TITLE: Minimal Clinically Important Differences for Measures of Pain, Lung Function, Fatigue, and Functionality in Spinal Cord Injury

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ABSTRACT

Objective: The objective of this study was to determine the MCIDs for the numerical pain rating scale (NPRS), peak cough flow (PCF), peak expiratory flow (PEF), fatigue severity scale (FSS), and London chest activities of daily living scale (LCADL) in patients with SCI after rehabilitation.

Methods: Inpatients with SCI from two rehabilitation centres participating in a daily rehabilitation programme were recruited. The NPRS, PCF, PEF, FSS, and LCADL were collected at baseline and discharge. The global rating of change (GRC) scale was performed at discharge. MCIDs were calculated using anchor (linear regression, mean change and receiver operating characteristic curves) and distribution-based methods (0.5 times the baseline standard deviation, standard error of measurement (SEM), 1.96 times SEM, and minimal detectable change) and pooled using arithmetic weighted mean.

Results: Sixty inpatients with SCI (36 males; 54.5 (15.9) years) participated. On average their rehabilitation programme lasted 7.3 (1.7) weeks. Pooled MCID estimates were -1.6 points for the NPRS, 69.8 L/min for the PCF, 77.4 L/min for the PEF, 1.1 points for the FSS, and 1.4 points for the LCADL.

Conclusion: Established MCIDs for NPRS, PCF, PEF, FSS, and LCADL will help health professionals to interpret results and guide rehabilitation interventions in patients with SCI.

INTRODUCTION

Spinal cord injuries (SCIs) represent a major public health problem with neurological deficits that lead to lifelong disabilities and handicaps affecting personal, familiar and social life.[1] Traumatic SCIs are mostly caused by road traffic accidents and falls, affecting 10.5 per 100000 people worldwide.[2,3] Non-traumatic SCIs are commonly associated with age-related problems, although, this incidence has not been widely studied, data from Spain showed to affect 11.4 per 1000000 people.[4]

After SCI, 36 to 83% of patients develop respiratory complications. This rate is twice the observed in age-matched healthy controls and is associated with high levels of morbidity and mortality, especially on higher spinal cord injury levels.[5-7] Such injuries lead to greater decreases in lung function parameters, diminishing the person's ability to cough and clear the airways and causing atelectasis, impaired gas exchange and respiratory infections.[5,8] Patients with SCI also report dyspnoea, at rest and during daily activities, pain and fatigue which contribute to reducing their mobility, participation and satisfaction with life.[9-11] These burdensome symptoms and the high mortality and morbidity associated with respiratory complications in patients with SCI demand appropriate monitoring, prevention and treatment.[12,13]

Most patients are cared for in specialized SCI hospitals, units, or centres, with multidisciplinary teams, focused on achieving their maximum functional potential and independence to overcome the barriers of societal reintegration.[14] Physiotherapy plays a key role in addressing the described needs of patients with SCI and is part of the fundamental rehabilitation process that should start as soon as the patient is medically stable.[15,16] Outcome measures are used during the rehabilitation process to monitor patients' progress; however, clinically relevant improvements are often difficult to interpret due to the absence of minimal clinically important differences (MCIDs).[17]

The MCID is defined as the smallest change in health-related scores that is perceived as meaningful by patients, being specific for each outcome measure and population.[17] Although MCIDs have been established for patients with SCI for surgical procedures and in some rehabilitation settings, MCID for outcome measures commonly used in rehabilitation of patients with SCI are still lacking and are urgently needed to monitor and interpret patients' progress and guide personalised interventions.[18-22]

This study aimed to determine MCIDs for numerical pain rating scale (NPRS), peak expiratory flow (PEF), peak cough flow (PCF), fatigue severity scale (FSS), and

London chest activities of daily living scale (LCADL) in patients with SCI after a rehabilitation programme.

[H1] METHODS

[H2] Ethical approval

This study was approved by the Institutions Ethical Committees prior to patients' recruitment (CMRA 2018 004). Written informed consent was obtained from all participants before any data collection.

[H2] Study design and recruitment

An observational prospective study was conducted between May 2018 and June 2019 in inpatients with SCI from two rehabilitation centres in Portugal.

Participants were considered eligible if they were: 18 years old or older, had a diagnosis of SCI, were able to understand and speak portuguese and able to give informed consent. Patients were excluded if they presented: signs of mental disorders or cognitive impairments; neurological, cardiovascular, or respiratory function limitations previous to the SCI; and thorax or spine structural injuries being concurrently managed that could affect or preclude their participation in the assessment and/or in the rehabilitation program.[23-26] The investigators informed eligible participants about the study and acquired their written informed consent.

[H2] Data Collection

Patients were assessed within two weeks of admission, when clinically stable, and at discharge. Each evaluation lasted approximately 20 minutes. All measures were collected by an experienced physiotherapist except lung function, maximal inspiratory pressure and maximal expiratory pressure, which were collected by a trained cardiopulmonary technician.

The following data were collected only at baseline to characterise the population. First, a structured questionnaire based on the International Classification of Functionality checklist which included sociodemographic and general clinical data was applied.[27] The Charlson Comorbidity Index was calculated to measure the burden of the disease, using the updated version from 2010.[28] Participants were classified into three groups according to their total score: Charlson Comorbidity Index ≤2, 3 to 4, or ≥5.[29]

Then, the Portuguese version of the International standards for neurological classification of spinal cord injury (ISNCSCI) was used to categorise the injury

extension, associated with the 5-grade classification system from American Spinal Injury Association (ASIA) Impairment Scale.[15,30]

Lung function was assessed with spirometry and respiratory muscle strength with maximal respiratory pressure tests as internationally recommended.[31,32] The equipment was adapted to wheelchair users, using a computer with specialised software (MasterScope version 4.5, JAEGER), in conformity with the standards from the European Respiratory Society and the American Thoracic Society.[33] A heated pneumotach was connected to the program, to measure and analyse lung function and respiratory muscle strength.[33] Absolute and percentage predicted values for forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FVC/ FEV1 ratio, maximal inspiratory and expiratory pressures were registered.[32,33]

The following outcome measures were acquired at admission and at discharge: NPRS, PCF, PEF, FSS, and LCADL.

The NPRS was used to rate patients' pain severity in the site of the most severe pain at admission, as recommended (the same site was used at discharge).[19,34,35] Each patient was asked to select a number between "0" and "10" that best represented her/his pain, being "0" the "absence of pain" and 10 "the worst imaginable pain".[35] The NPRS has been found to correlate significantly with the pain relief scale (r = 0.92).[36]

The PCF and PEF were measured using a peak flow meter (MicroPeak from CareFusion). In the sitting position and using a nose clip, patients were asked to inhale as much air as they could and to cough (for the PCF manoeuvre) as fast and as strong as they could or to exhale (for the PEF manoeuvre) through the mouthpiece of the peak flow meter. Each assessment was repeated three to five times with intervals of 30 seconds, and the best result was recorded.[37] The PEF has been considered an excellent discriminator for pneumonia in patients with motor incomplete SCI with a risk threshold value of 420 L/min, supporting the relevance of using this outcome measure in the target population.[38]

The portuguese version of the FSS was used to measure the severity of fatigue. Each patient was asked to score their agreement with eight sentences, between "1" – "strongly disagree" and "7" – "strongly agree".[39] Scores were summed and divided by eight, with a possible range of 1 to 7. A higher score corresponds to greater fatigue.[39] The FSS is validated for the portuguese population with multiple sclerosis, and has been used in patients with SCI.[39-41] The FSS has excellent internal validity and is moderately and positively correlated (r = .74) with the visual analogue scale for fatigue.[39]

The portuguese version of the LCADL, was used to assess dyspnoea during activities of daily living. The LCADL contains 15 items divided into four components:

self-care, domestic, physical, and leisure. Each patient was asked to score how much their dyspnoea interfered with each activity of daily living in a scale from 0 to 5: “0” – I would not do it anyway (or motor control does not allow), “1” – I have no lack of air doing this, “2” – I have a slight lack of air, “3” – I have a great lack of air, “4” – I no longer do this, “5” – I need help in doing this or someone to do it for me (“4” and “5” because of dyspnoea).[42] The final score was calculated by summing every item of the scale in each of the components for a possible range of 0 to 75. The LCADL has adequate psychometric properties, showing a strong test-retest reliability [intraclass correlation coefficient (ICC)=0.98] and internal consistency (Cronbach’s alpha=0.86).[42] To adjust the final score to the different levels of motor impairment, at discharge, the LCADL was applied considering just the activities of daily living that each patient was able to perform at baseline. This adjustment was needed to avoid the increase of the total score of the scale at discharge, due to the recovery of some abilities instead of dyspnoea increases performing the activities.

The global rating of change (GRC) scale was used to assess the perception of change for each outcome at discharge. GRC questions were designed for each outcome according to the best evidence available to optimise interpretability and reliability, i.e., mentioning the specific condition, the concept and the time frame.[43] Patients were asked to quantify their perception of change in each outcome, comparing discharge to admission, in a 11-point numerical scale with written descriptors at the ends (“-5” – “much worst”, and “5” – “much better”) and at the midpoint (“0” – “without changes”).[43] Significant and moderate correlations have been reported between the GRC and the magnitude of change in subjective self-report outcome measures, such as the NPRS [r=0.49, area under the curve (AUC)=0.68].[44] The 11-point GRC has shown adequate reproducibility ($ICC_{2,1}$=0.90), and good sensitivity to change (minimum detectable change of 0.45 points and minimal important difference (MID)=2 points) in patients with chronic low back pain.[45]

[H2] **Intervention**

Patients were admitted for a maximum length of stay of 9 weeks. The intervention was tailored to each patient through an interdisciplinary approach and included: optimisation of pharmacological treatment; one to three hours/day of physiotherapy; one hour/day of occupational therapy; thirty minutes/day of activities of daily living training; thirty minutes/week of psychology, and medical, pharmacological, nursery, dietary and social assistance support as needed.[46]

Physiotherapy intervention was individually planned and focused on the following components: respiratory management, sensorial stimulation and movement

facilitation, pain relief techniques, exercise and motor skills training, respecting the functional potential, neuromuscular electrical stimulation.[15,47,48,49,16,50,51]

Occupational therapy was planned depending on the personal, social and cultural characteristics and limitations of each patient. It included the practice of activities of daily living and occupational activities evolving pictures, music, crafts, ceramic work, sports, entertainment, home management skills, mobility, transfers, balance, strengthening, stretching, equipment evaluation, and adaptation of the wheelchair as an important tool for community reintegration.[52,53]

ADL training was performed as much as possible, with the support of the physiotherapists, occupational therapists and nurses, with the primary purpose of successful bed movements, and adaptation to sitting position to allow safe transfers.[46]

Psychology focused on depression, anxiety and adjustment management, and coping strategies, mostly through cognitive behavioural therapy.[54]

Nurses were responsible for managing patients at the nursery, including bladder and bowel management, pharmacological administration, skin inspection and cleaning and ensured that patients' position was regularly changed to prevent ulcers and contractures.[46,55]

Social assistance was in charge of the social reintegration of patients, house modifications and care providers when needed.[56]

Education of the patient and carers was reinforced by the whole rehabilitation team.[16 46]

If considered relevant, additional therapy resources were used as speech therapy, body weight-supported walking training and aquatic physiotherapy.[16,46,51,57]

[H2] **Statistical Analysis**

Statistical analysis was performed using IBM SPSS Statistics, version 24 (IBM Corporation, Armonk, NY, USA) and plots created using MetaXL 5.3 (EpiGear International, Queensland, Australia) for Windows. The significance level was set at 0.05.

Descriptive statistics were used to describe the sample, baseline characteristics were expressed as relative frequencies, mean and standard deviation for normally distributed data or median, minimum and maximum for non-normally distributed data. The Kolmogorov-Smirnov test was used to assess normality of data distribution. Analysis for the presence of outliers was conducted by plotting the studied variables on a graph and visually inspecting it for extreme points.[58] Outliers were removed for the MCID analysis. Significance of changes between admission and discharge were

calculated with paired t tests for normally distributed data or Wilcoxon signed-rank tests for non-normally distributed data.[23]

The best procedure to estimate MCIDs has not been defined yet however, it has been commonly recommended to use anchor- and distribution-based techniques.[23,59,60] Thus, both techniques were used.[17]

Anchor-based methods were calculated through patient-referencing, using the GRC as an anchor, when the Pearson rank correlations were significant and equal or superior to 0.3 in the selected outcome measures (ie, changes in NPRS, PCF, PEF, FSS, and LCADL).[23,60,61] A GRC total score of two points improvement was used as the MID for the GRC.[43,59] MCIDs were calculated using the mean change, linear regression analysis and receiver operating characteristic (ROC) curves. The mean change between admission and discharge scores was calculated for patients who achieved the MID improvement of the GRC (+2).[59] For linear regression analysis, statistically significant equations were used to estimate the MCID of the respective outcome measure corresponding to the stated MID improvement (+2). For each ROC curve, the AUC had to be statistically significant and superior to 0.7 and respective 95% confidence intervals were obtained, the closest point to the left corner, where specificity (SP) and sensitivity (SN) are both optimized was considered the optimal cut-off point and chosen for the MCID of each outcome measure.[60]

Distribution-based methods used to estimate MCID were the 0.5 times the baseline standard deviation (0.5SD); standard error of measurement (SEM) calculated as SEM= baseline SD x $\sqrt{(1-ICC)}$; 1.96 times SEM (1.96SEM) and minimal detectable change at the 95% level of confidence (MDC95) calculated as MDC95= 1.96 x SEM x $\sqrt{2}$.[19,60,61] The intraclass correlation coefficient used for the SEM calculation was based on reliability studies previously published for each outcome measure (i.e., 0.95 for the NPRS;[19] 0.746 for the PCF;[37] 0.87 for the PEF;[62] 0.899 for the FSS;[39] 0.98 for the LCADL and 0.96, 0.99, 0.92, 0.95 for the respective sections: self-care, domestic, physical, and leisure.[42] Pooling of data was performed based on what has been previously described.[59,63] The final MCID for each measure was pooled by calculating the arithmetic weighted mean with the MCID generated by each anchor and distribution-based method, which were then introduced into the MetaXL to create the MCIDs' plots. Anchor-based methods were weighed more than distribution methods (ie, 2/3 against 1/3), as recommended in previous studies.[60,64]

[H2] **Role of the funding source**

The funders played no role in the design, conduct, or reporting of this study.

[H1] RESULTS

[H2] Patient characteristics and health status

In total, sixty patients with SCI were referred for the study and included for baseline assessment. Three patients did not complete the study due to unexpected discharges. Therefore, 57 patients with a mean intervention time of 7.3 (1.7) weeks were included in the final analysis. A flow diagram of the included sample is provided in Figure 1.

Baseline characteristics of the included patients with SCI are shown in Table 1. Participants' mean age was 54.5 (15.9) years old. Most were male (n = 36; 60%) with 4 years of education (n = 17; 28.3%), and former or never smokers (same proportion, n = 28; 46.7%).

Most common type of SCI was traumatic (n = 33; 55%) classified as D (i.e., motor incomplete) according to the ASIA impairment scale (n = 29; 48.3%), and of cervical neurological level (n = 31; 51.7%).

At baseline, lung function tests could only be completed by 31 patients due to the absence of a trained cardiopulmonary technician, and maximal respiratory pressure tests were completed by 55 patients due to inadaptation to the mouthpiece of the pneumotachograph.

One patient at baseline and discharge and four patients at discharge failed to perform the PCF and the PEF due to skin damage (n = 2) which caused difficulties in assuming the sitting position or because they refused to perform it (n = 2). Three patients at baseline failed to perform PEF because the material to perform the assessments was not available onsite (n = 3). Therefore, 55 patients performed PCF and 52 performed PEF at baseline and discharge.

Forty patients (66.7%) reported pain at baseline. Most painful body regions were the lower limb (n = 13; 21.7%), the upper limb (n = 12; 20%), and the lumbar spine (n = 8; 13.3%).

After the rehabilitation programme, significant improvements were found in the PCF (mean difference of 27.7 L/min; $p < .001$; ES=0.22), and PEF (31.8 L/min; $p < .001$; ES=0.25). Baseline and post-intervention scores can be found in Table 2.

Non-significant improvements were found for NPRS (median difference of 0; $p = .14$; ES=0.2), FSS (median difference of -0.1; $p = .33$; ES=-0.09), and LCADL (mean difference of -0.4 points; $p= .06$; ES=0.17).

Participants were unable to complete the following activities at baseline: putting shoes/socks on (n = 35, 58.3%), going out socially (n = 45, 75%), walking at home (n = 42, 70%), walking up stairs (n = 50, 83.3%) and domestic activities (n = 53, 88.3%). Thirty-four patients (56%) recovered abilities after the rehabilitation programme, such as putting shoes/socks on (n = 11, 18.3%), washing hair (n = 5, 8.3%), walking up stairs (n = 12, 20%), bending (n = 6, 10%); walking in home (n = 9, 15%), and going out socially at the weekend (n = 22, 36.7%).

[H2] **Minimal Clinically Important Difference**

[H3] **Anchor-based methods**

Significant correlations were found between the GRC and changes in the NPRS (r = -.6; p = <.001) and in the PCF (r = .3; p = .04). No other significant correlations were found. Thus, anchor methods were only possible to be applied for the NPRS and the PCF.

In total, 27 patients (47.4%) perceived improvements higher than 2 points in the GRC for pain (NPRS mean difference of -2.2 (3.6) points), whereas 30 (52.6%) did not reach that threshold (NPRS mean difference of 1.1 (3.2) points). Thirty-two patients (65.3%) perceived improvements higher than 2 points in the GRC for PCF (PCF mean difference of 38.4 (49.6) L/min), whereas 17 (34.7%) did not reach that threshold (PCF mean difference of 10 (45.6) L/min).

Using linear regression, the estimated MCID for the NPRS was -0.8 points (95%CI= -2.3 to 1.2), and the estimated MCID for the PCF was 25.1 (95%CI= -11.3 to 61.6) (Fig. 2).

Using ROC statistics, the AUC generated for the NPRS and PCF did not show adequate discrimination between those improving above and below two points for the GRC (AUC=0.395; 95%CI=0.27 to 0.53; p=0.62 for NPRS; AUC=0.356; 95%CI=0.13 to 0.58; p=0.34 for PCF), thus MCIDs could not be computed.

[H3] **Distribution-based methods**

The SEM, 1.96SEM, MDC95, and 0.5SD were calculated for the NPRS, PCF, PEF, FSS and LCADL. Distribution-based MCID estimates ranged from 0.8 to 2.2 points for the NPRS, 63.1 to 178 L/min for PCF, 43.1 to 119.4 L/min for PEF, 0.6 to 1.7 points for the FSS, and 0.6 to 2.1 points for the LCADL (Tab. 3).

[H3] **Pooled MCID estimates for the clinical measures**

The weighted MCID estimates were -1.6 points on the NPRS, 69.8 L/min on the PCF, 77.4 L/min on the PEF, 1.1 points on the FSS, and 1.4 points on the LCADL (Fig. 3). Results for the LCADL dimensions were 4.1, 0.8, 1.8 and 2.5 points for self-care, domestic, physical activity and leisure, respectively.

[H1] DISCUSSION

The present study established the MCIDs for NPRS, PCF, PEF, FSS, and LCADL. The pooled MCID estimates were -1.6 points, 69.8 L/min, 77.4 L/min, 1.1 points, and 1.4 points for NPRS, PCF, PEF, FSS and LCADL, respectively.

After the rehabilitation programme, significant improvements were found for the PCF and PEF. It is likely that these improvements are related to the thoracic expansion exercises, diaphragmatic activation and breathing retraining performed daily in the physiotherapy intervention. Although no other studies were found corroborating our findings, after a comparable comprehensive rehabilitation programme in patients with SCI, these results are clinically important since low PCF and PEF are discriminators for pneumonia in patients with motor incomplete SCI.[38]

The scoring of LCADL is not well adapted to the expected functional improvement of patients with SCI, especially with motor incomplete injuries.[65] At admission, most of our patients were unable to perform some activities of daily living due to motor impairments, like walking and going up stairs, reported as the hardest for patients with SCI.[66,67] For this reason, the authors decided to score just the activities which patients were able to perform at baseline, to assure that the motor impairment did not influence the assessment of dyspnoea. More than half of the patients were able to perform more activities by the end of the rehabilitation programme, and if those activities were considered their score would have increased, not because they felt more dyspnoeic but because they were performing more activities, misleading the interpretation of the results. We have chosen to use the LCADL given the importance that dyspnoea might have on performing activities of daily living in this population, and considering the absence of measures to assess it.[9,21,66,68] However, the use of LCADL for routine clinical assessment in patients with SCI needs further reflection, as adaptions or different activities of daily living measures might be needed.

The pooled MCID calculated for the NPRS was slightly higher than the one previously reported for patients with SCI, specifically for back pain (MCID=-1.16) and similar to the one established for leg pain (MCID=-1.64).[19] Most patients included in our study performed spine surgery before the rehabilitation programme, and the worst pain site referred at baseline was located in the lower limb, which could have influenced the

similarity between our MCID estimate for the NPRS and the MCID established for NPRS when assessing back pain.[19]

No studies were found reporting MCIDs for PCF, PEF, FSS, and LCADL in patients with SCI. Our pooled MCID estimates are dependent on the specific sample variability between patients with SCI, being different from the previously reported values for other populations.[19]

It was not possible to use anchor-based methods to estimate MCIDs for PEF, FSS, LCADL due to non-significant correlations with the GRC, in agreement with the results of a recent study, the design of the anchor questions could have had a negative impact on those correlations.[69] The patient-referencing anchor method is highly dependent on the correlation between the selected outcome measures and the anchor instrument and on the accuracy of the anchor MCID.[61] The GRC may, therefore, not provide the best perception of change due to patients' limitations in recalling their health state at admission, which can be influenced by their current mood state, memory biases, and more recent health events.[70] Our MCIDs for PEF, FSS, LCADL were estimated with four distribution-based methods, without influence from the intervention nor the patient perception of change, which reduces the clinical significance.[60,64]

[H2] **Limitations and implications for future**

There are some limitations to this study that need to be acknowledged. First, the involvement of researchers in the assessment and treatment of patients may have affected the results obtained despite all efforts to avoid any influence on patients or measures. Additionally, most studies measuring PEF and FSS have revealed significant differences between patients with complete or incomplete motor SCI.[38,71] Most of our sample had incomplete injury according to the ASIA impairment scale. Although discrimination between completeness of injury has not been considered when establishing MCIDs in populations with different neurological levels of impairment[18-20], we acknowledge that the external validity of our findings may be reduced for patients with complete SCI. Future studies should explore MCIDs for patients with motor complete and incomplete SCI to corroborate or strengthen these findings.[21]

Moreover, MCIDs in this study were established for a comprehensive rehabilitation programme. It is unknown if these MCIDs would remain for stand-alone interventions, e.g., pharmacological treatment. Future studies may explore the validity of the established MCIDs for different interventions. Finally, the current study used only distribution-based methods to estimate MCIDs for the PEF, FSS, LCADL, due to the

non-significant correlations with GRC, which reduced clinical significance.[60,64] More studies with larger samples are needed to increase the power in data analysis and potentiate reaching significant values in both anchor- and distribution-based approaches. Additionally, future studies may explore the use of different anchors for PEF, FSS, and LCADL, possibly as the SCIM III.[21]

This study established MCIDs for NPRS, PCF, PEF, FSS, and LCADL, to be used in clinical practice for patients with SCI. The interpretation of the results of rehabilitation programmes may now be guided by the established MCID.

[H2] **Conclusion**

Improvements exceeding -1.6 points on the NPRS, 69.8 L/min on the PCF, 77.4 L/min on the PEF, 1.1 points on the FSS, and 1.4 points on the LCADL are currently considered clinically relevant for patients with SCI after a rehabilitation programme.

Author Contributions

Concept / idea / research design: M. Sobreira, A. Oliveira, A. Marques

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Ethics Approval

This study was approved by the Institutions Ethical Committees prior to patients' recruitment (CMRA 2018 004). Written informed consent was obtained from all participants before any data collection.

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Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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TABLES

Table 1. Baseline Characteristics of the Included Patients With Spinal Cord Injury[a]

Characteristics	Baseline
Age (y)	54.5 (15.9)
BMI (kg/m^2)	25.8 (5)
Sex	
Male	36 (60%)
Female	24 (40%)
Level of injury	
Cervical	31 (51.7%)
Thoracic	19 (31.7%)
Lumbar	10 (16.7%)
ASIA impairment scale classification	
A – complete	13 (21.7%)
B – sensory incomplete	7 (11.7%)
C – motor incomplete	11 (18.3%)
D – motor incomplete	29 (48.3%)
Time since SCI (months)	5.5 (1, 468)
Education	
Illiterate	4 (6.7%)
4th year	17 (28.3%)
6th year	13 (21.7%)
9th year	8 (13.3%)
12th year	6 (10%)
Professional course	2 (3.3%)
Higher education	10 (16.7%)
Smoking status	
Former	28 (46.7%)
Never	28 (46.7%)
Current	4 (6.7%)
Lung function	
FEV_1 %predicted (n=31)	81.1 (9.3)
FVC %predicted (n=31)	77.2 (19.1)
FEV_1/FVC (n=31)	86.2 (9.8)
Respiratory muscle strength	
MIP %predicted (n=55)	71.9 (32.7)
MEP %predicted (n=55)	49.2 (22.8)
Comorbidities	
Number of comorbidities	1.8 (1.5)
Charlson Comorbidity Index	
Mild	39 (65%)
Moderate	19 (31.7%)
Severe	2 (3.3%)
Abdominal binder	
No	49 (81.7%)
Yes	11 (18.3%)
Respiratory exacerbations during the past 12 months	
0	55 (91.7%)
1	5 (8.3%)
Ventilation	
Non-ventilated	55 (91.7%)
Bilevel positive airway pressure	4 (6.7%)
Continuous positive airway pressure	1 (1.7%)
Medication	
Medicine per patient	7.3 (4.5)
Pharmacotherapeutic group	

Modifiers of intestinal motility, propulsives	39 (65%)
Modifiers of gastric secretion	35 (58.3%)
Anxiolytics, hypnotics and sedatives	29 (48.3%)
Antidepressants	28 (46.7%)
Drugs for urinary problems	22 (36.7%)
Antiepileptics and anticonvulsants	22 (36.7%)
Analgesics and antipyretics	21 (35%)
Anti-thrombotics	20 (30.3%)
Centrally acting muscular relaxants	16 (26.7%)
Opioid analgesics	15 (25%)
Vitamins	14 (23.3%)
Renin-angiotensin-system-acting agents	14 (23.3%)
Antidyslipidemics	12 (20%)
Antibacterial	9 (15%)
Other antidiabetics	8 (13.3%)
Antipsychotics	7 (11.7%)
Anti-anaemics	7 (11.7%)
Venotropics	6 (10%)
Thyroid and antithyroid preparations	6 (10%)
Adrenoreceptor antagonists	5 (8.3%)
Gynaecological anti-infectives	5 (8.3%)
Calcium channel blockers	5 (8.3%)
Modifiers of gastric motility or prokinetics	5 (8.3%)
Nonsteroidal anti-inflammatory drugs	5 (8.3%)
Mineral salts	5 (8.3%)
Drugs for the treatment of haemorrhoids	4 (6.7%)
Diuretics	4 (6.7%)
Antiasthmatics and bronchodilators	3 (5%)
Antifungal	3 (5%)
Drugs for the treatment of arthrosis	3 (5%)
Insulins	3 (5%)

[a]Data is presented as mean (SD), median (minimum, maximum) or number (percentage%), unless otherwise stated. N = 60**.** ASIA = American Spinal Injury Association; BMI = body mass index; FEV_1 = forced expiratory volume in one second; FEV_1/FVC = ratio between FEV_1 and FVC; FVC = forced vital capacity; MEP = maximal expiratory pressure; MIP = maximal inspiratory pressure.

Table 2. Effects of the Rehabilitation Programme in Patients With Spinal Cord Injury[a]

Outcome Measure	Baseline	Post-intervention	Change	*P*	Effect Size
NPRS, points	5 (0, 10)	5 (0, 10)	0 (-9, 10)	.14	-0.20
PCF, L/m (n = 52[b])	358.1 (124.8)	385.8 (124.8)	27.7 (48.4)	<.001[c]	0.22
PEF, L/m (n = 49[d])	348.4 (120.9)	380.2 (131.4)	31.8 (49.9)	<.001*	0.25
FSS, points	3.4 (1, 7)	3.4 (1, 7)	-0.1 (-3.4, 4.3)	.33	-0.09
LCADL, points (n = 52[e])	6.1 (2.9)	5.7 (2.4.2)	-0.4 (1.6)	.06	-0,17
Self-care	3.5 (0, 8)	3 (0, 5)	0 (-4, 2)	.1	-0,12
Domestic	0 (0, 3)	0 (0, 3)	0 (-1, 0)	.32	-0,04
Physical	1 (0, 4)	1 (0, 3)	0 (-2, 1)	.06	-0,19
Leisure	1 (1, 4)	1 (1, 4)	0 (-2, 2)	.45	-0,06

[a]Values are presented as mean (standard deviation) or median (minimum, maximum), unless otherwise stated. n = 57. FSS = Fatigue Severity Scale; LCADL = London Chest Activities of Daily Living Scale; L/m = litters per minute; NPRS = Numerical Pain Rating Scale; PCF = peak cough flow; PEF = peak expiratory flow.
[b]8 Patients did not perform the test at baseline or discharge assessment.
[c] $p<.05$
[d]5 Patients did not perform the test at baseline or discharge assessment.
[e]2 Outliers and 3 extremes were removed.

Table 3. Minimal Clinically Important Difference Calculated With Distribution-Based Estimates for Numerical Pain Rating Scale, Peak Cough Flow, Peak Expiratory Flow, Fatigue Severity Scale, and London Chest Activities of Daily Living Scale in Patients With Spinal Cord Injury[a]

Outcome Measure	SEM	1.96SEM	MDC95	0.5SD
NPRS, points	0.8	1.6	2.2	1.7
PCF, L/m (n = 56[b])	64.2	125.9	178	63.1
PEF, L/m (n = 56[b])	43,1	84.4	119.4	62,7
FSS, points	0.6	1.2	1.7	0.9
LCADL, points	0.6	1.2	1.6	2.1
Self-care	2.7	5.3	7.5	0.9
Domestic	0.4	0.9	1.2	0.4
Physical	1.1	2.2	3.2	0.5
Leisure	1.6	3.2	4.5	0.5

[a] N = 60. 0.5SD = 0.5 times standard deviation; 1.96SEM = 1.96 times SEM; FSS = Fatigue Severity Scale; LCADL = London Chest Activities of Daily Living Scale; L/m = litters per minute; MDC95 = minimal detectable change; NPRS = Numerical Pain Rating Scale; PCF = peak cough flow; PEF = peak expiratory flow; SEM = standard error of measurement.

[b] *4* patients did not perform the test at baseline.

FIGURES

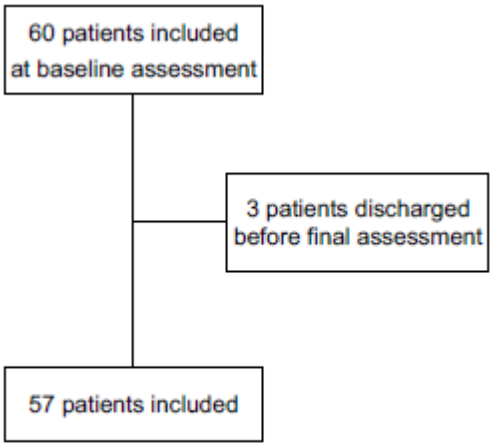

Figure 1. Flow diagram of the included sample of patients with spinal cord injury.

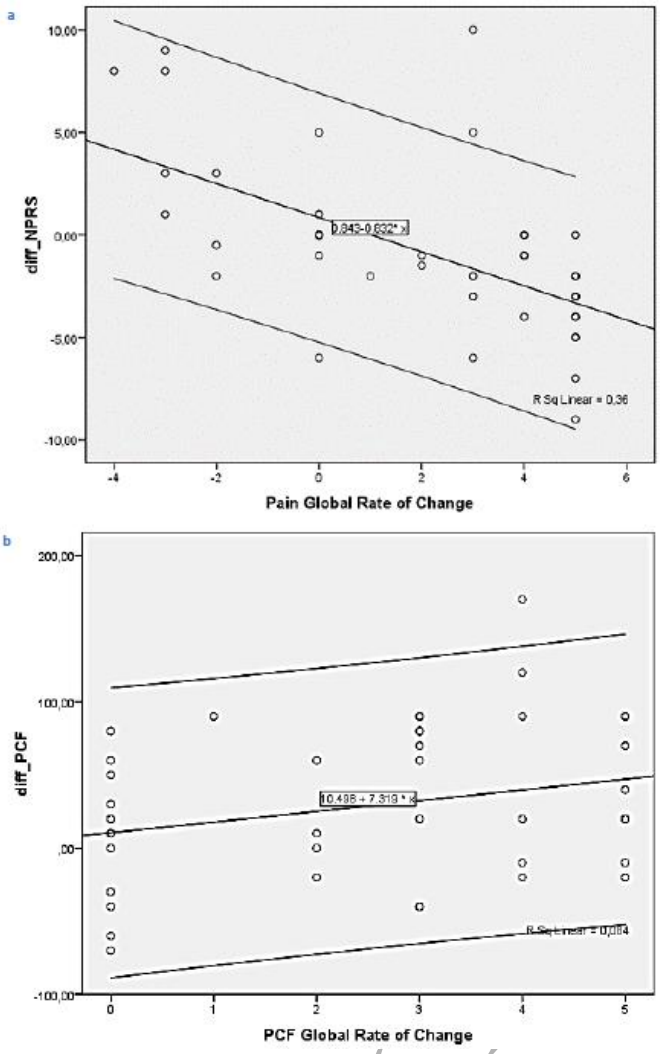

Figure 2. Linear regression to estimate the minimal clinically important difference according to the global rating of change, in patients with spinal cord injury for: a, numerical pain rating scale (n = 57); b, peak cough flow (n = 49).

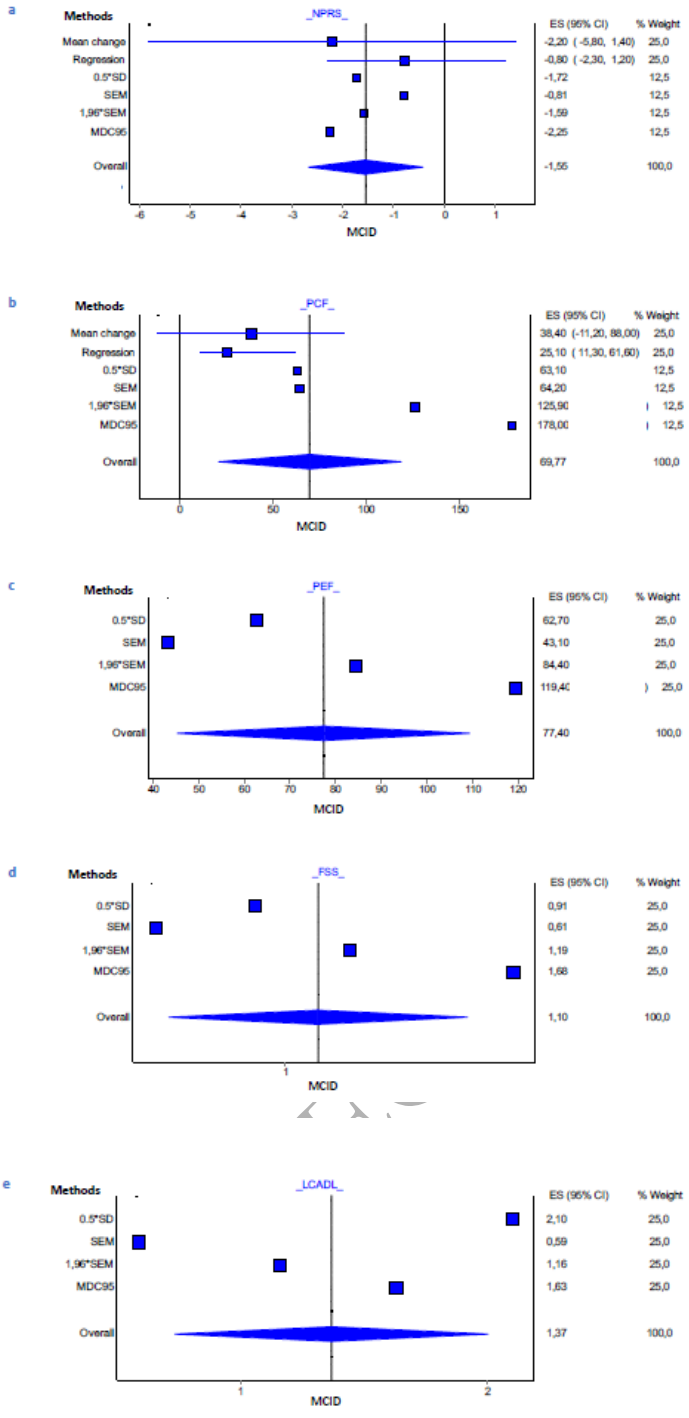

Figure 3. Pooled minimal clinically important difference (MCID) estimates for patients with spinal cord injury: a, numerical pain rating scale (NPRS) (N = 60); b, peak cough flow (PCF) (n = 59); c, peak expiratory flow (PEF) (n = 56); d, fatigue severity scale (FSS) (n = 60); and e, London Chest Activities of Daily Living Scale (LCADL) total score (N = 60)