The Ability to Walk After a Spinal Cord Injury with Emphasis on Exoskeletons: A Review

Lysanne van Silfhout[1*], Michael J.R. Edwards[2], Allard J.F. Hosman[3], Henk Van de Meent[4] and Ronald H.M.A. Bartels[5]

[1]Department of Surgery, Radboud University Medical Centre, The Netherlands

[2]Department of Trauma Surgery, Radboud University Medical Centre, The Netherlands

[3]Department of Orthopaedic Surgery, Radboud University Medical Centre, The Netherlands

[4]Department of Rehabilitation Medicine, Radboud University Medical Centre, The Netherlands

[5]Department of Neurosurgery, Radboud University Medical Centre, The Netherlands

*Corresponding author: Van Silfhout L, Department of Surgery, Radboud University Medical Centre, The Netherlands, Tel: +31243611111; E-mail: Lysanne.vanSilfhout@Radboudumc.nl

Abstract

Background: In recent years, an increasing number of patients with a spinal cord injury (SCI) have been reintegrating into community life and have been getting back to a more active and independent lifestyle. Consequently, rehabilitation therapies have altered, to address activity limitations that patients may experience, to increase participation in the community and to improve patients' overall quality of life. An innovative, supportive approach to locomotor training is through use of an exoskeleton, which could be used in those patients who are unable to ambulate by themselves.

Study design: Review.

Objective: To provide an overview of the current literature regarding ambulation in spinal cord injured patients with emphasis on outcome and the usage of exoskeletons, a new innovative way of rehabilitation therapy after a SCI.

Methods: This is a narrative review of the SCI literature on ambulation outcomes in patients with SCI. A systematic search was performed of all publications mentioning SCI, exoskeletons and ambulation. Relevant studies were included after screening of both title and abstract of the search results. Animal studies and non-English articles were excluded.

Results: Current literature shows that the final degree of motor-function recovery depends on neuronal plasticity, and that the largest amount of recovery can be achieved during the first-year post-injury. Training muscle strength and walking speed are important goals in rehabilitation therapy after a SCI. Furthermore, exoskeletons have been shown to be well tolerated by spinal cord injured patients and could be used by patients without any remaining ambulatory function.

Conclusion: This review showed that it is important to start early with the rehabilitation process after a SCI, to be able to fully benefit from neuroplasticity during the first-year post-injury. In patients without any remaining ambulatory function, such as patients with a complete SCI, exoskeletons have shown to reduce spasticity and improve ambulatory capacity.

Keywords: Spinal cord injury; Ambulation; Exoskeleton

Abbreviations:

10 MWT: 10 Meters Walking Test; SCI: Spinal Cord Injury; 6MWT: 6-minute walking test; SCIM: Spinal Cord Independence Measure; WISCI: Walking Index for Spinal Cord Injury

Introduction

Continuous advances in trauma care and in the recovery process after a spinal cord injury (SCI) have resulted in an increase in survival rates and life expectancy. The distribution of incomplete and complete lesions is currently about 50/50, tending more toward incomplete lesions and therefore with more potential for recovery [1]. In recent years, an increasing number of SCI patients have been reintegrating into community life and have been getting back to a more active and independent lifestyle. This may be a result of the increased number of people living with incomplete SCIs [1]. Consequently, rehabilitation therapies have altered, to address activity limitations that patients may experience, to increase participation in the community and to improve patients' overall quality of life [2]. One of the primary goals of the recovery after a SCI is often to reduce the acquired physical impairments, along with improving functional mobility [3,4]. Increased mobility can improve cardiovascular health and muscle function, prevent loss of bone quality and promote psychological well-

being [5]. According to a European multicentre study, four out of ten SCI patients will be able to walk independently again [6]. During the past decade, several pharmacological therapies have been developed to enhance the walking capacity of SCI patients [7]. These treatments result mainly in reducing spasticity. Further, task-specific locomotor training, combined with manual or robotic-assisted bodyweight-supported treadmill training, have improved the possibility that patients with incomplete SCI will regain ambulatory function [8].

One of the principal interventions to regain mobility after a SCI is muscle strengthening [9]. Following SCI, the central nervous system is able to recover locomotor function with the help of functional locomotor training [10,11]. Literature shows that the greatest recovery occurs during the first year after a SCI; even with continuous rehabilitation therapy, there are often no further improvements seen [12]. To regain locomotor function, patients with incomplete SCI depend strongly on visual input to compensate for proprioceptive deficits and impaired balance. In addition, they require additional attentional capacity to stand, walk and handle their walking aids [8]. However, when suffering from spasticity, a patient's potential for functional improvements from locomotor training may be limited [13]. Spasticity is a common secondary complication of SCI that is associated with deleterious effects on ambulation and mobility [14]. Combined with the inability or difficulty to recruit muscles below the lesion, spasticity leads to limitations in sensory-motor activities such as walking and posture [10].

An innovative, supportive approach to locomotor training is through use of an exoskeleton. An exoskeleton is a wearable brace-support suit featuring motors at the lower limb joints, rechargeable batteries and a computer-based control system [15]. This robotic suit could be used in those patients who are unable to ambulate by themselves, e.g. after a complete lesion, and assist in SCI patients with mobility and to facilitate locomotion therapy. The purpose of exoskeletons is to facilitate standing and walking, as well as assist in rehabilitation [12]. However, different applications of exoskeletons exist; to provide mobility in complete SCI and as rehabilitation system for incomplete SCI.

Over the years, many different exoskeletons have been developed. One can distinguish assistive exoskeletons and rehabilitative exoskeletons. Assistive exoskeletons (e.g. Rex-Bionics, Wearable Power-Assist Locomotor exoskeleton (WPAL), Re-Walk) allow patients to walk. Rehabilitative exoskeletons (e.g. Lokomat, Hybrid Assistive Limb (HAL), Kinesis and Ekso-Bionics) focus on improving gait in the long run. Besides this difference in application and clinical objective, there are differences in the control mechanism of the exoskeletons. Some are controlled by a joystick (Rex-Bionics, Lokomat, WPAL, and Kinesis), others have a posture controlled system (Re-Walk, Ekso-Bionics, Indego). The HAL exoskeleton has electromyographic (EMG) control [12]. Despite the many different exoskeletons, the ultimate goal is to help patients to walk as naturally as possible.

The aim of this review is to provide an overview of the current literature regarding ambulation in SCI patients. Requirements for ambulation will be discussed, and walking impairments in SCI patients as well as functional walking measures used in clinical practice will be covered. Finally, interventions such as medication and an exoskeleton, including their effect on walking capacity, will be discussed.

Methods

A systematic search was performed of all publications mentioning SCI and ambulation. The following search terms were used: 'spinal cord injury', and 'ambulation'/'walking'/'gait'. This resulted in the following search string: ('spinal cord injury' [All Fields] and 'spinal cord injury' [Title/Abstract]) and ('walking' [MeSH Terms] or 'walking' [All Fields] OR 'ambulation' [All Fields]) and ('walking' [MeSH Terms] OR 'walking' [All Fields])) and ('gait' [MeSH Terms] OR 'gait' [All Fields])). The literature search was conducted in PubMed without any time limits or other filters. All study designs, including case reports, were included, without restrictions on the ages of participants. All article abstracts were screened on relevance for this review. Non-English-language articles and animal studies were excluded. The reference lists of key articles, were searched to identify other potentially relevant articles for this study, as well as the Cochrane database and Google Scholar.

Due to the large variety in study populations, a systematic review was not possible; therefore, a narrative design for the review was chosen.

Results

Requirements for functional walking

Normal gait requires muscle strength, sufficient range of motion, coordination, proprioception and sensation of the lower limbs, as well as vision and planning of movements [16]. Significant muscle groups for ambulation include: flexors, extensors, and abductors of the hip; flexors and extensors of the knee; and dorsi-flexors and plantar-flexors of the ankle [17]. In patients with SCI, these capabilities might be limited due to the injury, resulting in limited ambulatory capacity, as well as reduced gait speed and endurance.

Besides the ability to walk, the walking speed is an important factor in community ambulation. Community ambulation is defined as being able to walk outdoors, potentially with the use of walking aids. Literature suggests that a walking speed of 1.20 to 1.31 m/s is required for independent community ambulation [18]. However, several studies show an average walking speed of patients with SCI around 0.36 m/s [19-21]. Together with factors such as the ability to transfer and manage curbs, stairs and crowded areas, this could lead to a reduced independence in walking in the community. In these situations, walking may not be the most practical method of mobility [22,23], and more efficient forms of mobility (e.g., wheelchairs, motorized scooters) are often used as compensation. Although these compensatory strategies enable patients with SCI to become more functionally mobile, paradoxically they contribute to a reduction in walking behavior [24]. According to Stevens et al. [19], therapeutic interventions designed to increase community ambulation in patients with SCI should focus on strengthening the legs through resistance training, engaging in locomotor training or regularly participating in other forms of weight-supported physical activity involving the legs.

Functional walking measures

There are several measures to assess functional walking after a SCI. Examples of gait outcomes are the walking speed for 10 metres (10 MWT), the preferred and maximum walking speed, 6-minute walking test (6 MWT), the Spinal Cord Independence Measure (SCIM) and the Walking Index for Spinal Cord Injury (WISCI).

The 6 MWT measures the distance (in meters) walked during 6 minutes, whereas the 10 MWT measures the time (in seconds) needed to walk 10 meters. The 10 MWT has been shown to be a valid clinical measure of walking capability and to reliably reflect walking performance in real-life settings [19]. Walking speed on the 10 MWT in SCI patients correlates well with ambulation categories based on ambulatory milestones, as defined by van Hedel et al. [25], (Table 1). The walking speed distinguishes between ambulation categories with high sensitivity and specificity. This means that in patients with SCI, the preferred walking speed as assessed in the clinic can be used to estimate functional ambulation during daily life. Another study showed that SCI patients who have a walking speed of 0.59 m/s on the 10 MWT tend to walk in the community instead of using their wheelchair [26,27]. However, the actual walking speed depends on many factors such as the motivation of the subject as well as environmental and psychological factors.

Category	Description	Average walking speed
1	Wheelchair-dependent patients who are able to perform some steps	0.01 m/s
2	Supervised walkers indoors for a short distance, wheelchair dependent for longer distances and outdoors	0.34 m/s
3	Independent indoors walkers, wheelchair for longer distances	0.57 m/s
4	Assisted walkers who require a walking aid	0.88 m/s
5	Walkers without walking aid	1.46 m/s

Table 1: Walking categories.

Another study showed that a combination of walking velocity and knee-extension strength is a good discriminant between household and community walkers, with a threshold of 0.42 m/s for the velocity variable [26,27].

In patients with SCI, the preferred walking speed as assessed with the 10 MWT in the clinic can be used to estimate functional ambulation during daily life. Moreover, Van Middendorp et al. [6] have developed the Dutch ambulation prediction rule, which provides a reliable prognosis of a patient's ability to walk independently at home after a traumatic SCI. This prediction is based on a combination of factors including age, motor scores of the quadriceps femoris and the gastrocsoleus muscles, and light touch sensation for two dermatomes (L3 and S1). This prediction rule has been validated externally [27] when being used in daily clinical practice and has shown to be accurate in giving an early prognosis in the first two weeks after a SCI.

Walking can be cognitively more challenging for SCI patients compared with healthy subjects [28]. This might minimally affect the performance of a 10 MWT, where the patient can fully concentrate on walking itself without consideration of variables such as irregular surfaces, obstacles, a dark environment or other disturbing factors.

Van Hedel et al. [29] showed that SCI patients walk slower than the able-bodied and that they favour walking closer to their maximum walking speed as compared with the able-bodied. The slower walking speed of SCI patients has been shown to be associated with an increased duration of the double-support phase [30]. Balance requirements are lower during the double-support compared with the single-support phase of walking [28]. Even in SCI patients with good walking ability, the duration of double support is slightly increased. By walking as fast as possible, SCI patients can automatically further improve balance during walking [31].

Both the SCIM and WISCI are assessments of functional capacity. The SCIM scores independence and activities during daily life, e.g. self-care (feeding, grooming, bathing, and dressing), respiration and sphincter management, and mobility (bed, transfers, indoors and outdoors). The WISCI assesses the amount of physical assistance needed and devices required for walking a distance of 10 meters.

Morganti et al. [12] showed a significant positive correlation between the WISCI and SCIM (r=0.97, p<0.001).

Walking impairments in SCI patients

As described before, SCI affects the leg muscles to a certain degree, which correlates with functional walking measures such as 10 MWT and ambulatory capacity. Ambulatory capacity is the degree of walking independence at home and in the community. Kim et al. [32] showed that, for walking speed at the 10 MWT, the strongest correlations were produced by the hip flexors and hip abductors on both sides. The less-affected hip flexor strength explained more than 50% of the variance in these two functional measures. The hip flexors play an important role during the initial swing phase of gait to pull the swinging limb forward, and the hip abductors are important for stability during stance [33]. It is possible that patients with strong hip flexors and abductors are able to better control balance during stance and pull their swinging limb forward to increase stride length and consequently increase gait speed. The less-affected hip extensor strength explained up to 64% of the variance in ambulatory capacity, which suggests that the stabilizing role of these muscles is essential for a higher level of community mobility. Tasks such as transfers, standing and stairs, which are important activities for functioning in the community, have different strength demands from gait. Finally, Kim et al. [32] showed that, for all three of the functional walking measures, the strength of the less-affected limb was more important than that of the more-affected limb. These results suggest that patients with at least one strong limb may be able to compensate for the weakness on the more-affected side and thus demonstrate higher functional performance.

Perry [34] described three categories of ambulation difficulties in SCI. The first category involves inadequate hip extension during the stance phase, which is usually due to weakness of the gluteal muscles and results in poor stability during stance with limitations of the step length of the opposite extremity. It also contributes to pelvic drop. The second category, excess of plantar flexion during the swing phase and impaired initial foot contact, results in problems with foot clearance during swing and poor foot placement at heel strike. The last category is limited hip and knee flexion during the swing phase, which is due to weakness of the iliacus, rectus femoris and sartorius muscles. Besides

that, knee flexion is limited during the swing phase due to antagonistic action of the rectus femoris and vastus lateralis. This gait impairment results in a stiff leg, often associated with increased spasticity, and problems with foot clearance. This pattern of walking in SCI patients is due to not only weakness of the muscles but also spasticity and it differs in patients with thoracic lesions compared with lumbar lesions [22].

Pharmacology

In general, locomotor training results in better ambulation capacity than any pharmacological therapy. However, there is some literature which suggests that drugs could facilitate the recovery of walking function after a SCI [35].

Tizanidine, an anti-spasticity drug, has been shown to reduce hypertonia in SCI patients, and may thus facilitate locomotor training in chronic SCI patients [13,36,37]. Cyproheptadine, an anti-serotonergic and antihistamine drug, has shown to increase the maximal walking speed, improve muscle coordination and reduce clonus [38]. However, side effects are drowsiness and fatigue, which could have negative effects on walking outcome and outweigh the benefits of taking the drug [35].

The combination of cyproheptadine and clonidine has shown to reduce clonus and spasticity, and improve muscle activity and joint kinematic patterns, what resulted in an improvement of functional ambulation [35,39]. GM-1 ganglioside has been shown to improve walking speed and walking distance [35,40]. Baclofen is commonly used to treat spasticity after a SCI with the intent to enhance motor function [35]. A systematic review showed that intrathecal administered baclofen can potentially reduce spasticity, while orally administered had no effects [41].

Literature shows that there are no benefits from the drugs Levodopa [35,42] and 4-Aminopyridine [43,44].

Exoskeletons

As mentioned in the introduction, there are many different kinds of exoskeletons, each with their own purposes and benefits. Depending on the way the exoskeleton is controlled, different applications are possible. Exoskeletons controlled with a joystick or by posture enable the patient to compensate for the functional loss of their lower limbs, thus regaining mobility while wearing the suit. EMG controlled exoskeletons however, require an active contribution of the lower limbs of the patient. This way, the patient's voluntary drive is integrated in the walking pattern. This mechanism could lead to neuronal plasticity and possibly result in increased mobility even when not wearing the exoskeleton [12].

Both patients with complete and those with incomplete SCI can benefit from using an exoskeleton. Whereas patients with complete SCI will benefit primarily from the ability to stand up and walk, those with incomplete SCI will benefit mostly from the ability to walk longer distances, and potentially an increased walking ability [15]. In the study of Benson et al., [15] both patients with complete and those with incomplete SCI showed an improvement in ambulatory capacity when using an exoskeleton. This is consistent with previous studies [45-47], which showed improvements in mobility outcomes in patients with complete SCI using an exoskeleton.

Zeilig et al. [45] showed that an exoskeleton is safe in usage and stability during standing. Ambulation can be achieved by using walking aids such as crutches, a walker and/or railing for stairs climbing. Benson et al. [15] observed that walking speeds are higher and walking distances are longer in exoskeleton users when compared with non-users. Walking speed with an exoskeleton ranged from 0.33 to 1.45 m/s in the 10 MWT. In the 10 MWT, patients with lower levels of injury walk significantly faster than those with higher levels of injury [45]. Duffell et al. [48] compared exoskeleton training to no intervention, and found that patients with a high baseline walking capacity (high 10 MWT walking speed, high 6 MWT distance and fast Timed-Up-and-Go (TUG) test times;) had more improvement in 10 MWT walking speed with the exoskeleton compared with no intervention at 4 weeks of follow-up; patients with low baseline walking capacity (low 10 MWT walking speed, low 6 MWT distance and slow TUG test times) showed no difference for either treatment.

However, a recent systematic review [12] showed that in general, there were no differences in change from baseline among patients undergoing exoskeleton training compared with non-exoskeleton training (e.g. treadmill-based training, over-ground ambulation training, body weight-supported treadmill training (BWSTT), no training, or treatment with tizanidine (dose ¼ 0.03 mg/kg)). There were no differences found in the 10 MWT and 6 MWT comparing exoskeleton and non-exoskeleton training in SCI patients. There were mixed results for the WISCI/WISCI II; most of the included studies found no difference between rehabilitation strategies, only a few studies reporting significantly improved scores in the exoskeleton group.

Patients with spasticity have shown to experience a reduction in spasticity after training sessions with an exoskeleton [46,49]. An explanation for this could be that the activation of neuronal circuits involved in walking is able to reduce the non-physiological hyper-activation present in spasticity after a SCI [49].

Multiple studies have shown that use of an exoskeleton is generally well tolerated, with no increase in pain and a moderate level of fatigue after use [45,49].

Discussion

This review covers many different aspects regarding the recovery of ambulation capacity after a SCI. In the acute phase after a SCI, a reliable prognosis of the ability to walk can be given to a patient based on the Dutch clinical ambulation prediction rule developed by Van Middendorp et al. [6] The final degree of motor function recovery depends on neuronal plasticity, as shown in current literature [50], which has been shown to be the largest during the first year after a SCI. This shows that it is important to start as early as possibly with the rehabilitation process after a SCI, to be able to fully benefit from the time the most recovery can be achieved.

There are several different strategies that can be followed during the rehabilitation process, which all have the same goal: to regain the best possible walking capacity. However, this can be complicated by the occurrence of spasticity. The effects of pharmacological therapies on spasticity and walking function are highest when combined with locomotor training; however, the literature is inconsistent regarding the reported effects of these drugs. In this training, walking aids and body-weight support can be used to help SCI patients walk and thus activate the neuronal systems involved in ambulation [51]. During these trainings, progress can be measured using functional walking measures.

The exoskeleton is an innovative form of rehabilitation therapy, which can also be used for patients with a complete SCI and patients who do not yet have any ambulatory capacity. However, a recent systematic review showed that the 10 MWT walking speed and SCIM scores were not significantly different after exoskeleton training compared with various other rehabilitation therapies. The 6 MWT and WISCI showed mixed results, with some studies indicating no significant difference in change from baseline between exoskeleton training and other therapies, some indicating benefit of exoskeletons and some indicating benefit of comparator therapies over exoskeleton. There is no consistent benefit from rehabilitation using an exoskeleton versus a variety of conventional methods in patients with chronic SCI [12].

Exoskeletons have shown to potentially improve ambulatory capacity after a SCI, is safe in usage and is well tolerated by patients [45,49]. A significant disadvantage of the current exoskeletons is the relatively low mean walking speed of 0.26 m/s [52]. As described in this review, it has been suggested that a walking speed of 1.20 to 1.31 m/s is required for independent community ambulation [18]. However, for community ambulation, it is necessary to be able to achieve a walking speed of at least 0.49 m/s, which is necessary, for example, to cross an intersection as set by traffic signals [53]. Another study showed that a walking speed of 0.59 m/s is feasible for patients to prefer walking over using their wheelchair whilst ambulating in the community [27]. This might make exoskeletons for now an unsuitable method of ambulation in the community for most SCI patients without sufficient ambulatory function on their own.

Besides exoskeletons having a potential positive on walking ability, it could also be beneficial for mental health, pain, spasticity as well as bladder and bowel function.

Limitations

This review has limitations due to the nature of the articles that were examined. Some of the studies are based on small numbers of patients, and the definitions of walking function and follow-up time points vary across the studies. Moreover, different SCI populations were used in the studies; varying in severity of injury as well as time since SCI. There are many types of non-exoskeleton therapies that can be used in rehabilitation of SCI, e.g. treadmill-based training, over-ground ambulation training, BWSTT, besides the different types of exoskeletons, which results in a large heterogeneity in the literature. In order to still provide an overview regarding ambulation after a SCI with emphasis on exoskeletons, a narrative review was chosen as a study design.

Furthermore, these studies do not represent the standards of care of the whole world. Since the management of SCI may be different internationally, the recovery of walking function might vary. Finally, the examined articles are not distributed regularly in time.

Clinical relevance

Based on this review, it is important that rehabilitation therapy during the first-year post-injury focuses on regaining muscle strength and walking speed. Most neurologic recovery occurs within the first few months after injury; early initiation of the rehabilitation process is therefore considered fundamental to maximize the recovery. However, the best timing for treatment interventions is not known [1]. For patients who are not (yet) able to walk, an exoskeleton could be used to ambulate in the rehabilitation process.

Conclusion

This review showed that muscle strength and walking speed are important goals in rehabilitation therapy after a SCI. To be able to fully benefit from the neuroplasticity during the first-year post SCI, it is important to start as soon as possible with rehabilitation. This way patient has the best chances to regain as much walking ability as possible. In patients without any ambulatory function, e.g. patients with a complete SCI, or patients who do not (yet) have sufficient muscle power to ambulate following conventional rehabilitation therapies such as treadmill-based training, over-ground ambulation training and BWSTT, exoskeletons have shown to potentially increase walking ability. Literature has shown that exoskeletons are safe when used, and they could reduce spasticity.

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