and having cervical injury resulting in a complete or partial dependency on MV were included. Patients who received DPS implants were followed for up to 1 year for device usage and safety. ***Results:*** Across 3 centers, 47 patients with high SCI were evaluated for DPS, and 34 were implanted. Twenty-one patients had 12 months of follow-up data with a median DPS use of 15 h/day (interquartile range 4, 24). Eight patients (38.1%) achieved complete MV weaning using DPS 24 h/day. Two DPS-related complications were surgical device revision and a wire eruption. No other major complications were associated with DPS use. ***Conclusions:*** Diaphragm pacing represents an attractive alternative stand-alone treatment or adjunctive therapy compared to MV in patients with high SCI. After a period of acclimation, the patients were able to reduce the daily use of MV, and many could be completely removed from MV.

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Introduction

Spinal cord injury (SCI), which is usually of the traumatic origin, has an annual incidence rate of approximately 1.6 per 100,000 inhabitants in western Europe. Approximately half of these cases occur at cervical levels resulting in tetraplegia, and depending on the lesion level, the complete or partial loss of respiration [1]. The level of cervical injury affects the ability of the patient to maintain adequate ventilation. The phrenic nerves (PNs) which originate from the C3, C4, and C5 levels of the spinal cord serve as the conduit for brain stem-generated respiratory impulses to stimulate the primary muscle of respiration, the diaphragm [2]. Lesions occurring at or above C3 cause a complete interruption of communication between the respiratory centers and phrenic motor neurons, and therefore causing complete diaphragmatic paralysis. Lower cervical lesions at the C4/C5 spinal levels usually result in partial reduction of diaphragm activity. Mechanical ventilation (MV) via a tracheostomy is standard therapy for patients with tetraplegia after complete cervical SCI at or above the C3, and it is common among those with complete cervical injuries distal to C3 [3].

The chronic use of MV is associated with significant complications that effect quality of life including difficulty in speech, loss of smell, increased secretions requiring regular suctioning, and noise associated with the ventilator. Ventilated patients also experience high rates of complications, including posterior lobe atelectasis, pneumonia, barotrauma, tracheomalacia, and a significant reduction in life expectancy [3]. To address these negative effects of MV, technologies to stimulate the diaphragm through direct electrical stimulation of the PN motor points or indirectly through stimulation of the PNs have been developed. Pacing of the diaphragm allows patients to breath in a more natural manner and has been shown to be effective for reducing or completely eliminating the dependence on MV in many patients [4].

Herein, we report our European multicenter experience with the NeuRx DPS™ (Synapse Biomedical, Oberlin, OH, USA) in patients with cervical SCI through 1-year of post-implant follow-up. Specifically, we report on screening patients for diaphragmatic motor activity, the use of the diaphragm pacing system (DPS), and success at weaning patients from MV.

Materials and Methods

This study was conducted as a multicenter, retrospective, observational registry in tetraplegic patients who were evaluated for DPS implants with continued data evaluation of patients who received the DPS device. Ethics Committee approvals were not required as it was determined that the DPS placement was an implementation of a new, approved treatment, and did not constitute scientific/medical research. Patients or their legal representatives provided written informed consent for the use of their medical information. Patients were included in the evaluation if they met the following prospectively defined criteria: at least 1 year of age, and having a cervical SCI that resulted in a complete or partial dependency on MV. Exclusion criteria were an abolished response of the diaphragm to stimulation, and any significant comorbidity, psychiatric disorders, or complete social isolation.

The pre-inclusion assessment data for all patients evaluated for DPS implant were collected retrospectively after pacemaker implantation, and all evaluations were carried out as a part of the usual follow-up of the patient. Information collected included patient demographics, lesion characteristics, MV weaning/DPS usage data, and safety information including intraoperative complications and adverse events related to device use.

Patients were screened for DPS by evaluating the stimulability of the diaphragm. Each center had used its own protocol for identifying patients with diaphragms which could be stimulated with DPS. Some utilized PN conduction studies using previously described protocols [5]. Other centers evaluated diaphragm stimulability as a part of motor point mapping at the outset of laparoscopic implant procedure as described below. Patients with nonstimulable diaphragms did not receive implants.

DPS was implanted laparoscopically using previously described procedures [6]. Briefly, electrodes are placed near the PN motor points, and electrical stimulation was applied to identify the optimal electrode placement for chronic use. Electrodes were exited from the body and connected to a 4-channel external stimulator; so that the multistrand stainless steel electrode leads are the only portions of the device that dwell internally. Stimulus parameters and respiratory timing were set for each patient and programmed into the stimulator [7].

In the first few days of post-implant, each patient began a conditioning period to prepare for weaning off the ventilator by reversing the disuse atrophy of the diaphragm, thereby providing fatigue resistance and muscle strengthening. The stimulus parameters vary widely from patient to patient and depend on a number of factors. The breaths per minute and inspiration time are programmed to match the MV settings for this patient. Other adjustable settings include pulse width and pulse amplitude. These settings are titrated based on stimulating the diaphragm to best support basal tidal volume requirements. Conditioning was an incremental process, where patients could only tolerate short periods of DPS due to rapid muscle fatigue and low diaphragm strength, resulting in low tidal volumes. Over a period of days to weeks, as individualized for each patient, the diaphragm built up endurance and strength allowing patients to tolerate longer durations on DPS.

Data were collected at baseline and through 1-year of follow-up. Collected data included patient demographic and disease characteristics, MV and DPS use data, and adverse events. Continuous data are presented as mean ± standard deviation, the median and

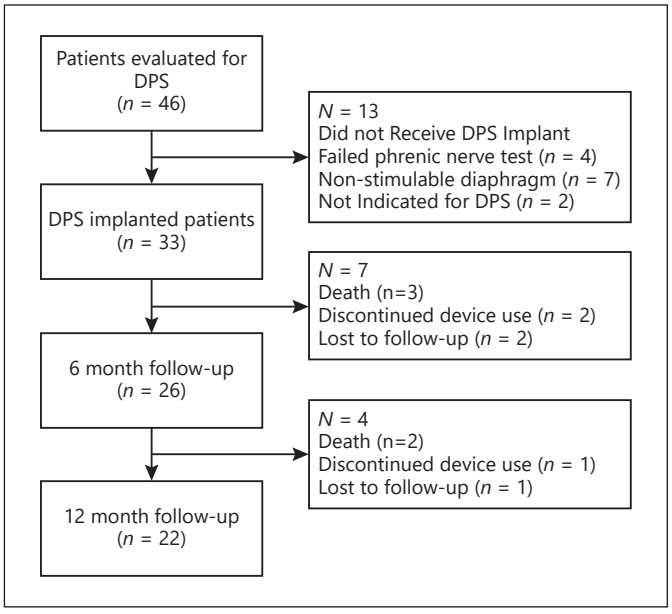

Fig. 1. Patient flow consort diagram. DPS, diaphragm pacing system.

interquartile range, and minimum/maximum values. Categorical data are presented as number and percentage of patients. Adverse events collected included any event deemed to be related to the device or the procedure to implant the device, respiratory-related events, and any events that resulted in hospitalization.

Results

Figure 1 summarizes patient flow through the study. Forty-six patients (20 in Spain, 16 in Italy, and 10 in The Netherlands) were evaluated for DPS. The first patient received a DPS implant on December 14, 2007 and the last collection of 12-month follow-up data occurred on October 21, 2019. Thirteen patients did not receive implants. The reasons for not receiving a DPS implant were nonstimulable diaphragms during motor point mapping (53.8%), failed PN conduction tests (30.8%), and 2 (15.4%) patients were not appropriate candidates for DPS. The patients were not appropriate candidates due to (1) a transdiaphragmatic pressure of 30% which was considered too good for DPS therapy; and (2) the determination that patient's obstructive sleep apnea would become worse with DPS. Of the 33 patients who received DPS implants, 26 and 22 had follow-up data at 6 and 12 months, respectively. Five patients died during the follow-up period and 3 discontinued device use. Causes of death are summarized below. Other patients were lost to follow-up as continued patient care was performed outside the centers participating in this study.

Patient baseline demographics and clinical characteristics by implant status and overall are presented in Table 1. The patients were primarily male (72.7%), and most of the injuries were caused by trauma (80.0%). Injuries at C3 or above predominated (77.8%). As would be expected for patients with these characteristics, most required MV for ≥20 h/day (81.8%), and all patients used MV for at least 6 h/day. The median time from injury to DPS surgery or the PN test (nonimplanted patients) was 581 days.

Table 2 describes DPS use following the acclimation period. Usage of DPS increased with increasing time of device use. The median hours of DPS use were 11 and 14 h/day at 6 and 12 months post-implant, respectively. At 6 months, 19 (73.1%) and 11 (42.3%) patients were using DPS for ≥4 and ≥15 h a day, respectively. Six (23.1%) patients used DPS for 24 h a day, and were completely liberated from MV. After further use and acclimation, the number of patients using DPS for ≥4 and ≥15 per day were 17 (77.3%) and 11 (50.0%), respectively, and 8 (36.4%) patients were completely liberated from MV use.

Adverse events are summarized in Table 3. Nine patients experienced 11 cases of pneumonia. Of note, pneumonia was most commonly seen (7/11; 63.6%) in patients during the first 3 months post-implant, during a period when they were using MV for time periods ranging from 16 to 24 h/day. Most pneumonia cases responded to antibiotic therapy, but 3 required hospitalization and 2 patients died. The 2 pneumonia deaths occurred at 134 and 369 days post-implant, and no patient was successfully weaned with both using MV 24 h a day. Other causes of death were euthanasia (2 patients) and from a fever of unknown origin. Other respiratory events that occurred in more than one patient included pneumothorax (3 patients) and atelectasis (2 patients). These are not unexpected in patients under MV. Device-related events included a DPS revision procedure hospitalization, a wire eruption that was remedied by reattachment of the wire, and stimulation of the abdominal muscles, which required changing the stimulation parameters. Procedure-related events included capnothorax (2 events), which occurs commonly in laparoscopic procedures, an access site hemorrhage treated with a transfusion, and a pneumothorax at 1-day post-surgery requiring thoracocentesis.

Table 1. Demographic and clinical characteristics

Characteristic	Patient status		
	implanted (*N* = 33)	not implanted (*N* = 13)	all patients (*N* = 46)
Gender, *n* (%)			
Male	24 (72.7)	10 (76.9)	34 (73.9)
Female	9 (27.3)	3 (23.1)	12 (26.1)
Age at injury, years			
Mean ± SD	33.0±19.9	24.6±20.2	30.6±20.2
Median (IQR)	35.3 (17.1, 45.9)	17.9 (11.6, 33.0)	29.0 (17.0, 45.6)
Min/Max	2.4/65.1	1.2/65.8	1.2/65.8
Injury caused by trauma, *n* (%)*	*N* = 32	*N* = 13	*N* = 45
Yes	26 (81.3)	10 (76.9)	36 (80.0)
No	6 (18.7)	3 (23.1)	9 (20.0)
Level of injury, *n* (%)	*N* = 32	*N* = 13	*N* = 45
C0	0 (0)	1 (7.7)	1 (2.2)
C1	8 (25.0)	2 (15.4)	10 (22.2)
C1/C2	4 (12.5)	0 (0)	4 (8.9)
C2	8 (25.0)	6 (46.2)	14 (31.1)
C3	3 (9.4)	2 (15.4)	5 (11.1)
C3/C4	1 (3.1)	0 (0)	1 (2.2)
C4	7 (21.9)	2 (15.4)	9 (20.0)
C4/C5	1 (3.1)	0 (0)	1 (2.2)
Injury type, *n* (%)	*N* = 32	*N* = 13	*N* = 45
Complete	22 (68.8)	11 (84.6)	33 (73.3)
Incomplete	10 (31.2)	2 (15.4)	12 (26.7)
Mechanical ventilation per day, hours	*N* = 32	*N* = 12*	*N* = 44
Mean ± SD	21.9±4.7	20.2±7.1	21.5±5.4
Median (IQR)	24 (23, 24)	24 (21, 24)	24 (23, 24)
Min/Max	8/24	6/24	6/24
n ≥20 h/day, *n* (%)	27 (84.4)	9 (75.0)	36 (81.8)
n <20 h/day, *n* (%)	5 (15.6)	3 (25.0)	8 (18.2)
Time from injury to DPS surgery or PN test, days	*N* = 33	*N* = 12	*N* = 45
Mean ± SD	1,407±2,091	1,310±1,474	1,381±1,930
Median	581 (257, 1,498)	854 (146, 1,719)	581 (243, 1,612)
Min/Max	103/10,346	107/4,315	103/10,346

* One patient used bilevel positive airway pressure. DPS, diaphragm pacing system; PN, phrenic nerve.

Discussion/Conclusion

This is the first multicenter evaluation in Europe to demonstrate that DPS is a successful strategy for managing respiration in patients with high SCI. Patients with diaphragm motor points who were able to be stimulated with electrical impulses could be partially or completely removed from MV. Further, there were minimal adverse events associated with the implant or the use of the device.

This device initially obtained marketing approval in the US based on the ability to achieve at least 4 h of independent DPS use. The 4-h time frame was selected based on the user being able to participate in community-based activities such as attending church services, going to a movie, and dining out without the onerous burdens associated with MV. We showed that 73 and 77% of patients achieved this threshold at 6 and 12 months of follow-up, which is similar to the experience reported by others that 88 and 86% of patients used the device for at least this length of time [4, 8]. Further, we demonstrated complete liberation from MV in 36% of patients, which is within the range of 25–73% reported in other studies [4, 8–11].

A key feature for the use of DPS is that it requires a period of acclimation to achieve full effectiveness of the therapy. As use and follow-up increased from 6 to 12 months, greater percentages of patients were able to use

Table 2. DPS use

Parameter	Month 6 (n = 26)	Month 12 (n = 22)
Length of ventilatory autonomy, h/day		
Mean ± SD	11.3±9.1	13.6±9.7
Median (IQR)	11 (2, 18)	14 (4, 24)
Min/Max	0/24	1/24
≥4 h/day, n (%)	19 (73.1)	17 (77.3)
≥15 h/day, n (%)	11 (42.3)	11 (50.0)
24 h/day, n (%)	6 (23.1)	8 (36.4)
Nighttime stimulation, n (%, yes)	12 (46.2)	12 (57.1)*

* n = 21. DPS, diaphragm pacing system.

Table 3. Patient adverse events

	Number of patients with event, n (%)
Death, n (%)	
Euthanasia	2 (6.1)
Pneumonia	2 (6.1)
Fever of unknown origin	1 (3.0)
Hospitalization, n (%)	
Pneumonia	3 (9.1)
Pleural drainage due to infection	1 (3.0)
Deep vein thrombosis	1 (3.0)
Respiratory events (not related to procedure/device), n (%)	
Pneumonia	9 (27.3)*
Pneumothorax	2 (6.1)
Atelectasis	2 (6.1)
Bronchial congestion	1 (3.0)
Respiratory arrest	1 (3.0)
Device and/or procedure-related events, n (%)	
Capnothorax	2 (6.1)
Pneumothorax	1 (3.0)
Revision of DPS requiring hospitalization	1 (3.0)
DPS wire eruption	1 (3.0)
Hemorrhage (access site)	1 (3.0)
Co-contraction of abdominal muscle	1 (3.0)

* Two patients had 2 separate occurrences of pneumonia. DPS, diaphragm pacing system.

DPS for both longer periods of time and completely wean from MV use altogether. This finding is not surprising that it is well-documented, and even short periods of MV use unloads the diaphragm resulting in reduced functional capacity and disuse atrophy, with longer periods of use leading to increased levels of atrophy and greater dependence on MV [3, 12, 13]. Interesting in this respect is the study by Masmoudi et al. [14] showing that mechanically ventilated sheep DPS could protect against ventilator-induced diaphragm dysfunction. They hypothesized that DPS might have an anti-inflammatory effect or that it may prevent strain injuries induced by the MV through stretching of the diaphragm [14]. Further benefit of DPS was shown by Posluszny et al. [10], who indicated that early implant with DPS facilitates improved weaning from MV. Kerwin et al. [15] showed improved inhospital outcomes, reduced incidences of ventilator-associated pneumonia, and shorter time on MV by implanting patients with acute cervical CSI with DPS. Our study cohort consisted primarily of patients who had been on longer term MV with a median of 581 days and a minimum of 103 days to a maximum of 28 years. Even with this longer term use, over 1/3 of the patients achieved complete liberation from MV and half used DPS for at least 15 h/day.

Removal from MV confers multiple benefits to patients in the form of improved quality of life, reduced incidences of respiratory disease, and increased longevity. Due to high SCI injuries, tetraplegic patients have substantially greater annual health care and living expenses than those with other SCIs [16]. Patients on a ventilator have an impaired ability to cough, which increases the risk of respiratory tract infections. Because of this, pneumonia is the most common cause of morbidity and mortality in ventilator-dependent SCI patients [17]. Regular suction of secretions can reduce complications, but suctioning is intrusive and increases patient dependence on a health care provider. In our study group, pneumonia primarily occurred during the first 3 months post-implant in a time period during which MV was used for 16 or more hours per day. Further, only 2 patients died from pneumonia during the 1-year follow-up period. Longer term follow-up would be required to ascertain if this outcome is maintained over time.

Other published studies have shown evidence for long-term benefits of DPS therapy when compared to MV. Watt et al. [18] conducted a 25-year retrospective single-center evaluation of survival in patients requiring ventilation following SCI. In this study, a subset of 55 patients required ventilatory support, of which 19 used DPS. They reported that the patients who used DPS part-time or full-time had "significantly improved" survival when compared to those who used MV. However, they further noted that patients who used DPS were younger than the MV group [18]. More recently, Onders et al. [4] reported a

single-center experience of DPS with long-term follow-up of 92 patients. Thirty-one patients died during the follow-up period, of which 17 had a known cause of death. Pneumonia was reported as the cause of death in only one case. Further, at the time of this analysis, the median survival time was 22.2 years (95% confidence interval; 14.0, not reached) [4]. The survival time reported by Onders et al. [4, 7] is much greater than would be predicted had these patients been maintained on MV. One study showed that the median survival time for patients requiring ventilatory support was approximately 6 and 16 years for patients aged ≥40 and <40 years, respectively [17]. Another evaluation has shown an age-dependent survival in MV-dependent patients ranging from 16.9 to 7.9 years for those injured at ages 20 and 60, respectively [16].

An important limitation of this study is that although the data collection parameters were prospectively identified, it is a retrospective evaluation. Only patients who received an implant of the DPS system were followed, and there was no contemporary comparator group of patients on MV for direct comparison of outcomes. Further, outcome measures are limited to the ability to wean or reduce the use of MV and adverse medical events.

In conclusion, diaphragm pacing is a viable and an attractive alternative stand-alone treatment or adjunctive therapy to MV for patients with high CSI. Patients who were previously on long-term chronic ventilation can be safely and successfully transitioned to a partial or complete use of DPS to support respiration.

Statement of Ethics

This registry was conducted in accordance with the World Medical Association Declaration of Helsinki. Ethics Committee approval was not required as it was determined that the DPS placement was an implementation of a new treatment and the treatment did not constitute medical/scientific research.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

P.J.W., F.C., M.G., F.X.C.C., J.B.-P., and J.V. conceived and designed the study. H.v.d.A., H.S.H., F.C., M.G., G.S., M.A.D.A., and C.M.-B. participated in the implant procedure. H.v.d.A., F.C., M.G., G.S., M.A.D.A., F.X.C.C., J.B.-P., C.M.-B., and J.V. participated in patient follow-up procedures and collected data. P.J.W. and J.V. analyzed the data and drafted the manuscript. All of the authors reviewed and approved the final version of the manuscript. All authors agreed to be accountable for all aspects of the work.

References

1 Lee BB, Cripps RA, Fitzharris M, Wing PC. The global map for traumatic spinal cord injury epidemiology: update 2011, global incidence rate. Spinal Cord. 2014;52(2):110–6.
2 Mitchell RA, Berger AJ. Neural regulation of respiration. Am Rev Respir Dis. 1975 Feb; 111(2):206–24.
3 Gonzalez-Bermejo J, LLontop C, Similowski T, Morélot-Panzini C. Respiratory neuromodulation in patients with neurological pathologies: for whom and how?. Ann Phys Rehabil Med. 2015;58(4):238–44.
4 Onders RP, Elmo M, Kaplan C, Schilz R, Katirji B, Tinkoff G. Long-term experience with diaphragm pacing for traumatic spinal cord injury: early implantation should be considered. Surgery. 2018;164(4):705–11.
5 Resman-Gaspersc A, Podnar S. Phrenic nerve conduction studies: technical aspects and normative data. Muscle Nerve. 2008;37(1): 36–41.
6 DiMarco AF, Onders RP, Kowalski KE, Miller ME, Ferek S, Mortimer JT. Phrenic nerve pacing in a tetraplegic patient via intramuscular diaphragm electrodes. Am J Respir Crit Care Med. 2002;166:1604–6.
7 Onders RP, Dimarco AF, Ignagni AR, Aiyar H. Mapping the phrenic nerve motor point: the key to a successful laparoscopic diaphragm pacing system in the first human series. Surgery. 2004;136:819–26.
8 Lammertse D, Charlifue S, Berliner J. Longitudinal follow-up of individuals with implanted diaphragm pacing systems. Philadelphia (PA): American Spinal Injury Association Annual Scientific Meeting; 2016.
9 Alshekhlee A, Onders RP, Syed T, Elmo M, Katirji B. Phrenic nerve conduction studies in spinal cord injury: applications for diaprhragmatic pacing. Muscle Nerve. 2008;38:1546–52.
10 Posluszny JA, Onders R, Kerwin AJ, Weinstein MS, Stein DM, Knight J, et al. Multicenter review of diaphragm pacing in spinal cord injury : successful not only in weaning from ventilators but also in bridging to independent respiration. J Trauma Acute Care Surg. 2014;76:303–10.
11 Tedde ML, Vasconcelos Filho P, Hajjar LA, de Almeida JP, Flora GF, Okumura EM, et al. Diaphragmatic pacing stimulation in spinal cord injury: anesthetic and perioperative management. Clinics. 2012;67(11):1265–9.
12 Levine S, Nguyen T, Taylor N, Friscia ME, Budak MT, Rothenberg P, et al. Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. N Engl J Med. 2008; 358(13):1327–35.
13 Jaber S, Petrof BJ, Jung B, Chanques G, Berthet JP, Rabuel C, et al. Rapidly progressive diaphragmatic weakness and injury during mechanical ventilation in humans. Am J Respir Crit Care Med. 2011;183:364–71.

14 Masmoudi H, Coirault C, Demoule A, Mayaux J, Beuvin M, Romero N, et al. Can phrenic stimulation protect the diaphragm from mechanical ventilation-induced damage? Eur Respir J. 2013;42(1):280–3.
15 Kerwin AJ, Yorkgitis BK, Ebler DJ, Madbak FG, Hsu AT, Crandall ML. Use of diaphragm pacing in the management of acute cervical spinal cord injury. J Trauma Acute Care Surg. 2018;85(5):928–31.
16 National Spinal Cord Injury Statistical Center. Spinal cord injury facts and figures at a glance: 2020 SCI data sheet [Internet]. 2020. Available from: https://www.nscisc.uab.edu/Public/Facts and Figures 2020.pdf.
17 Shavelle RM, DeVivo MJ, Strauss DJ, Paculdo DR, Lammertse DP, Day SM. Long-term survival of persons ventilator dependent after spinal cord injury. J Spinal Cord Med. 2006;29(5):511–9.
18 Watt JWH, Wiredu E, Silva P, Meehan S. Survival after short-or long-term ventilation after acute spinal cord injury: a single-centre 25-year retrospective study. Spinal Cord. 2011;49(3):404–10.