MARGARIDA DE ALMEIDA SANTOS SOBREIRA

Mínimas diferenças de importância clínica para medidas de dor, função pulmonar, fadiga e funcionalidade na lesão medular

Minimal clinically important differences for measures of pain, lung function, fatigue and functionality in spinal cord injury

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Escola Superior de Saúde de Aveiro

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Dissertação apresentada à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Fisioterapia, realizada sob a orientação científica da Doutora Alda Marques, Professora Adjunta da Escola Superior de Saúde da Universidade de Aveiro e coorientação científica da Doutora Ana Oliveira, Professora Assistente da Escola Superior de Saúde da Universidade de Aveiro

Dedico este trabalho aos participantes com lesão medular que permitiram e motivaram a sua realização.

O júri

Presidente	Professora Doutora Ana Rita Pinheiro Professora Adjunta da Escola Superior de Saúde da Universidade de Aveiro
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Palavras-chave Lesão medular; mínima diferença de importância clínica, pico de fluxo, atividades da vida diária

Resumo

Introdução: As lesões medulares (LM) são atualmente um problema de saúde pública mundial. A dor, a fadiga, a redução do fluxo expiratório e da eficácia da tosse e o aumento da dispneia são sinais e sintomas frequentes, que contribuem para o aumento do risco de infeções respiratórias. As infeções respiratórias constituem a principal causa de morte nestes doentes e podem ser prevenidas, desde que exista uma monitorização regular. As Mínimas diferenças de importância clínica (MDICs) de instrumentos de medida são essenciais, para interpretar os resultados desta monitorização e orientar a intervenção, mas são escassas as que se encontram estabelecidas para doentes com LM que realizam programas de reabilitação.

Objetivo: Determinar as MDICs para a Escala Numérica da Dor (END), Pico de Fluxo Expiratório (PFE), Pico de Fluxo de Tosse (PFT), Escala de Severidade da Fadiga (ESF), e Escala *London Chest Activities of Daily Living* (LCADL) em doentes com LM após reabilitação.

Métodos: A END, PFE, PFT, ESF e LCADL foram aplicadas na admissão e no momento da alta dos doentes do Centro de Medicina e Reabilitação de Alcoitão que realizaram programa de reabilitação. A escala de perceção global de mudança (EPGM) foi aplicada no momento de alta. As MDICs foram calculadas através de métodos de âncora (característica de operação do recetor e regressão linear) e de distribuição (erro padrão da medida (EPM), 1,96 vezes o EPM, 0,5 vezes o desvio-padrão e a mínima diferença detetável). As MDICs finais foram calculadas agrupando os métodos de âncora e de distribuição.

Resultados: Trinta e um doentes com LM participaram no estudo (17 homens; 55±16,2 anos). Foi encontrada uma correlação significativa entre a END e a EPGM, resultando numa MDIC, através de métodos de âncora, de -1,5 pontos. As MDICs estimadas através de métodos de distribuição variaram de 0,8 a 2.3 pontos para a END, 37 a 102,6 L/min para o PFE, 59,4 a 166,5 L/min para o PFT, 0,6 a 1,8 pontos para a ESF, e de 0,6 a 2 pontos para a LCADL.

Conclusão: Melhorias que excedam as estimativas de -1,6 pontos para a END, 67,1 L/min para o PFE, 100,9 L/min para o PFT, 1,1 pontos para a ESF, e 1,4 pontos para a LCADL devem ser considerados clinicamente relevantes para doentes com LM após reabilitação.

Keywords Spinal cord injury; minimal clinically important difference; peak flow; activities of daily living

Abstract

Introduction: Spinal cord injuries (SCIs) represent a major public health problem. Pain, fatigue, reduced expiratory flow and cough efficacy and increased dyspnoea are frequent signs and symptoms that contribute to the increased risk of having respiratory infections. Respiratory infections are the most common cause of mortality and morbidity in this population, but can the prevented if regular monitoring of these patients is performed. Minimal clinically important differences (MCIDs) of outcome measures are essential to interpret results of this monitoring and guide interventions, but MCIDs established for patients with SCI after rehabilitation programmes are missing.

Aim: To determine MCIDs for the 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 rehabilitation.

Methods: The NPRS, PEF, PCF, FSS and LCADL were performed at baseline and at discharge of patients who underwent a rehabilitation programme treatment at the Medicine and Rehabilitation Centre of Alcoitão. The global rating of change (GRC) scale was performed at discharge. MCIDs were calculated using anchor (receiver operating characteristic and linear regression analysis) and distribution-based methods (standard error of measurement (SEM), 1.96 times SEM, 0.5 standard deviation and minimal detectable change) and pooled using Meta XL.

Results: Thirty-one inpatients with SCI (17 males; 55±16.2 years) participated. A significant correlation with GRC was found for the NRS resulting in an anchor-based MCID estimate of -1.5 points. Distribution-based MCIDs estimates ranged from 0.8 to 2.3 points for the NPRS, 37 to 102.5 L/min for PEF, 59.4 to 166.5 L/min for PCF, 0.6 to 1.8 points for the FSS, and 0.6 to 2 points for the LCADL.

Conclusion: Improvements exceeding the pooled MCID estimate of -1.6 points on the NPRS, 67.1 L/min on the PEF, 100.9 L/min on the PCF, 1.1 points on the FSS, and 1.4 points on the LCADL should be considered clinically relevant for patients with SCI after rehabilitation.

Abbreviations and/ or acronyms

AUC – Area under the curve

ADL – Activities of daily living

ASIA – American Spinal Injury Association

AIS – ASIA impairment scale

COPD – Chronic Obstructive Pulmonary Disease

ES – Effect size

ESL – Erythematous systemic lupus

ICC – Intraclass correlation coefficient

ICF – International Classification of Functionality

ISNCSCI – International standards for neurological classification of spinal cord injury

FSS – Fatigue severity scale

GRC – Global rating of change

LCADL – London chest activities of daily living scale

LS – Laryngotracheal stenosis

L/min – Litres per minute

MCID – Minimal clinically important difference

MDC95 - Minimal detectable change at the 95% level of confidence

MID – Minimal important difference

MRCA – Medicine and Rehabilitation Centre of Alcoitão

NPRS – Numerical pain rating scale

PCF – Peak cough flow

PEF – Peak expiratory flow

PFM – Peak flow meter

ROC – Receiver operating characteristic

SCI – Spinal cord injury

SEM – Standard error of measurement

0.5SD – 0.5 times the standard deviation of the baseline session

1.96SEM – 1.96 times the standard error of measurement

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INTRODUCTION

Spinal cord injuries (SCIs) represent a major public health problem that leads to significant disabilities in patients and affects not only the patients themselves but also their family and, ultimately, the society as a whole (van den Berg, 2010). Traumatic SCIs are mostly caused by road traffic accidents and falls, affecting 10.5 per 100000 people worldwide (Jazayeri, Beygi, Shokraneh, Hagen, & Rahimi-Movaghar, 2015; Kumar et al., 2018). Non-traumatic SCIs are commonly associated with age-related problems and affect approximately 11.4 per 1000000 people in Spain. However, this incidence has not been widely studied (van den Berg, Castellote, Mahillo-Fernandez, & de Pedro-Cuesta, 2012).

After SCI, 36 – 83 % of the patients are affected by respiratory complications, the most common cause of death in this population, twice the expected rate for a same age person without SCI (Tollefsen & Fondenes, 2012; Lidal at al., 2007). Respiratory failure and retention of secretions represent significant complications (Hagen, Eide, Rekand, Gilhus, & Gronning, 2010).

As higher is the neurological level of the injury, greater is the reduction of pulmonary function parameters, leading to a reduced ability to cough and to clear airways, atelectasis, impaired gas exchange and respiratory infections (Linn et al., 2001; Brown, DiMarco, Hoit, & Garshick, 2006; Schilero, Spungen, Bauman, Radulovic, & Lesser, 2009; Schilero, Bauman, & Radulovic, 2018). Respiratory infections have a negative effect on the physical independence and long-term survival of patients with SCI, irrespective of age and severity (Kopp et al., 2017). Additionally, findings from a 5-year follow-up study showed that beyond respiratory function impairments and reduced ability to cough (30.9% of the patients had a forced vital capacity (FVC) below the 80% predicted value, 35.9% poor or moderate self-reported cough strength), 18.4% of the patients reported rest dyspnoea and 29.0% during activity, being associated with worse health-related quality of life (Postma et al., 2016). Patients with SCI also report pain and fatigue as relevant symptoms, with a statistically significant negative association with reduced mobility, participation, and satisfaction with life (Marcondes et al., 2016; Smith et al., 2016).

The pertinence of these signs and symptoms, and the mortality and morbidity associated with respiratory complications in patients with SCI demand appropriate monitoring, prevention and treatment (Schilero et al., 2018; Tollefsen & Fondenes, 2012; Wyndaele & Wyndaele, 2006; Anton et al., 2017; Kopp et al., 2017).

According to a report from the European Spinal Cord Injury Federation about primary rehabilitation services offered to people with SCI, most of the patients are cared

for in specialized SCI hospitals, units, or centres, with multidisciplinary teams, focused on achieving their maximum functional potential and independence, overtaking the barriers of societal reintegration (Horsewell, 2007).

Physiotherapy for patients with SCI comprises a comprehensive assessment and intervention, focusing on different problems in many body systems, including respiratory and sensorimotor function, impact on functionality and pain (Harvey, 2016). It plays a key role to address 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 (Fehlings, Tetreault, Wilson, et al., 2017; Harvey, 2016).

The use of outcome measures during a rehabilitation intervention is essential to monitor patients' evolution however, clinically relevant improvements are difficult to interpret in the absence of minimal clinically important differences (MCIDs) (Ekstrom et al., 2015).

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 (Ekstrom, Currow, & Johnson, 2015). MCIDs for the neck disability index, the oswestry disability index, the physical component summary of the 36-item short form of the medical outcome measures, the physical and mental component summaries of the 12-item short form health survey, EuroQol-5D health survey, the numerical rating scale for back and for leg pain, the visual analogue scale have been determined for patients with SCI after undergoing surgery (Parker et al., 2013; Copay et al, 2008; Parker et al, 2012). MCID for the spinal cord independence measure III was established after rehabilitation in spinal cord units (Corallo et al., 2017). Minimal important difference (MID) for the walking index for SCI and gait speed were established for patients with incomplete SCI, after an out-patient body weight-supported treadmill training programme (Musselman, 2007). However, MCID for other outcome measures commonly used in rehabilitation including physiotherapy interventions of patients with SCI are lacking and are urgently needed to monitor and interpret patients' progress and guide personalised interventions.

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.

METHODS

Ethical approval

This study was approved by the Ethical Commission of the Medicine and Rehabilitation Centre of Alcoitão (MRCA) on the 21th May of 2018 (CMRA 04) (Annex I). Written informed consent (Appendix I) was obtained from all participants before any data collection.

Study design and recruitment

An observational prospective study was conducted from May to November of 2018 in patients with SCI admitted to the MRCA.

Participants were first identified by the investigator according to the eligibility criteria. Patients were considered eligible for the study if they were at least 18 years old, had a diagnosis of SCI (without limitations about the time or extension of the injury), were currently inpatients at the MRCA, and were able to understand and speak Portuguese and to give an informed consent to participate. 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's structural injuries being managed; that could affect or preclude them of participating in data collection (Chan et al., 2018; Mueller, Hopman, & Perret, 2013; Roth et al., 2010; Tamplin et al., 2013). The investigator informed eligible participants about the study, and gave them a Participant Information Sheet (Appendix II). Only those interested to participate were included for further assessments.

Data Collection

Patients were assessed within two weeks of admission and at discharge from the MRCA. Each evaluation session lasted approximately 20 minutes and was performed at the MRCA. All measures were collected by an experienced physiotherapist except the lung function, maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP), which were collected by a trained cardiopulmonary technician. Patients were admitted for approximately 60 days.

The following data were collected only at baseline to characterise the population. A structured questionnaire based on International Classification of Functionality (ICF) checklist and American Spinal Injury Association (ASIA)/ International Spinal Cord Society working group, which included sociodemographic (i.e., age, weight, height, body mass index gender, education, current occupation, marital status), and general clinical data (i.e., smoking status, comorbidities, respiratory complications in the last year,

ventilatory assistance, medication, time and cause of the SCI) was first applied (DeVivo, 2017; Krassioukov A., 2010; WHO, 2010).

The Charlson Comorbidity Index (CCI) was calculated to measure disease burden, using the updated version from 2010 (Quan et al., 2011). CCI have been used in patients with SCI (Bertling et al., 2016; Burns, Weaver, Chin, Svircev, & Carbone, 2016). Each comorbid condition was weighted according to the related risk of mortality in one year: congestive heart failure – 2 points; dementia – 2 points; chronic pulmonary disease – 1 point; rheumatologic disease – 1 point; mild liver disease – 2 points/ moderate or severe liver disease – 4 points; diabetes with chronic complications – 1 point; hemiplegia or paraplegia – 2 points; renal disease – 1 point; any malignancy, including leukaemia and lymphoma – 2 points/ metastatic solid tumour – 6 points, acquired immunodeficiency syndrome or human immunodeficiency virus – 4 points (Quan et al., 2011). All points are summed, and the total score can range from 0-24 points, a higher score means a greater disease burden and predicts an earlier mortality (Quan et al., 2011). The total score was classified as mild – CCI ≤2, moderate – 2<CCI≤4, or severe – CCI≥5 (Charlson, Pompei, Ales, & MacKenzie, 1987).

The Portuguese version of the International standards for neurological classification of spinal cord injury (ISNCSCI) was used to categorise the injury extension (Fehlings, Tetreault, Wilson, et al., 2017; Kirshblum, 2011). The ISNCSCI is divided into a motor and sensory assessment (Fehlings, Tetreault, Wilson, et al., 2017). The motor score was defined by the sum of the left and right upper and lower extremities motor scores, evaluating 10 key myotomes (Fehlings, Tetreault, Wilson, et al., 2017). The sensory assessment comprised light touch and pin prick sensation tests of the left and right dermatomes compared to the patient's face sensation (Fehlings, Tetreault, Wilson, et al., 2017). The neurological level was the lower spinal cord level where both sensory and motor function were preserved (Kirshblum, 2011).

The ASIA Impairment Scale (AIS) was used to classify the injury extension in a 5-grade classification system. Grade A – complete injury, B – sensory incomplete, C and D – motor incomplete, E– normal sensation and motor function (Fehlings, Tetreault, Wilson, et al., 2017).

Lung function was assessed with spirometry and respiratory muscle strength with maximal respiratory pressure tests. The equipment was adapted to wheelchair users, using a computer with a specialised software (MasterScope version 4.5, JAEGER), in conformity with the relevant standards from European Respiratory Society and the American Thoracic Society (Jaeger, 1999). A heated pneumotach was connected to the MasterScope program, to measure and analyse the lung function and respiratory muscle strength (Jaeger, 1999). Absolut and percentage predicted values from FVC, forced

expiratory volume in one second (FEV1), FVC/ FEV1 ratio, MIP and MEP were registered for each participant (Jaeger, 1999; Miller, 2005).

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

The NPRS was used to quantify the perception of the patient about her/his pain severity in the worst pain site. The scale is recommended by the Portuguese Health General Direction and has been used in other studies with patients with SCI (Copay et al., 2008; DeSantana & Sluka, 2009; DGS, 2003). The patient was asked to select the number between “0” and “10” that best represented her/his pain. The scale was presented as a horizontal sequence of squares with a number inside. Higher numbers represent worse pain, i.e., “0” means “no pain” and “10” means “the worst pain you can imagine” (DGS, 2003). The NPRS correlates significantly to the pain relief scale (r=0.92) (Lee et al., 2015).

The PEF and PCF were measured using a peak flow meter (PFM) (MicroPeak from CareFusion), which is simple and economic instrument. A nose clip was placed on the patients nose and patients were asked to inhale as much air as they could, and exhale (PEF) as fast and as strong as they could or cough (PCF) through the mouth piece of the PFM, in the sitting position. Each assessment was repeated three to five times with intervals of 30 seconds, and the best result was recorded for PEF and PCF (Tzani et al., 2014). PEF and PCF are two commonly used outcome measures in patients with SCI (Postma et al., 2016; Postma et al., 2015; Rose et al., 2018). The PEF is 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 the outcome measure for the target population (Raab et al., 2016). The PCF has also been considered a relevant measure for patients with SCI, a cut-off value of 270 L/min is recommended as clinically important to start techniques to increase cough effectiveness, including lung volume recruitment, manually assisted cough, and mechanical insufflation-exsufflation devices (Rose et al., 2018). A cut-off value of 160 L/min has been reported as minimum to allow an effective airway clearance, considered a specific and sensitive predictor of severe respiratory infections and hospital admissions due to respiratory complications (Tzani et al., 2014; Bianchi, Baiardi, Khirani, & Cantarella, 2012).

The Portuguese version of the FSS, was used to measure the severity of the fatigue. Each patient was asked to score her/his agreement with eight sentences, between “1” – “strongly disagree” and “7” – “strongly agree”, as the authors suggested the elimination of item 1, considering eight sentences instead of the nine from the original version, presenting better internal consistency (Chronbach’s alpha=0.899) (Gomes, 2011). Scores were summed and divided by eight, with a possible range of 1 to 7, a

higher score reveals greater fatigue (Gomes, 2011). In the absence of an outcome measure validated for the Portuguese population with SCI, the FSS is validated for the Portuguese population with multiple sclerosis, and have been used in patients with SCI (Fawkes-Kirby et al., 2008; Gomes, 2011; Nooijen et al., 2015). The FSS has an excellent internal validity, revealing a moderate and positive significant correlation (r=0.74) with the visual analogue scale applied to assess fatigue severity (Gomes, 2011).

The portuguese version of the LCADL, was used to assess dyspnoea during activities of daily living (ADL). The LCADL contains 15 items divided in four components: self-care, domestic, physical, and leisure. Each patient was asked to score how much dyspnoea interferes, to each ADL 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) (Pitta et al., 2008). The final score was calculated by summing every item of the scale in each of the components with a possible range of 0 to 75. In the absence of an outcome measure validated for Portuguese patients with SCI, the LCADL is validated for patients with chronic obstructive pulmonary disease (COPD) and has been reported to be adjustable to different levels of motor impairment due to SCI (Pitta et al., 2008). 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) (Pitta et al., 2008). Positive poor to moderate significant correlations have been reported between the LCADL total score and each section and total score of the Saint George Respiratory Questionnaire components ($0.36<r<0.74$; $p<0.05$), and a negative moderate significant correlation between the LCADL total score and the 6 minutes walking test distance (r=-0.48; p=0.006) (Pitta et al., 2008).

The global rating of change (GRC) scale was used to assess the perception of change for each outcome measure used at discharge. In order to optimise interpretability and reliability, GRC questions were designed for each outcome measure according to the best evidence available, i.e., mentioning the specific condition, the concept, and the time frame (Kamper, Maher, & Mackay, 2009). Patients were asked to quantify their perception about each measure's change, comparing discharge to the admission, in a balanced 11-point numerical scale with written descriptors at the ends ("-5" – "much worst", and "5" – "much better") and at the midpoint ("0" – "without changes") (Kamper, Maher, & Mackay, 2009). The GRC has been used before in patients with SCI (Stewart, Maher, Refshauge, Bogduk, & Nicholas, 2007) and significant and moderate correlations have been reported between the GRC and the magnitude of change scored by subjective self-report measures as the NPRS (r=0.49, area under the curve (AUC)=0.68) (Stewart

et al., 2007). The 11-point GRC has shown an adequate reproducibility, with excellent $ICC_{2,1}$ (ICC=0.90), and a good sensitivity to change (minimum detectable change of 0.45 points and MID=2 points) in patients with chronic low back pain (Costa et al., 2008).

Intervention

The intervention was tailored to each patient and included: one to three hours/day of physiotherapy; one hour/day of occupational therapy; thirty minutes/day of ADL training; thirty minutes/week of psychology; pharmacological therapy; medical; nursery; and social assistance support.

The physiotherapy intervention was individually planned and focused in the following components:

- Respiratory management enhancing thoracic expansion, breathing control, respiratory muscle training, and airway clearance techniques to prevent complications, such as atelectasis and pneumonia, and achieve the best possible exercise tolerance (Berlowitz & Tamplin, 2013; Fehlings, Tetreault, Wilson, et al., 2017; Reid, Brown, Konnyu, Rurak, & Sakakibara, 2010);
- *Bobath concept*, an inclusive, personalised problem-solving approach, based on contemporary principles of motor control, neuromuscular plasticity and motor learning, emphasising movement analysis and recovery through the integration of sensory information, postural control and task performance; with the final purpose of optimising the movement selectivity, activity, participation and quality of life of neurological patients (Vaughan-Graham, Cott, & Wright, 2015a, 2015b).
- Sensorial stimulation, crucial to guide postlesional neuroplasticity, and movement facilitation, a selective manipulation of sensory input to enhance motor control and perception (Gjelsvik B., 2016; Vaughan-Graham et al., 2015b);
- Pain relief techniques to avoid maladaptive plastic changes involved in the development of neuropathic pain and allodynia (Onifer, Smith, & Fouad, 2011);
- Exercise to enhance positive plastic changes, including aerobic, strength, flexibility, and postural control training (Harvey, 2016; Rank et al., 2015; van Langeveld et al., 2011);
- Neuromuscular electrical stimulation, to enhance motor function (Fehlings, Tetreault, Aarabi, et al., 2017; Harvey, 2016);

- Motor skills training including wheelchair abilities and walking, respecting the functional potential of the patients, to improve their functionality (Gjelsvik B., 2016; Harvey, 2016);
- Education of the patient and carers, to facilitate discharge and maintenance of the improvements (Harvey, 2016).

If in the best judgement of the physiotherapist, she/he considered relevant, additional therapy resources could be used such as: body weight-supported treadmill training (promoting plasticity in an activity-dependent manner), lokomat robotic walking training, exoskeleton walking training, and aquatic physiotherapy (if the patient had sphincters control) (Ellapen, Hammill, Swanepoel, & Strydom, 2018; Fehlings, Tetreault, Aarabi, et al., 2017; Gjelsvik B., 2016; Harvey, 2016).

Statistical Analysis

SPSS software Version 24.0 (IBM Corporation, Armonk, NY, USA) and Meta XL 5.3 (EpiGear International, Queensland, Australia) for Windows were used for statistical analysis. 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 and interquartile range for non-normally distributed data. The Shapiro-Wilk test was used to assess normality of data distribution. The analysis of outliers was achieved by plotting the studied variables (i.e., NPRS, PEF, PCF, FSS, and LCADL) on a graph and visually inspect for extreme points and outliers were removed for MCID analysis (Aggarwal & Ranganathan, 2016). Significance of changes between admission and discharge were calculated with paired t-tests for normally distributed data or Wilcoxon signed-rank tests for otherwise (Chan et al., 2018).

The best way to measure MCID has not been defined yet, however it has been commonly recommended to use anchor- and distribution-based techniques (Alma et al., 2016; Chan et al., 2018; Oliveira, Machado, & Marques, 2018). Thus, both techniques were applied in this study to determine the proposed MCIDs (Ekstrom et al., 2015).

Anchor based methods were calculated through patient-referencing methods, using the GRC as an anchor, when significant correlations, tested with the Pearson rank correlation, were equal or superior to 0.3 in the selected outcome measures (i.e., NPRS, PCF, PEF, FSS, and LCADL) (Chan et al., 2018; Oliveira et al., 2018; Revicki, Hays, Cella, & Sloan, 2008). A GRC total score of two points improvement was used as the MID for the GRC (Alma et al., 2016; Kamper et al., 2009). MCIDs were calculated using linear regression analysis and receiver operating characteristic (ROC) curves. For linear

regression analysis, the statistically significant equations were used to estimate the MCID of the respective outcome measure corresponding to the MID improvement of the GRC (+2). For each ROC curve, the AUC and respective 95% confidence intervals were obtained and the pair of coordinates where the sensitivity and specificity were simultaneously maximised were chosen for the MCID of each outcome measure (Oliveira et al., 2018).

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 $\sqrt{2}$ (Copay et al., 2008; Oliveira et al., 2018; Revicki et al., 2008). The intraclass correlation coefficient used for the SEM calculation was based on the reliability studies previously published for each outcome (i.e., 0.95 for the NPRS (Copay et al., 2008); 0.87 for the PEF (Fonseca et al., 2005); 0.746 for the PCF (Tzani et al., 2014); 0.899 for the FSS (Gomes, 2011); 0.98 for the LCADL and 0.96, 0.99, 0.92, 0.95 for the respective sections: self-care, domestic, physical, and leisure (Pitta et al., 2008).

The pooling of data was performed based on what has been previously described (Alma et al.,2016; Oliveira et al., 2018). MCIDs estimated with each of the anchor- and distribution-based methods for the PEF, PCF, FSS, NPRS and LCADL were pooled using Meta XL 5.3. The input data were the estimated MCID with each method and respective confidence interval, when appropriated. Since anchor-based methods are considered to be more adequate for establishing clinical significance than distribution-based methods, a quality effects model was used in which anchor methods weighted 2/3 and distribution methods weighted 1/3 for the final pooled MCID (Alma et al., 2018; Oliveira et al., 2018).

RESULTS

Patient characteristics and health status

In total, 31 patients with SCI were referred for the study and included for baseline assessment. However, three patients did not complete the study due to unexpected discharges. Therefore, 28 patients with a mean intervention time of 7.5 ± 1.4 weeks were included in the final analysis. A flow diagram of the included sample is provided in Figure 1.

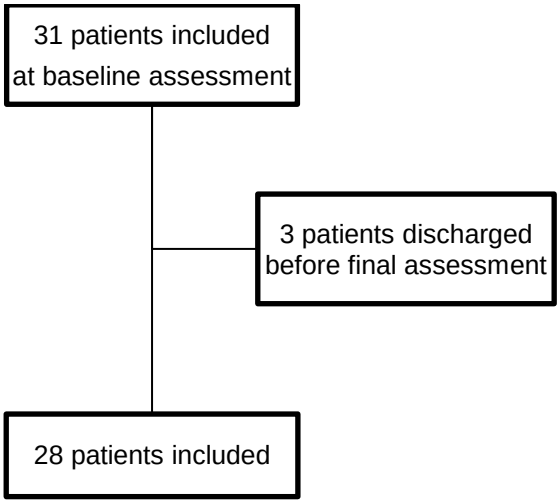

Figure 1. Flow diagram of the included sample of patients with spinal cord injury.

Baseline characteristics of the included patients with SCI are shown in Table 1. Patients were aged 55 ± 16.2 years old. Most of them were male (n=17; 54.8) with 4 years of education (n=8; 25.8%), were retired (n=14; 45.2%), married (n=16; 51.8%) and were former smokers (n=16; 51.8%).

At baseline, lung function tests could only be completed by 27 patients and maximal respiratory pressures tests by 26 patients due to the inadaptation to the mouth piece of the pneumotachograph. Overall, patients presented normal lung function (mean FEV_1 %predicted=80.9 ± 20.1; FVC %predicted=78.5 ± 19.8; FEV_1/FVC=85.1 ± 9.8) and almost half of the maximal respiratory pressure values predicted (MIP %predicted=59.3 ± 21.7; MEP %predicted=57.9 ± 20.4).

Mean comorbidities per patient was 2±1.4, 67.7%, meaning a mild CCI (n=21). Only two patients presented respiratory exacerbations during the past 12 months and no patients used non-invasive ventilation. Patients were taking a mean of 9.3±3.6 medicines, being the most common modifiers of intestinal motility (n=29; 93.5%); modifiers of gastric secretion (n=23; 74.2%); antidepressants (n=21; 67.7%); anxiolytics, sedatives, and hypnotics (n=16; 51.6%); and drugs for urinary problems (n=15; 48.4%).

The most common type of SCI was traumatic (n=17; 54.8%) classified as D (i.e., motor incomplete) according to the AIS (n=13; 41.9%), and of cervical neurological level (n=16; 51.8%).

Table 1. Baseline characteristics of the included patients with spinal cord injury (n=31).

Characteristics	***Baseline***
Age (years)	55 ± 16.2
BMI (kg/m^2)	25.9 ± 4.7
Gender	
Male	17 (54.8)
Female	14 (45.2)
Education	
Illiterate	4 (12.9)
4th year	8 (25.8)
6th year	5 (16.1)
9th year	5 (16.1)
12th year	3 (9.7)
Higher education	6 (19.4)
Current occupation	
Retired	14 (45.2)
Sick leave	11 (35.5)
Student	2 (6.5)
Housework	2 (6.5)
Unemployed	1 (3.2)
Remunerated work	1 (3.2)
Marital status	
Married	16 (51.8)
Single	8 (25.8)
Unmarried couple	2 (6.5)
Widower	2 (6.5)
Divorced	2 (6.5)
Separated	1 (3.2)
Smoking status	
Former	16 (51.8)
Never	12 (38.7)
Current	3 (9.7)
Lung function	
FEV_1 %predicted (n=27)	80.9 ± 20.1
FVC %predicted (n=27)	78.5 ± 19.8
FEV_1/FVC (n=27)	85.1 ± 9.8
Respiratory muscle strength	
MIP %predicted (n=26)	59.3 ± 21.7
MEP %predicted (n=26)	57.9 ± 20.4
Comorbidities	
Number of comorbidities	2 ± 1.4
Charlson Comorbidity Index	
Mild	21 (67.7)
Moderate	9 (29.0)
Severe	1 (3.2)
Respiratory exacerbations during the past 12 months	
0	29 (93.5)
1	2 (6.5)
Ventilation	
Non-invasive ventilation	0 (0)
Medication	
Medicine per patient	9.3 ± 3.6
Pharmacotherapeutic group	

Modifiers of intestinal motility, Propulsives	29 (93.5)
Modifiers of gastric secretion	23 (74.2)
Antidepressants	21 (67.7)
Anxiolytics, hypnotics and sedatives	16 (51.6)
Drugs for urinary problems	15 (48.4)
Antiepileptics and anticonvulsants	14 (45.2)
Centrally acting muscular relaxants	12 (38.7)
Anti-thrombotics	11 (35.5)
Vitamins	10 (32.3)
Renin-angiotensin-system-acting agents	8 (25.8)
Antipsychotics	7 (22.6)
Antidyslipidemics	7 (22.6)
Other antidiabetics	7 (22.6)
Venotropics	5 (16.1)
Antibacterial	4 (12.9)
Analgesics and antipyretics	4 (12.9)
Opioid analgesics	4 (12.9)
Adrenoreceptor antagonists	4 (12.9)
Anti-anaemics	4 (12.9)
Drugs for the treatment of haemorrhoids	4 (12.9)
Thyroid and antithyroid preparations	4 (12.9)
Gynaecological anti-infectives	5 (16.1)
Diuretics	3 (9.7)
Calcium channel blockers	3 (9.7)
Adrenergic inhalants	3 (9.7)
Antifungal	3 (9.7)
Modifiers of gastric motility or prokinetics	2 (6.5)
Nonsteroidal anti-inflammatory drugs	2 (6.5)
Drugs for the treatment of arthrosis	2 (6.5)
Bisphosphonates	2 (6.5)
Calcium	2 (6.5)
Peripherally acting muscular relaxants	1 (3.2)
Antiemetic and antinauseants	1 (3.2)
Repolarization prolongers antiarrhythmics	1 (3.2)
Other antihypertensives	1 (3.2)
Vasodilators	1 (3.2)
Other vasodilators	1 (3.2)
Digestive antispasmodics	1 (3.2)
Enzyme supplements, lactobacillus, and analogues	1 (3.2)
Choleretic and cholagogues	1 (3.2)
Drugs for erectile dysfunction	1 (3.2)
Insulins	1 (3.2)
H1 non-selective histamines	1 (3.2)
Sodium	1 (3.2)
Immunomodulators	1 (3.2)
Dressings for chronic wounds	1 (3.2)

Data is presented as mean ±standard deviation or number (percentage), unless otherwise stated.
Abbreviations: BMI, body mass index; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity, FEV_1/FVC, ratio between FEV_1 and FVC; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure.

One patient at baseline and at discharge, and four patients at discharge assessments failed to perform the PEF and the PCF due to difficulties in assuming the sitting position due to skin damage (n=2) or because they refused to perform it (n=2). Therefore, 23 patients performed the PEF and the PCF at baseline and discharge.

Twenty-two patients (71%) reported pain at baseline. The most painful body regions were the lower limb (n=8; 25.8%), the upper limb (n=7; 22.6%), and the thoracolumbar region (n=7; 22.6%).

After the rehabilitation programme, significant improvements were found for the NPRS (median difference of -1, with interquartile range of -3 points; p<0.001; effect size (ES)=-0.5), the PEF (mean difference of 46.1 L/min; p<0.001; ES=0.59), the PCF (21.3 L/min; p=0.03; ES=0.37), the FSS (-0.5 points; p=0.03; ES=-0.27), and the leisure component of the LCADL (median difference of 0, with interquartile range of 1 point; p=0.02; ES=0.45). No other significant improvements were found. Baseline and post intervention scores can be found in Table 2.

Table 2. Effects of the rehabilitation programme in patients with spinal cord injury (n=28).

Outcome measure	*Baseline*	*Post-intervention*	*Change*	*p value*	*Effect size*
NPRS, points (n=28)	7 [8]	4.5 [6]	-1 [3]	<0.001*	-0.50
PEF, L/m (n=23[a])	358.7 ± 99.6	404.8 ± 123.3	46.1 ± 51.3	<0.001*	0.59
PCF, L/m (n=23[a])	367.8 ± 113.7	389.1 ± 118.6	21.3 ± 43	0.03*	0.37
FSS, points (n=27[b])	3.8 ± 2	3.3 ± 1.8	-0.5 ± 1.0	0.03*	-0.27
LCADL, points (n=27[b])	7.6 ± 3.5	7.7 ± 3.2	0.2 ± 2.1	0.72	0.04
Self-care	4 [0]	4 [1]	0 [1]	0.17	-0.17
Domestic	0 [0]	0 [0]	0 [0]	0.85	0.04
Physical	1 [1]	1 [1]	0 [0]	0.25	-0.14
Leisure	2 [2]	2 [2]	0 [1]	0.02*	0.45

Notes: Values are presented as mean ± standard deviation or median [interquartile range], unless otherwise stated. [a]5 patients did not perform the test at discharge assessment; [b]1 outlier was removed; * p<0.05
Abbreviations: NPRS, Numerical Pain Rating Scale; PEF, peak expiratory flow; PCF, peak cough flow; FSS, Fatigue Severity Scale; LCADL, London Chest Activities of Daily Living Scale; L/m, litters per minute.

Participants were unable to complete the following activities in the LCADL at baseline: putting shoes/socks on (n=15, 48.4%), going out socially (n=21, 67.7%), walking in home (n=22, 71%), walking up stairs (n=25, 80.6%) and domestic activities (n=26, 83.9%). After the rehabilitation programme, 13 patients recovered some abilities, such as dressing upper body (n=1, 3.6%), putting shoes/socks on (n=1, 3.6%), make beds (n=1, 3.6%), change sheet (n=1, 3.6%), wash up (n=2, 7.1%), bending (n=1, 3.6), walking up stairs (n=1, 3.6%), walking in home (n=3, 10.7%), and going out socially at the weekend (n=9, 32.1%).

Comparing the LCADL score at admission and discharge, the results were not statistically significant (mean difference of 0.2 points; p=0.72; ES=0.04). However, almost half of the patients (n=13, 46.4%) were able to perform more activities at discharge, which increased their final score of the LCADL. After removing the activities

that scored “0” at baseline from the total score, there was a statistically significant improvement of dyspnoea during ADL (-0.6 points; p=0.008; ES=-0.19).

Minimal Clinically Important Difference

Anchor-based methods

A negative and statistically significant correlation was found between the GRC and changes in the NRPS (r=-0.7; p=<0.001). No statistically significant correlations were found between the GRC and the PEF (r=-0.09; p=0.68), the PCF (r=-0.06; p=0.77), the FSS (r=-0.25-; p=0.21), and LCADL (r=-0.17, p=0.39; and r=-0.26, p=0.21 with the final score adjustment without the activities which scored 0 points at admission). Thus, anchor methods were only possible to be applied for the NRPS.

In total, 17 patients (60.7%) perceived improvements higher than 2 points in the GRC for pain (NPRS mean difference of -2.9 ± 2.3), whereas 11 (39.3%) did not reach that threshold (NPRS mean difference of -0.1 ± 0.5).

Using linear regression, the estimated MCID for the NPRS was -1.5 points (95%CI -2.9 to -0.1) (Figure 2).

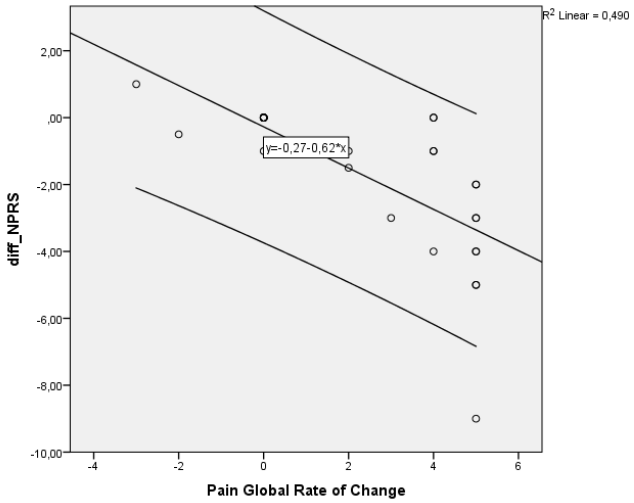

Figure 2. Linear regression to estimate the minimal clinically important difference for numerical pain rating scale according to the global rating of change, in patients with spinal cord injury (n=28).

Using ROC statistics, the AUC generated for the NPRS did not show adequate discrimination between those improving above and below two points for the GRC (AUC=0.45; 95%CI=0.26 to 0.65; p=0.82), thus a MCID could not be computed using ROC methods.

Distribution-based methods

The SEM, 1.96SEM, MDC95, and 0.5SD were calculated for the NPRS, PEF, PCF, FSS and LCADL. Distribution-based MCID estimates ranged from 0.8 to 2.3 points for the NPRS, 37 to 102.5 L/min for PEF, 59.4 to 166.5 L/min for PCF, 0.6 to 1.8 points for the FSS, and 0.6 to 2 points for the LCADL (Table 3).

Table 3. Minimal clinically important difference distribution-based estimates for numerical pain rating scale, peak expiratory flow, peak cough flow, fatigue severity scale, and london chest activities of daily living scale in patients with spinal cord injury (n= 31).

Outcome measure	*SEM*	*1.96SEM*	*MDC95*	*0.5SD*
NPRS, points (n=31)	0.8	1.7	2.3	1.8
PEF, L/m (n=30[a])	37	72.5	102.5	56.5
PCF, L/m (n=30[a])	60.1	117.7	166.5	59.4
FSS, points (n=31)	0.6	1.2	1.8	0.9
LCADL, points (n=31)	0.6	1.3	1.8	2
Self-care	3.3	6.4	0.3	2.7
Domestic	0.4	0.7	0.8	0.4
Physical	1.4	2.8	0.2	1.2
Leisure	1.7	3.4	0.4	1.5

Notes: [a]1 patient did not perform the test at baseline.
Abbreviations: NPRS, Numerical Pain Rating Scale; PEF, peak expiratory flow; PCF, peak cough flow; FSS, Fatigue Severity Scale; LCADL, London Chest Activities of Daily Living Scale; SEM, standard error of measurement; 1.96SEM, 1.96 times SEM; MDC95, minimal detectable change; 0.5SD, 0.5 times standard deviation; ; L/m, litters per minute.

Pooled MCID estimates for the clinical measures

The weighted MCID estimates were -1.6 points for NPRS, 67.1 L/min for the PEF, 100.9 L/min for the PCF, 1.1 points for the FSS (Figure 3), and 1.4 points for the LCADL (Figure 4). Results for the LCADL dimensions were 3.2, 0.6, 1.4 and 1.8 points for self-care, domestic, physical, and leisure, respectively (Figure 4).

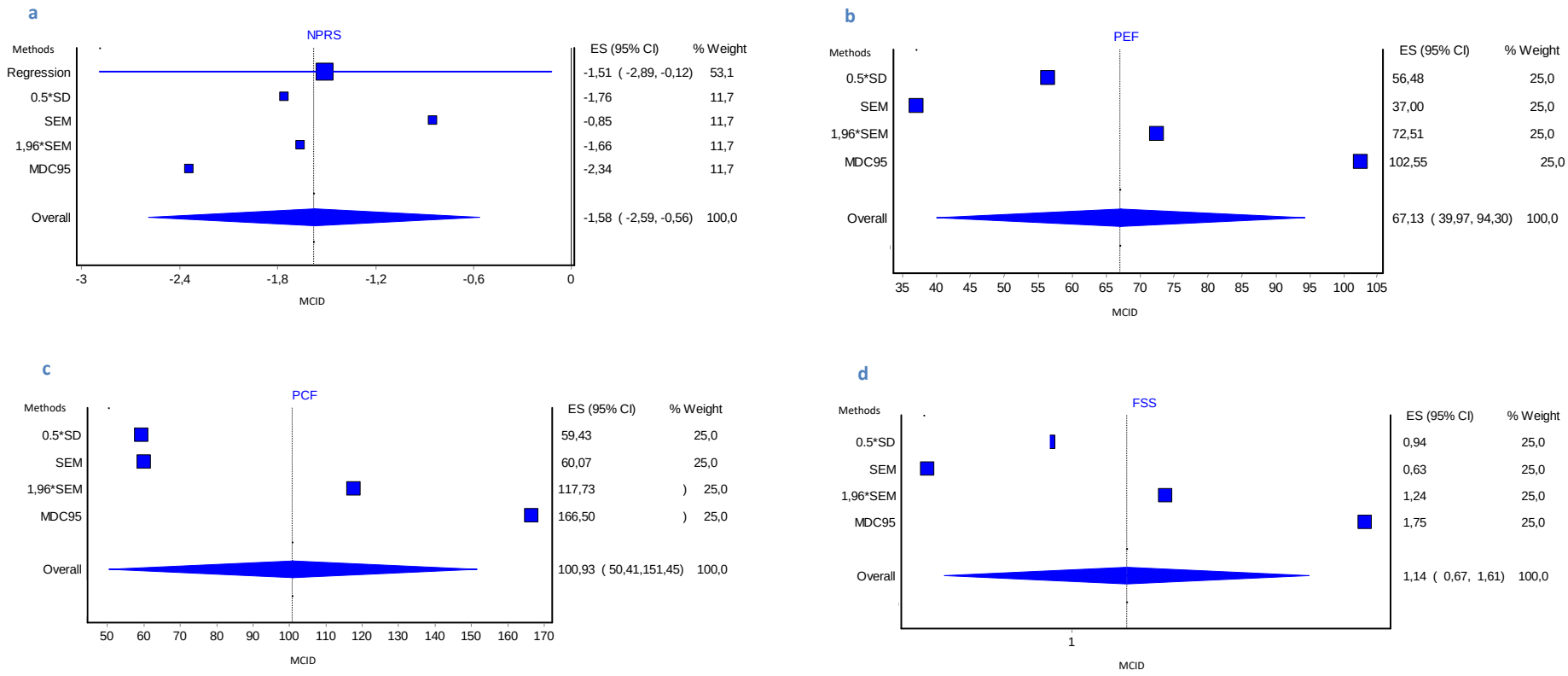

Figure 3. Pooled minimal clinically important difference (MCID) estimates for patients with spinal cord injury: a, numerical pain rating scale (NPRS) (n=31); b, peak expiratory flow (PEF) (n=30); c, peak cough flow (PCF) (n=30); and d, fatigue severity scale (FSS) (n=31).

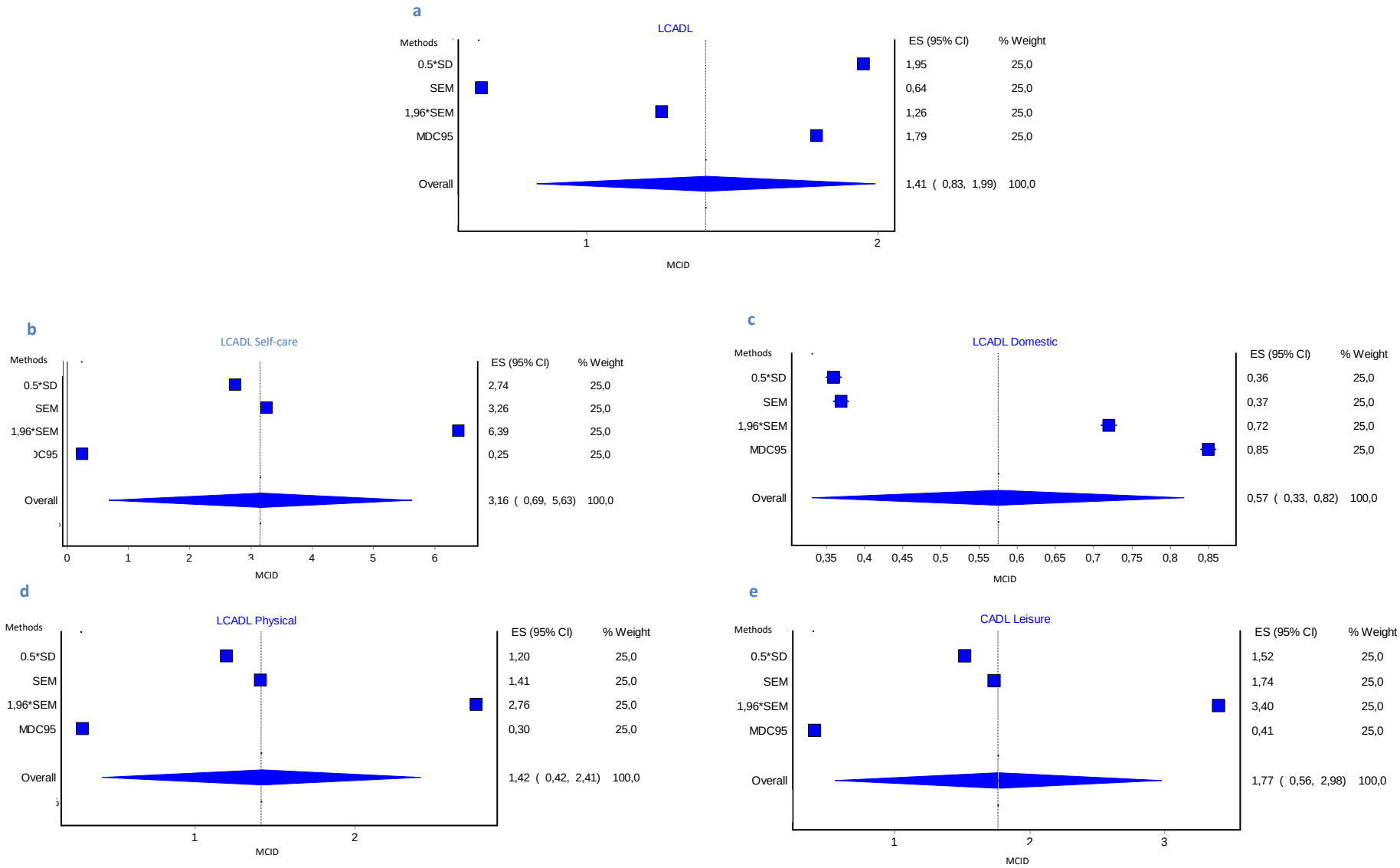

Figure 4. Pooled minimal clinically important difference (MCID) estimates for patients with spinal cord injury: a, London Chest Activities of Daily Living Scale (LCADL) total score, b, LCADL, Self-care; c, LCADL, Domestic; d, LCADL, Physical; e, LCADL, Leisure (n=31).

DISCUSSION

The present study established the MCIDs for NPRS, PEF, PCF, FSS, and LCADL. The distribution-based estimated values ranged from 0.8 to 2.3 points for NPRS, from 37 to 102.5 L/min for PEF, from 59.4 to 166.5 L/min for PCF, from 0.6 to 1.8 points for FSS, and from 0.6 to 2 points for LCADL. The pooled MCID estimates were -1.6, 67.1, 100.9, 1.1 and 1.4 for NPRS, PEF, PCF, FSS, and LCADL, respectively.

After the rehabilitation programme, significant improvements were found for NPRS, PEF, PCF, FSS, and the leisure component of LCADL. Medium ES were found for the NPRS and for the PEF, meaning that these outcome measures may be moderately sensitive to changes in patients with SCI who underwent a rehabilitation programme (Fritz, Morris, & Richler, 2011). A small ES was found for PCF, FSS, and LCADL, revealing poor sensitivity to change after the intervention (Fritz et al., 2011). No studies were found corroborating the positive results reported for pain, respiratory function and fatigue obtained after a comprehensive rehabilitation programme in patients with SCI.

The results of LCADL were not statistically significant, suggesting that patients did not change their dyspnoea during ADL. However, these results need to be interpreted with caution as the domestic component of LCADL is not suitable to inpatients, and the scoring of LCADL is not well adapted to the expected functional improvement of patients with SCI, especially with motor incomplete injuries (AIS grades C and D) (Wilson et al., 2012). At admission, most of our patients scored “0” in domestic activities, as they were inpatients and did not need to do it; and in the ADLs like putting shoes on, going out socially, walking in home, and walking up stairs; as they were unable to perform these activities due to motor impairments. Walking and going up stairs have been reported as the hardest items in other instruments such as the functional independence measure (FIM), or spinal cord independence measure (SCIM) self-report, assessing ADL in the SCI population (Bode, Heinemann, Kozlowski, & Pretz, 2014; Prodinger,et al., 2016). The SCIM was updated to SCIM III, an increasingly used scale of independence in the ADLs validated and designed for patients with SCI, with established MCIDs after rehabilitation, for total score and for the respective subscales: self-care, respiration and sphincter management, mobility in the room, mobility indoors/outdoors) (Corallo et al., 2017). Nevertheless, some of our patients were able to do more activities by the end of the rehabilitation programme, and their score increased, not because they felt more dyspnoeic but because they were now doing more activities. Although, FIM and SCIM III have been used in this population, and spinal cord injury activities of daily living measure

(SCI_ADL) was recently developed, none of these measures assess dyspnoea impact on ADLs (Bode et al., 2014; Corallo et al., 2017; Li et al., 2018). We have chosen to use LCADL given the importance that dyspnoea might have on performing ADL in this population (Postma et al, 2016). However, the use of LCADL for routine clinical assessment in patients with SCI needs further reflection, as adaptions or different ADL measures might be necessary.

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) (Copay et al., 2008). Most of the patients included in our study performed a spine surgery before the rehabilitation programme, and the worst pain site referred at baseline was located in the lower limb, which possibly could have influenced the similarity between our MCID estimate for the NPRS and the MCID established for NPRS when assessing leg pain (Copay at al., 2008).

No studies were found reporting MCIDs for PEF, PCF, FSS and LCADL in patients with SCI. MCID were only found in patients with laryngotracheal stenosis for the PEF (90 L/min) (Nouraei et al., 2014), with erythematous systemic lupus (ESL) for the FSS (0.4 points) (Pettersson et al., 2015) and in patients with COPD for the LCADL (4 points) (Bisca, Proenca, Salomao, Hernandes, & Pitta, 2014). Overall, the values found for other populations tended to be higher than the ones reported in our sample. The functional impairment and treatment of patients with SCI is particularly different from patients with LS, ESL or COPD without neuromuscular conditions. 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 (Copay et al., 2008).

It was not possible to use anchor-based methods to estimate MCIDs for PEF, PCF, FSS, LCADL due to non-significant correlations with GRC, in agreement with the results of a recent study, estimating MCIDs for COPD assessment test and clinical COPD questionnaire, reporting the design of the anchor questions as a possible reason (Alma et al., 2018). Designing appropriate anchors has been reported as a problem, since 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 (Revicki et al., 2006; Revicki et al., 2008). GRC may therefore not provide the best perception of change, due to patients limitation in recalling their health state at admission, being influenced by their current mood state, memory biases, and more recent health events (Crosby, Kolotkin, & Williams, 2003). Our MCIDs for PEF, PCF, FSS, LCADL were estimated with four distribution-based methods of baseline data, without influence from the intervention nor the patient perception of

change, which reduces the clinical significance (Alma et al., 2018; Oliveira et al., 2018). Nevertheless, in the absence of established MCID with anchor-based methods for patients with SCI, the MCIDs established may be carefully used to interpret the results post-intervention in future studies.

Strengths and Limitations

This study applied multiple anchor- and distribution-based approaches and determined the MCID for the NPRS, PEF, PCF, FSS, and LCADL in patients with SCI who participated in a rehabilitation programme. Estimates are valid for patients with traumatic and non-traumatic SCI, with different severity and neurological levels.

There are however, some limitations that need to be acknowledged. First, involving only one investigator in the assessment and treatment of the patients, may influence patients' answers, especially in questionnaires. This potential bias was minimised by following standard procedures when applying the different measures and active efforts were made not to influence patients' answers. Secondly, a relatively small sample size to determine MCID was included in this study due to the timeframe and human resources constraints to perform this dissertation which may have reduced the strength of the statistical analysis (Terwee et al., 2007). Additionally, most studies measuring PEF and FSS revealed statistically significant differences between patients with complete or incomplete motor SCI, but our small sample size did not allow the discrimination of patients according to AIS, which may reduce the applicability of the MCID found in patients with different levels of SCI (Grimm, Schilero, Spungen, Bauman, & Lesser, 2006; Raab et al., 2016). Finally, the current study used distribution-based methods to estimate MCIDs for the PEF, PCF, FSS, LCADL, instead of using both distribution- and anchor-based approaches. However, this could not be performed due to the non-significant correlations between those outcome measures and GRC. Anchor-based methods would enrich the estimated MCIDs with clinical significance, and probably the correlations with GRC would have improved with a higher sample size (Alma et al., 2018; Oliveira et al., 2018).

Implications for future research, policy, and practice

The present study established MCIDs for NPRS, PEF, PCF, FSS, and LCADL which can be used in clinical practice for patients with SCI. The interpretation of the results of rehabilitation programmes may now be guided considering the established MCID as a minimum goal to reach. Thus, the establishment of MCID for several outcome measures commonly used to assess patients with SCI may enable a better tailoring of measurable goals and treatment for patients.

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, studies may explore the use of different anchors for PEF, PCF, FSS, and LCADL, possibly as the SCIM III (Corallo et al., 2017). A statistically significant negative association was found between FVC and self-reported cough strength ($p < 0.0001$) (Postma et al., 2016). FVC might therefore be a useful measure to be used as an anchor to estimate the MCID for PCF. Future studies should also discriminate patients with motor complete and incomplete SCI, since they present different functional prognosis, which may also influence the MCID.

Conclusion

Improvements exceeding -1.6 points on the NPRS, 67.1 L/min on the PEF, 100.9 /min on the PCF, 1.1 points on the FSS, and 1.4 points on the LCADL may be considered clinically relevant for patients with SCI after a rehabilitation programme.

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Annex I – Ethics approval

CENTRO
DE MEDICINA
DE REABILITAÇÃO
ALCOITÃO

SANTA CASA Misericórdia de Lisboa, Rua Bento Coelho,

Exma. Senhora
Directora Clínica do Centro de Medicina de Reabilitação de Alcoitão
Dra. Maria de Jesus Rodrigues

A Comissão de Ética para a Saúde deste Centro, reunida no dia 21 de maio deste ano, deu os seguintes pareceres:

- Estudo **CMRA2018 004:** "Mínima diferença de importância clínica do débito máximo da tosse, débito expiratório máximo instantâneo, força muscular respiratória, escala de severidade da fadiga, escala London Chest Activities of Daily Living, e escala numérica da dor, em utentes com lesão vertebro medular após fisioterapia"; solicitado por Margarida de Almeida Santos Sobreira, aluna de mestrado em Fisioterapia na Escola Superior de Saúde da Universidade de Aveiro.

A Comissão considerou que estão garantidos os requisitos éticos para a realização do estudo após:
a revisão do documento do Consentimento Informado, Esclarecido e Livre; o conteúdo do Termo de Consentimento Livre e Esclarecido e da Folha de informação ao participante, deve constar num só documento;

retificação do nome do Serviço onde a Terapeuta Margarida Sobreira exerce funções no CMRA, no documento de Consentimento Informado, Esclarecido e Livre.

Alcoitão, 21 de maio de 2018

Appendix I – Written Informed consent

Termo de Consentimento Livre e Esclarecido

Orientadora: Prof. Doutora Alda Sofia Pires de Dias Marques
Coorientadora: Mestre Ana Luísa Araújo Oliveira
Aluna de mestrado: Margarida de Almeida Santos Sobreira

Por favor leia o que se segue e assine abaixo caso concorde com as 5 afirmações. (Caso não consiga assinar será pedido a uma testemunha externa ao estudo que assista a toda a explicação e assine por si caso consinta com os seguintes pressupostos)

1. Eu confirmo que percebi a informação que me foi dada e tive a oportunidade de questionar e de me esclarecer.

2. Eu percebo que a minha participação é voluntária e que sou livre de desistir, em qualquer altura, sem dar nenhuma explicação, sem que isso afete qualquer serviço de saúde ou qualquer outro que me é prestado.

3. Eu compreendo que os dados recolhidos durante a investigação são confidenciais e que só os investigadores do projeto da Universidade de Aveiro têm acesso a eles. Portanto, dou autorização para que os mesmos tenham acesso a esses dados.

4. Eu compreendo que os dados recolhidos durante o estudo podem ser utilizados para publicação em Revistas Científicas e usados noutras investigações, sem que haja qualquer quebra de confidencialidade. Portanto, dou autorização para a utilização dos dados para esses fins.

5. Eu concordo então em participar no estudo.

_____	_____	_____
Nome do utente/ testemunha	Data	Assinatura
_____	_____	_____
Nome da Investigadora	Data	Assinatura

Appendix II – Participant information sheet

Folha de informação ao participante

O Sr./Sra. está a ser convidado/a para participar no estudo de investigação clínica intitulado: "*Mínima diferença de importância clínica do débito máximo da tosse, débito expiratório máximo instantâneo, força muscular respiratória, escala de severidade da fadiga, escala London Chest Activities of Daily Living, e escala numérica da dor, em utentes com lesão medular*". Mas, antes de decidir, é importante que compreenda porque é que a investigação está a ser realizada e o que é que a mesma envolve. Por favor, leia a informação com atenção e discuta a sua participação com outros, se assim o entender.

Se houver algo que não esteja claro para si ou necessitar de informação adicional, por favor pergunte aos investigadores (contactos no final deste documento). Use o tempo que precisar para decidir se deseja ou não participar.

Muito obrigada desde já por ler a informação.

Qual é o propósito do estudo?

Este estudo visa quantificar a melhoria mínima que os utentes com lesão medular sentem como sendo importante após a fisioterapia. Estes valores, denominados valores de mínima diferença de importância clínica, serão estabelecidos para as alterações ao nível da função respiratória, força dos músculos respiratórios, intensidade da tosse, fadiga, dificuldade respiratória em atividades e dor. Após estabelecidos, estes valores serão muito úteis para os fisioterapeutas interpretarem os resultados da avaliação de utentes com lesão medular.

Para que seja possível alcançar estes objetivos vimos então solicitar a sua participação neste estudo que será realizado no Centro de Medicina e Reabilitação de Alcoitão (CMRA) e na Escola Superior de Saúde da Universidade de Aveiro.

Porque é que fui escolhido/a?

Foi escolhido/a porque é um adulto (≥18 anos de idade) com lesão medular que fala e compreende o Português e está internado no CMRA. Para o estudo, precisamos de dados de aproximadamente 50 pessoas, com uma condição clínica semelhante à sua, que aceitem participar.

Tenho de participar?

A decisão de participar, ou não, é completamente sua. Se decidir participar vai-lhe ser pedido que assine um formulário de consentimento informado mas, é totalmente livre de desistir a qualquer momento, sem que para tal tenha de dar qualquer justificação. A decisão de desistir ou de não participar, não afetará a qualidade dos serviços de saúde ou qualquer outro, que lhe são prestados agora ou no futuro.

O que me acontecerá caso decida participar?

No início e no final do seu internamento, o cardiopneumologista fará consigo as provas de função respiratória e avaliará a força dos seus músculos respiratórios. Adicionalmente, o seu fisioterapeuta vai avaliá-lo. Estes procedimentos fazem parte da rotina habitual do serviço do CMRA. Se decidir participar neste estudo, algumas medidas adicionais simples e que não causam qualquer desconforto, ser-lhe-ão explicadas e efetuadas após ter concordado com as mesmas e assinado o consentimento informado. Após assinar e entregar aos investigadores o

consentimento informado, ser-lhe-á então feita uma avaliação do seu estado de saúde geral e a fisioterapeuta investigadora irá avaliar a intensidade da sua tosse, e da sua expiração máxima recorrendo a um instrumento simples que mede a quantidade e a velocidade de ar expirado pela boca através de um pequeno tubo, ao mesmo tempo que o nariz está tapado com uma mola. Irá preencher também 3 escalas através de uma entrevista com a fisioterapeuta investigadora, para avaliar a severidade da sua fadiga, a dificuldade respiratória em atividades e a sua dor. Estes procedimentos serão repetidos pouco antes da sua alta, idealmente após 8 semanas.

Além disso, na data da avaliação final, a fisioterapeuta investigadora irá perguntar-lhe qual a sua perceção global de mudança relativamente à tosse, força da expiração, fadiga, dificuldade respiratória e dor, utilizando questões preparadas de acordo com a melhor evidência científica.

Quais são os efeitos secundários, desvantagens e riscos se eu resolver participar?

Não existem efeitos secundários, desvantagens ou riscos de participar no estudo.

Quais são os possíveis benefícios se eu resolver participar?

Será alvo de uma avaliação mais completa do funcionamento do seu aparelho respiratório, bem como do impacto deste na sua vida diária, e os dados poder-lhe-ão ser disponibilizados, caso tenha interesse.

A longo prazo, a informação obtida neste estudo, através da sua participação, irá ajudar a estabelecer as mínimas diferenças de importância clínica para utentes com a sua condição, facilitando a monitorização da evolução e o planeamento da intervenção do fisioterapeuta nestes utentes de uma forma mais personalizada.

A minha participação será confidencial?

Toda a informação recolhida no decurso do estudo será mantida estritamente confidencial e o anonimato será garantido. Os dados recolhidos serão salvaguardados com um código e palavra-passe, para que ninguém o/a possa identificar. Apenas os investigadores do projeto terão acesso aos seus dados.

O que acontecerá aos resultados do estudo?

Os resultados do estudo serão analisados e incorporados em Dissertações de Mestrado e Teses de Doutoramento e alguns serão publicados em Jornais Científicos. No entanto, em nenhum momento o Sr./Sra. será identificado/a. Se gostar de obter uma cópia de qualquer relatório ou publicação, por favor diga à fisioterapeuta investigadora.

Contactos para mais informações sobre o estudo

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