BMJ Open

Protocol for rapid onset of mobilisation in patients with traumatic spinal cord injury (PROMPT-SCI) study: a single-arm proof-of-concept trial of early in-bed leg cycling following acute traumatic spinal cord injury

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ABSTRACT

Introduction Activity-based therapy (ABT) is an important aspect of rehabilitation following traumatic spinal cord injury (SCI). Unfortunately, it has never been adapted to acute care despite compelling preclinical evidence showing that it is safe and effective for promoting neurological recovery when started within days after SCI. This article provides the protocol for a study that will determine the feasibility and explore potential benefits of early ABT in the form of in-bed leg cycling initiated within 48 hours after the end of spinal surgery for SCI.

Methods and analysis PROMPT-SCI (protocol for rapid onset of mobilisation in patients with traumatic SCI) is a single-site single-arm proof-of-concept trial. Forty-five patients aged 18 years or older with a severe traumatic SCI (American Spinal Injury Association Impairment Scale grade A, B or C) from C0 to L2 undergoing spinal surgery within 48 hours of the injury will be included. Participants will receive daily 30 min continuous sessions of in-bed leg cycling for 14 consecutive days, initiated within 48 hours of the end of spinal surgery. The feasibility outcomes are: (1) absence of serious adverse events associated with cycling, (2) completion of 1 full session within 48 hours of spinal surgery for 90% of participants and (3) completion of 11 sessions for 80% of participants. Patient outcomes 6 weeks and 6 months after the injury will be measured using neurofunctional assessments, quality of life questionnaires and inpatient length of stay. Feasibility and patient outcomes will be analysed with descriptive statistics. Patient outcomes will also be compared with a matched historical cohort that has not undergone in-bed cycling using McNemar and Student's t-tests for binary and continuous outcomes, respectively.

Ethics and dissemination PROMPT-SCI is approved by the Research Ethics Board of the CIUSSS NIM. Recruitment began in April 2021. Dissemination strategies include publications in scientific journals and presentations at conferences.

Trial registration number NCT04699474.

Strengths and limitations of this study

► Activity-based therapy will be applied for the first time in humans during the acute hospitalisation following a traumatic spinal cord injury (SCI).
► This study is a single-arm proof-of-concept trial of early in-bed leg cycling after a traumatic SCI.
► A 14-day regimen of daily in-bed leg cycling initiated within 48 hours of the end of spinal surgery for a traumatic SCI will be implemented.
► We will assess the feasibility of early in-bed leg cycling after a traumatic SCI in terms of safety and adherence to protocol.
► We will assess the benefits of early in-bed leg cycling after traumatic SCI with respect to neurofunctional recovery, quality of life and inpatient length of stay.

INTRODUCTION

Following a traumatic spinal cord injury (SCI), individuals often remain with life-long limitations and secondary multisystemic complications. SCI also impacts independence, social integration and quality of life. Recovery depends on neuroplasticity, which refers to the capacity of the central and peripheral nervous systems to modify, reorganise and adapt to the injured state. Spontaneous recovery in the presence of spared neural tissue occurs when neurons form new 'detour circuits' that relay information from above the lesion to below the lesion, or vice-versa.[1] Neurons from descending motor pathways above or below the lesion then can sprout onto these new 'detour' neurons, leading to circuit reorganisation below the lesion. Similarly, via the remaining ascending pathways, neuroplasticity within the spinal

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cord can further induce changes in the brain and remapping of the circuits that connect the brain to the spinal cord.[2] Repetitive position, movement and weight-bearing (limb loading) inputs are essential to direct circuit reorganisation for promoting recovery[3–9] through adaptive (or appropriate) neuroplasticity of the brain and spinal cord. Conversely, inappropriate sensory inputs may produce maladaptive (or inappropriate) neuroplasticity, which may impair locomotor recovery, generate neuropathic pain and/or trigger spasticity.

There is a general consensus from animal studies that initiating early activity-based therapy (ABT) involving rhythmic loading of the limbs within days after an acute SCI is both safe and effective for enhancing neurological function.[10 11] Indeed, ABT stimulates recovery through a relearning process that involves adaptive neuroplasticity driven by repetitive neuromuscular activation below the level of the SCI.[12–14] This can be achieved through appropriate sensory stimulation and task-specific movement practice such as locomotor training and cycling. Early ABT parallels the critical importance of adaptive neuroplasticity during the early phase after an SCI ('window of plasticity') for promoting motor and sensory recovery.[15] Brown *et al*[15] exposed rats to locomotor training 1 day after an SCI. Improved locomotion, reduced neuropathic pain and decreased spinal cord damage were observed in comparison to rats that started training 8 days after the SCI. Similarly, forced use and weight-bearing of the impaired forelimb immediately following SCI in rats improved motor recovery.[16] Other studies showed that locomotor training in rats started 2–5 days after the SCI improved motor recovery[5 17–19] and prevented neuropathic pain.[20 21] These findings strongly suggest that there is a window of opportunity (or 'window of plasticity') after an SCI during which adaptive neuroplasticity and neurological recovery can be harnessed by early ABT.[15 22]

In the current management paradigm of traumatic SCI, ABT is used during the rehabilitation phase after a traumatic SCI, in order to induce neuroplasticity, reduce inflammation and preserve muscle mass and so on.[4 23–25] It can also help restore motor and sensory function through various neuroprotective and neuroregenerative mechanisms.[4 25] However, it has never been applied early during acute care in individuals who sustained a traumatic SCI. The objective of this article is therefore to provide the protocol for the rapid onset of mobilisation in patients with traumatic SCI (PROMPT-SCI) study, which is a single-arm proof-of-concept trial aimed at evaluating the feasibility and probable benefits (superiority) of applying early in-bed leg cycling as a form of early ABT during acute care after a traumatic SCI.

Hypotheses
Regarding the feasibility of early in-bed leg cycling initiated within 48 hours after the end of surgery for a traumatic SCI, we hypothesise that:
1. There will be no serious adverse events associated with early in-bed leg cycling.

2. 90% of participants will complete at least one session of in-bed leg cycling within 48 hours after the end of spinal surgery.
3. 80% of participants will complete at least 80% of all planned sessions (at least 11 of 14 planned sessions).

We further hypothesise that initiating early in-bed leg cycling in addition to standard care is associated with improved patient outcomes, as compared with standard care alone. Specifically, our hypotheses are:
1. Primary: recovering independent walking 6 months after the injury is more likely with early in-bed leg cycling.
2. Secondary: neurological recovery, functional status, spasticity, quality of life and inpatient length of stay are improved with early in-bed leg cycling.

METHODS AND ANALYSIS
Study design
The PROMPT-SCI study is a single-arm proof-of-concept trial involving a prospective cohort of 45 patients admitted to a single level-1 trauma centre specialised in SCI care (Hôpital du Sacré-Coeur de Montréal, Québec, Canada), and followed for 6 months after a traumatic SCI. The study was registered to ClinicalTrials.gov prior to enrolment and complies with the Standard Protocol Items: Recommendations for Interventional Trials checklist.

Participants
Forty-five participants with severe traumatic SCI will be recruited prospectively after admission to our trauma centre. Inclusion and exclusion criteria are described in table 1. Enrolment began in April 2021 and is anticipated

Table 1	Inclusion and exclusion criteria
Inclusion criteria	**Exclusion criteria**
Adult aged 18 years or older	Condition limiting patient's ability to engage into cycling (eg, pelvis or lower extremity injury or deformity, body mass index 35 kg/m^2, etc)
Blunt (non-penetrating) traumatic SCI	Medical condition that might endanger patients if submitted to cycling (eg, haemodynamic instability, active myocardial infarction, etc)
Neurological level of injury from C0 to L2	Moderate or severe brain injury
Severe SCI with AIS grade A, B or C	Inability to walk independently prior to SCI
Spine surgery performed within 48 hours of SCI	Pre-existing neurological disorder (eg, Parkinson's disease, cerebrovascular disease, etc)
	Complete spinal cord transection confirmed by MRI and/or surgery
	Unwilling or unable to comply with scheduled follow-up visits (eg, living in another country, incarcerated)

AIS, American Spinal Injury Association Impairment Scale; SCI, spinal cord injury.

to end by November 2022. All patients admitted for an SCI will be screened for eligibility by research assistants uninvolved in care and data analysis. The research assistants will provide information pertaining to the study and the informed consent form to eligible patients. Patients will be given the contact information of the research team and of an independent physician for any further questions they could have during the recruitment process or throughout the trial. Participants will be enrolled on a voluntary basis up to 48 hours after spinal surgery, and will be required to provide informed consent to participate in the study. Participants will be compensated for their travel and expenses ($C100) for each follow-up visit.

Routine acute care

Patients undergo initial medical resuscitation and stabilisation in the emergency room, before being transferred to the intensive care unit (ICU) for cardiorespiratory and haemodynamic management. Most patients (90%) undergo surgery to decompress the spinal cord and/or stabilise the spine, before returning to the ICU after surgery. Unless contraindicated due to associated injuries, patients are allowed to mobilise as tolerated immediately after spine surgery. Starting on postoperative day 1, routine physical therapy is initiated. For the first 2 weeks, it consists of 15 min sessions of passive mobilisation of all paralysed joints 6 times/week. Passive mobilisation is performed manually by the attending physical therapist until reaching full range of motion of the joint. Thereafter, focus is shifted on antigravity strengthening and postural exercises (no ABT) with 30 min sessions 4 times/week. Following acute care, 80% patients with severe SCI are transferred to our affiliated inpatient rehabilitation unit specialised in SCI care (Institut universitaire sur la readaptation en déficience physique de Montréal, Québec, Canada), and the remainder are transferred to nursing homes. The mean and median acute length of stay for American Spinal Injury Association Impairment Scale (AIS) grade A, B or C SCI at our institution are respectively 37.0 (SD: 34.7) and 28 (IQR: 18–44) days.

Early in-bed leg cycling

In addition to routine acute care, participants will receive daily 30 min continuous sessions of in-bed leg cycling for 14 consecutive days, starting within 48 hours after spine surgery as soon as the patient is fit for cycling (table 2). We will use an ergometer mounted on an adjustable frame (APT-5 Active Passive Trainer on Hi-Lo Stand, Tzora Active Systems, Beachwood, Ohio, USA). Adjusted socks and shoes will be put on the patients' feet so as to prevent any friction during the pedalling. Patients' legs will then be positioned on the pedals equipped with leg support, in order to ensure stability and protection of the limbs. Three cycling modes are available on the ergometer: passive (motor-driven), active-assisted (partially initiated by patient but with motor assistance) and active (fully initiated by patient without motor assistance). Patients will adopt a semi-reclined position (30 torso inclination) with knee flexed at 30 when pedal located at the 3 o'clock position. Each session will start with a 1 min warm-up of passive cycling at five revolutions per minute (RPM). Following the warm-up, unless participants actively reach the target cadence of 40 RPM, motor assistance will be titrated so that the target is reached. This target cadence has been used safely in chronic SCI individuals,[26] and replicates a low-normal step frequency of 80/min for normal individuals.[27]

Before each session, participants will be screened to ensure that they are fit for cycling (table 2). Setup of the cycling sessions will be supervised by a research assistant. Participant's condition and physiological parameters will be closely monitored by a research assistant during each session to minimise the risk of adverse events and improve adherence to the protocol. Stopping criteria

Table 2 Daily exemption and stopping criteria to determine if patient is fit for cycling

Daily exemption criteria	Stopping criteria
In-bed leg cycling should not be delivered if:	*In-bed leg cycling should cease if:*
► Caring team determines that patient is haemodynamically or medically unstable ► Resting heart rate <40 or >140 bpm ► Unstable or uncontrolled arrhythmia ► Active coronary ischaemia ► Mean arterial pressure <60 or >110 mm Hg ► SpO$_2$<90% ► Pressure ulcer at sacrum, buttock or heel area grade 2* ► Severe agitation† ► Uncontrolled pain ► Caring team considers that in-bed cycling is not appropriate for a condition other than above criteria (eg, active bleeding, incision or wound precluding cycling, risk of compartment syndrome, etc) ► Patient refuses in-bed cycling	► Sustained or symptomatic heart rate <40 or >140 bpm ► New arrhythmia ► Concern for coronary ischaemia (eg, chest pain, changes on ECG) ► Sustained or symptomatic mean arterial pressure <60 or >110 mm Hg ► Unplanned extubation or endotracheal tube dislodgment ► Sustained SpO$_2$<90% ► Clinical signs of cardiorespiratory distress ► Severe agitation† ► Termination of in-bed cycling session requested by patient or caring team

*According to the pressure injury staging system of the National Pressure Ulcer Advisory Panel.[61]
†With a Richmond Agitation and Sedation Scale >2.[62]
bpm, beats per minute.

for each session are detailed in table 2. If a participant has not performed or completed a planned session, the participant will still be eligible to perform a cycling session the following day *as per* the planned protocol. In case the acute length of stay exceeds 14 days following the initiation of cycling sessions, participants will not perform additional cycling sessions.

Haemodynamic and respiratory status

Arterial pressure will be assessed from the arterial line if available; otherwise, it will be measured intermittently every 2 min for the first 4 min and every 5 min thereafter using a digital monitor with an arm cuff. Heart rate and blood oxygen saturation will be measured using pulse oximetry. Respiratory rate will be monitored by visual assessment every 2 min for the first 4 min and every 5 min thereafter, or continuously from ventilator parameters if mechanical ventilation is used. In the ICU, the ECG will be monitored for the presence of cardiac events.

Musculoskeletal response

The musculoskeletal impact of cycling will be monitored during the first, seventh and last sessions. Spontaneous electromyographic (EMG) responses in key muscles will be monitored using a wireless EMG system (Ultium EMG Sensor System, Noraxon, Scottsdale, Arizona, USA). Surface electrodes will be placed bilaterally on four muscles: (1) tibialis anterior, (2) gastrocnemius, (3) vastus medialis, and (4) vastus lateralis. EMG waveforms will be analysed to determine peak amplitudes and compute the area under the curve during pedal cycle periods. To assess the loads transferred to the lower extremities (simulated weight-bearing) during cycling, smart insoles synchronised with the EMG system (SmartLead, Noraxon, Scottsdale, Arizona, USA) will be placed under the patient's feet to monitor plantar pressures. Temporal variations in plantar pressure distribution and EMG responses throughout the cycle period will be synchronised with an optic multiple-camera 6 degree-of-freedom tracking system (V120:Trio, Opti-Track, Corvallis, Oregon, USA).

Outcomes measures

The schedule of assessments of the outcome measures is presented in table 3. The research team is not blinded to the intervention since this is a single-arm trial. Patients will be contacted for follow-up visits 6 weeks and

Table 3	Schedule of assessments			
	Study period			
Outcome measure	**Intensive care unit***	**Ward**	**Hospital discharge**	**Outpatient follow-up visits‡**
Feasibility outcome				
Adherence to cycling protocol	X	X		
Safety: adverse events	X	X	X	X
Neurofunctional outcome				
Neurological status: International Standards for Neurological Classification of SCI	X†	X§	X	X
Spasticity: Spinal Cord Assessment Tool for Spastic Reflexes	X†	X§	X	X
Functional status: 3rd version of Spinal Cord Independence Measure (SCIM)			X	X
Independent walking ability: Item 12 of SCIM (Mobility indoors)			X	X
Quality of life				
Short-Form 36				X
WHO Quality of Life-BREF				X
Inpatient length of stay				
Intensive care unit	X			
Acute care			X	
Inpatient rehabilitation unit				X

*Starting with first cycling session.
†Before and after first cycling session.
‡6 weeks and 6 months after injury.
§After last cycling session.
SCI, spinal cord injury.

6 months after the SCI. The three feasibility outcomes have been described earlier. In addition to adherence to the protocol, adverse events will be monitored daily during the acute period and outpatient follow-up visits. A particular attention will be given to adverse events occurring during cycling sessions (see stopping criteria in table 2). Other adverse events occurring during acute care will be collected from communications with the caring team and chart review. During outpatient follow-up visits, adverse events will be collected by the research team. The onset, duration, severity and required treatment of adverse events will be recorded. The principal investigator (J-MM-T) will examine the relationship of the adverse event to in-bed cycling to determine whether it is a suspected adverse reaction. Severity of adverse events will be graded according to the Common Terminology Criteria for Adverse Events Version 5.0.[28]

The primary patient outcome that will be used to evaluate the probable benefits of early in-bed leg cycling consists in the recovery of independent walking ability 6 months after the SCI. Independent walking will be assessed with Item 12 (Mobility indoors) of the 3rd version of the Spinal Cord Independence Measure (SCIM), and is defined by a score 4 on this item.[29] The SCIM is a valid and reliable questionnaire to evaluate the ability to perform daily living activities (self-care, respiration and sphincter, and mobility) independently after SCI.[30 31]

Secondary patient outcomes will be used to further describe neurofunctional status, quality of life and inpatient length of stay. Functional recovery will be measured with the SCIM total score (from 0 to 100), which consists in the sum of all individual item scores. Neurological recovery will be assessed using the International Standards for Neurological Classification of SCI.[32] The ISNCSCI provides the AIS grade, the neurological level of injury, as well as the motor and sensory scores. Spasticity will be assessed using the Spinal Cord Assessment Tool for Spastic Reflexes (SCATS), a validated scale specific to SCI.[33 34] The SCATS is split into three subscales, accounting for clonus, flexor and extensor spasms rated with a score that ranges from 0 to 3. Quality of life will be assessed using the Short-Form 36 (SF-36) and WHO Quality of Life-BREF (WHOQoL-Bref) instruments, which are both validated for SCI patients.[35–37] In addition to domain scores (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, mental health), the physical component score and the mental component score of the SF-36 will be reported.[38] The WHOQoL-Bref is divided into four domains (physical health, psychological health, social relationships, environment), and comprises two specific items measuring overall quality of life and general health. Inpatient length of stay at the ICU, acute care hospital and intensive functional rehabilitation centre will also be collected.

Data collection and management

All data will be collected by research assistants uninvolved in patient care and data analysis. We will collect baseline characteristics of participants including patient-related (age, sex, comorbidities, body mass index), trauma-related (mechanism of injury, level of energy associated with injury, associated injuries) and injury-related (spine injury, neurological status) variables. Variables characterising the course of acute care (eg, timing of surgery, management of other injuries, complications, physical therapy treatments) will also be collected. A research assistant will enquire about the participants' perspectives through a standardised questionnaire to identify barriers and facilitators of using in-bed cycling prior to discharge from the acute care centre. Data will be recorded via the REDCap system[39] using electronic case report forms (eCRF) for each participant. Accurate and reliable data collection will be assured by verification and cross-check of the eCRF by the data manager (statistician). The data manager will inspect the data management system quarterly to verify the adherence to the protocol and the completeness and accuracy of the data. A comprehensive validation check strategy will be defined for data entry, including verification by an archivist of all data transferred from paper forms to electronic records. Data from the eCRF will be accessible to the statistician for performing the statistical analyses. The principal investigator will have full access to the final trial dataset, while coinvestigators will have access to the anonymised dataset. Data sharing will be in line with the recommendations from the Committee on strategies for Responsible Sharing of Clinical Trial Data.[40]

Analysis
Sample size calculation
We will recruit 45 participants who will receive early in-bed leg cycling, and we expect that at least 36 participants with complete data will be available for final analysis when accounting for potential 20% dropout rate (losses to follow-up and withdrawals). This estimation is consistent with the sample size required for observing an increased likelihood to recover independent walking 6 months after the injury (primary patient outcome), when compared with a matched historical cohort who has not received early in-bed leg cycling. In a previous study, we have reported that 36% of our SCI patients (with same inclusion/exclusion criteria as the current study) recovered independent walking.[41] In the absence of prior data on ABT during acute care after SCI in humans, we have determined that an increase in the percentage of individuals recovering independent walking from 36% to 50% would be considered as a clinically meaningful increase. Assuming that 50% of trial participants will walk independently—versus 36% for our current patients who have not received in-bed leg cycling[41]—, at least 36 patients in the trial and matched historical cohorts will provide 80% power to detect a statistically significant increase in the

ability to walk independently for patients who received early in-bed leg cycling, using a one-tail McNemar test with a level of significance of 0.05.

Matched historical cohort

A matched historical cohort of 45 patients (allocation ratio of 1) will be used as a reference for assessing the probable benefits of receiving early in-bed leg cycling. The historical cohort will be matched based on age, sex, AIS grade (A, B or C) and neurological level of injury (high-cervical from C1 to C4, low-cervical from C5 to T1, thoracic from T2 to T10 or thoracolumbar from T11 to L2). This matched historical cohort will be retrieved from our local database of 600+ patients admitted to our centre for a traumatic SCI between May 2010 and April 2021. These patients are participating in a long-term observational study approved by the ethics board of the CIUSSS Nord-de-L'Ile-de-Montréal. They have been followed for a minimum of 6 months after the injury with various patient outcomes, including those collected in this trial. Therefore, all primary and secondary outcomes that will be collected in the current study are already available for our historical cohort, and will be used for the comparative analyses. The historical cohort did not receive in-bed leg cycling or any form of structured ABT during acute care. Their management was otherwise similar to the routine acute care described for trial participants.

Statistical analysis

All statistical analyses will be conducted by a statistician uninvolved in collecting the data. There is no planned interim analysis. Descriptive analyses will be used to assess the feasibility of early in-bed leg cycling and verify the corresponding hypotheses in terms of safety and adherence to the protocol.

To assess the probable benefits of early in-bed leg cycling, data will be analysed and reported using intention-to-treat principles. A per-protocol analysis will be conducted if a significant variation from the planned protocol (daily session for 14 consecutive days) occurs for more than 20% of participants. The per-protocol analysis will include participants receiving at least 80% of cycling sessions (minimum 11 sessions). These thresholds have been defined because it is often believed that the percentage of missing data or participants should not exceed 20% to preserve the quality of the statistical analysis.[42–45]

In addition to descriptive statistics, comparison between the trial and matched historical cohorts will be achieved using a one-tail McNemar test for the primary patient outcome (independent walking 6 months after SCI). Comparisons between trial and matched historical cohorts will also be achieved using one-tail McNemar and paired Student's t-tests for secondary binary and continuous patient outcomes, respectively. Considering that the historical group will be matched for age, sex, AIS grade and neurological level of injury, we do not a priori plan to adjust for other potential confounders. However, we will compare the other baseline characteristics between the two cohorts, and may adjust if a potential confounder differs significantly between groups. A generalised linear mixed model may be used to examine the association between musculoskeletal measures (from smart insoles and EMG) and patient outcomes.

Trial management

The principal investigator will oversee and monitor the conduct of the trial. He will supervise the recruitment process, and oversee the training and coordination of the research personnel. A Trial Steering Committee (TSC) composed of all investigators (J-MM-T, AR-D, FB, YP, DB, DSKM) will monitor trial progress and advise on scientific credibility. While we expect seasonal variations in recruitment, an average accrual rate of 2.5 participants/month is planned. A contingency plan (eg, identifying and overcoming deficiencies in the enrolment process, providing additional support for eligible participants, reassessing inclusion/exclusion criteria, etc) will be implemented if we fail to recruit at least five participants per quarter.

Risk management

Different measures will be taken to ensure patient's safety, including the strict monitoring and exemption/stopping criteria described above. In addition to the daily neurological assessments that are already performed by caring teams, scheduled neurological assessments by our research team will ensure that there is no neurological deterioration associated with in-bed cycling, particularly for the first cycling session. Qualified personnel (including attending medical teams) will be available on site for managing adverse events. Serious adverse events will be reported to the study coordinator and principal investigator within 24 hours of their onset. Serious adverse events and suspected adverse reactions will be discussed between the investigators, and reported to the Data and Safety Monitoring Committee (DSMC) composed of two independent physicians from other institutions. The DSMC will be responsible for assessing the relationship of serious adverse events to in-bed cycling, and for determining if modifications to the protocol are required. The TSC will act, as appropriate, on the recommendations of the DSMC, and decide when to communicate with the ethics committee and trial participants. Post-trial care will be provided as per current standards through our public healthcare system.

PATIENT AND PUBLIC INVOLVEMENT STATEMENT

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

ETHICS AND DISSEMINATION

PROMPT-SCI has been approved by the ethics board of the CIUSSS Nord-de-L'Ile-de-Montréal (REB 2020

1901). To preserve participants confidentiality, all case report forms, personal data and study reports will identify subjects by a unique identification number specific to this trial. Data coding, security and storage will be ensured according to applicable privacy laws and regulations.

The study results will be disseminated regardless of effect direction and size through publications in peer-reviewed journals, presentations at conferences and media appearance. Authorship will be consistent with the recommendations from the International Committee of Medical Journal Editors.[46]

DISCUSSION

One main strength of the PROMPT-SCI study is the clinical implementation of early ABT during acute care—rather than during the rehabilitation phase—, using a protocol adapted to individuals with severe SCI. In-bed leg cycling is safe and feasible for critically ill (neurologically intact) patients in the ICU,[47–49] but in-bed leg cycling—or any other structured method of ABT—has never been applied early during acute care after SCI.

In addition to feasibility outcomes that will be used to assess safety and adherence to the protocol, we will evaluate patient outcomes that are highly relevant for individuals with SCI. We have defined independent ambulation as the primary patient outcome because it is a life priority in this population and it is strongly associated with long-term quality of life.[50 51] The neurological recovery, functional status and quality of life are also important outcomes measures to consider when conducting clinical trials for SCI,[52] as is inpatient length of stay since it relates to the efficiency of healthcare delivery for the SCI population.[53 54]

Because it is suggested that proprioceptive feedback and weight-bearing in a rhythmic fashion is essential for harnessing adaptive neuroplasticity,[3–9] our protocol includes the assessment of plantar pressures to estimate the loads transferred to the lower extremities. These measurements will bring insights on the effectiveness of in-bed leg cycling to provide appropriate sensory input even in severe SCI patients who cannot engage into active pedalling. We will also monitor EMG responses in the lower extremities since it has been shown that leg cycling, even if performed passively, has a potential to attenuate muscle atrophy.[26 55] Furthermore, monitoring EMG responses will be invaluable to better understand the development of spasticity.[56–58]

As shown in our previous animal study,[59] the main concern of introducing ABT early during the acute period is the potential risk of exacerbating spinal cord damage. However, there is a general consensus from animal studies that it can be initiated safely during the acute phase after SCI if the activity is performed in a proper environment where intense stress or supra-physiological demands from strenuous exercise are avoided.[11] Our risk management plan is based on two main strategies. First, psychological and physiological stresses are not likely to be increased with in-bed leg cycling when compared with two current interventions safely initiated the day after surgery: assisted transfer from bed to sitting (or standing) and passive range of motion of all joints by a physical therapist. Second, our clinical investigators (J-MM-T, AR-D, FB) specialised in acute and critical care of SCI have adapted the risk management plan and will train the personnel specifically for this trial.

The main limitation of this study is that it is conducted in a single centre and therefore the findings will need to be interpreted rigorously. The 14-day duration of the protocol was selected to maximise adherence to the planned intervention at our acute centre, in order to assess whether adding early ABT before the subsequent rehabilitative phase was feasible and potentially beneficial. This duration is adapted to the clinical reality of our patients since the mean and median acute length of stay at our centre for AIS grade A, B or C SCI are respectively 37.0 and 28 days. Implementing a 2-week protocol of in-bed cycling during acute care would therefore be easier in a healthcare system similar to our Canadian healthcare system in which the typical acute length of stay for severe SCI is approximately 3–4 weeks.[60] The protocol may not be readily applicable to other countries or healthcare systems, without interfering with interventions given at specialised rehabilitation centres or with the care pathway. For acute settings with a shorter length of stay, applying a 14-day protocol of in-bed cycling may require that final sessions be performed at home or in a rehabilitation unit.

This proof-of-concept trial will provide insights on the barriers and facilitators for using early in-bed leg cycling on a larger scale. The results will be used to design an updated protocol and estimate the sample size required for a multicentre randomised controlled trial to confirm the benefits of early in-bed leg cycling. Future work stemming from this trial has the potential to define a paradigm shift in acute SCI care, considering that patients with severe SCI are otherwise immobilised during the acute period between surgery and transfer to an intensive functional rehabilitation unit. Beyond the potential benefits on patient outcomes included in this protocol, early mobilisation through in-bed cycling also has the potential to decrease the rate of secondary complications associated with immobilisation such as pneumonias, thromboembolism, contractures and so on. In addition, early mobilisation could also minimise deconditioning and enhance patient engagement in care, thereby accelerating and improving the patient's ability to undergo intensive functional rehabilitation after the acute period.

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