Acta Neurologica Belgica
https://doi.org/10.1007/s13760-022-02011-1

REVIEW ARTICLE

Wearable powered exoskeletons for gait training in tetraplegia: a systematic review on feasibility, safety and potential health benefits

Gonzalo Rodriguez Tapia[1] · Ioannis Doumas[1,2] · Thierry Lejeune[1,2] · Jean-Gabriel Previnaire[3]

Received: 21 March 2022 / Accepted: 16 June 2022
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Abstract

Background Recent developments in wearable powered exoskeletons (WPE) allow gait training (GT) for patients after spinal cord injury (SCI). Two recent meta-analyses on GT using WPE showed promising results for paraplegic patients (PP). To this date, there is no review focusing on tetraplegic patients (TP).

Objectives The main objective of this review was to assess feasibility and safety of GT using WPE in patients after tetraplegia.

Method This systematic review was performed according to PRISMA-S guidelines. Two independent reviewers searched several databases for studies on GT using WPE for TP. Primary outcomes concerned the number, type and severity of reported adverse events (AE). Secondary outcomes examined potential additional health benefits (AHB).

Results Forty-one studies (6 randomized trials, 24 cohorts and 11 cases series) were selected, including 166 TP, 26 with complete lesions (AIS A) and 71 with level of injury above C6. Minor AE were reported in 17 TP, concerning cutaneous, cardiovascular or musculoskeletal systems. Occurrence of AE is significantly higher in a PP population compared to TP (p value = 0.001). Only one major AE concerned a TP. Studies of low level of evidence suggest that GT using WPE could lead to improvements in walking parameters, cardiovascular efficiency and to a reduction of spasticity.

Discussion and conclusion GT using WPE is a feasible and safe intervention for TP. To minimize occurrence of AE, a good patient selection and preparation is proposed. Future clinical trials should be performed to confirm current trends in terms of efficacy and potential AHB.

Keywords Spinal cord injury · Tetraplegia · Gait rehabilitation · Wearable powered exoskeleton

Abbreviations

WPE	Wearable powered exoskeletons
GT	Gait Training
SCI	Spinal cord injury
PP	Paraplegic patients
TP	Tetraplegic patients
AE	Adverse effects
AHB	Additional health benefits
NLI	Neurological level of injury
AD	Assistive device
TAGT	Therapist-assisted gait training
RAGT	Robotic-assisted gait training
BWSS	Body weight support systems

Background

Annual worldwide incidence of spinal cord injury (SCI) is estimated between 40 and 80 people per million [1]. Among them, approximately 50% of survivors present with tetraplegia and 15% have a C4 or above neurological level of injury (NLI) [1, 2]. One year post-SCI, up to 40% of patients with SCI achieve independent, indoor, walking ability among which only 18% without an assistive device (AD) [2]. Traditionally, severity of neurological impairments and ambulation ability determine gait training modalities after SCI [3]. During therapist-assisted gait training (TAGT), most patients require two or more therapists to support and guide lower

✉ Thierry Lejeune
thierry.lejeune@uclouvain.be

[1] Secteur des Sciences de la Santé, Neuro Musculo Skeletal Lab (NMSK), Institut de Recherche Expérimentale Et Clinique, Université Catholique de Louvain, Avenue Mounier 53, 1200 Brussels, Belgium

[2] Service de Médecine Physique Et Réadaptation, Cliniques Universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Brussels, Belgium

[3] Centre Jacques Calvé, Fondation Hopale 72, Esplanade Parmentier, 62600 Berck-sur-Mer, France

Published online: 17 July 2022

limbs during overground or treadmill training [4]. Rehabilitation programs exclusively using TAGT have demonstrated limited efficacy with only 1% of patients reaching full recovery [2].

In recent years, new technology-based rehabilitation therapies have emerged such as robot-assisted gait training (RAGT) with body weight support systems (BWSS) and wearable powered exoskeletons (WPE). In this review, we defined WPE as computer-guided systems using motorized orthoses to facilitate autonomous over ground movement in people with disabilities. Activation of these systems can be triggered by patients' voluntary movements or by a computer algorithm depending on the patients' capabilities and the exoskeleton characteristics [5–7]. WPE differ from other RAGT systems in terms of the following aspects and consequently offer new possibilities in gait rehabilitation. First, WPE allow self-balancing, overground, gait training, with or without upper limb assistance. Second, assistance during gait can be triggered voluntarily by the participant through muscle contraction and body movements [8, 9]. Third, gait training, through task specific rehabilitation, can be performed in more ecological environments, promoting a more human-like gait pattern (including activation of trunk muscles during over ground or treadmill training) [7, 10]. Finally, WPE enable walking with a lower energetic cost compared to other systems [7, 10].

Nowadays, Food and Drugs Administration has authorized the use of WPE in walking programs for paraplegic patients (PP). Regarding tetraplegic patients (TP), FDA has approved three devices: Ekso® (allowed only for C7–T3 Asia Impairment Score (AIS) D patients), Indego® (C7 or below) and Hal® (C4–L5 AIS C or D). These three exoskeletons can be used after SCI if upper limb strength is enough to allow use of assistive devices (AD), such as crutches or walkers [11]. Other self-balancing WPE, like Atalante® or Rex®, allow ambulation without upper limb help or use of AD [12].

Previous studies mainly focused on the use of WPE for gait rehabilitation in paraplegia. Compared to tetraplegia, PP present greater autonomy during transfers, fit quicker into robotic devices and control independently AD during autonomous walking. To this day, safety and feasibility of WPE during gait rehabilitation are only validated after paraplegia [6]. Two recent meta-analyses on walking assisted by powered exoskeletons after paraplegia demonstrated safety and indicated an improvement in walking capacities [6, 13]. In addition, some studies suggested that gait training using WPE constitutes a way to perform physical activity after SCI [6, 14, 15]. Gait training after tetraplegia is more challenging due to greater motor impairments concerning both the trunk and upper limbs, increased energy expenditure and cardiovascular autonomic dysfunction [5, 12, 16]. At the best of our knowledge, no systematic review has been conducted to assess feasibility, safety and potential health benefits of gait rehabilitation using WPE in TP.

The primary objective of this systematic review is to study whether gait training using WPE is feasible and safe after tetraplegia due to SCI. We have addressed the following question in PICO form: "Is gait training using WPE feasible and safe for adult patients with tetraplegia after traumatic or vascular SCI"? A secondary objective is to assess if walking ability improved after gait training using WPE and whether this treatment leads to additional health benefits (AHB) regarding gastro-intestinal, urological, or musculoskeletal systems.

Method

Design

This review was performed according to PRISMA-S guidelines [17] and was registered in PROSPERO (CRD42020216070).

Identification and study selection

Two independent reviewers systematically searched three electronic databases (Scopus, PubMed and Embase). The final search (Table 1) was conducted on the 1st February 2022. All references were stored in EndNote© and FileMaker© pro version 16. After removal of duplicates, a first selection was performed through titles and abstracts screening. Studies eligibility was assessed according to the following criteria: study design of randomized and non-randomized controlled trials, prospective or retrospective cohorts, case series and case studies; participants were adults with tetraplegia, at all stages, after traumatic or vascular SCI; the intervention consisted of gait training using WPE; reported outcomes concerned occurrence of adverse events and/or relevant outcomes concerning gait at function or

Table 1 Search strategy for PubMed database

Database	Search strategy
PubMed	(Rex OR ReWalk OR HAL OR Ekso* OR Indego OR WPAL OR mindWalker OR Elegs OR Exo-H2 OR Exoskelet* OR Robotic gait OR Robotic rehabilitation OR Lower extremit* robotic* OR wearable robot*) AND (Spinal cord injur* OR spinal injur* OR spine injur* OR spine injur* OR Paraplegi* OR Tetraplegi* OR Quadriplegi* OR SCI)

activity level and potential health benefits regarding gastrointestinal, urological, or musculoskeletal systems, according to the International Classification of Functioning, Disability and Health (ICF) of the World Health Organisation (WHO) model; articles written in French or English were included. All other gait rehabilitation programs or devices, including RAGT such as the Lokomat©, were excluded. Also, studies combining gait training with any other orthosis, electrical stimulation or invasive treatment were excluded.

Then, a selection based on full text was conducted by the same two reviewers. Disagreements were resolved through discussion.

Quality and risk-of-bias assessments

The Downs and Black checklist (D&B) was used to assess risk of bias in included cohort or randomized controlled studies.

Data extraction

Data extraction was performed using the following sequence. First, we verified the type of study and whether it included a mixed population (PP and TP) or a specific population (only TP). Then, we identified in each study the number of TP. TP were classified according to the severity of the lesion (motor complete: AIS A or B, motor incomplete: AIS C or D) and the NLI (*high* = at or above C6; *low* = below C6). Finally, we specified the following characteristics for rehabilitation program used by each study: type of WPE used, intensity and duration of training, overground vs treadmill training, task specificity, BWSS or other walking AD used.

Outcome measurements

As primary outcome, we collected all reported adverse effects (AE) and, in case of studies including both PP and TP, we specified whether they affected a PP or a TP. If the AE could not be precisely attributed to a specific patient, authors were contacted by mail to request access to additional information. AE were classified according to the following categories: musculoskeletal, cutaneous, cardiovascular, pain, falls, and fractures. AE were characterized as minor or serious. We defined serious AE as events requiring a definitive interruption of the gait training program using WPE. Finally, WPE software defects or manipulation errors were treated separately.

As secondary outcomes, we collected all the information concerning the potential additional health benefits (AHB) of gait rehabilitation using WPE. We focused on various parameters in accordance with the ICF-WHO model: body function and structure (walking parameters, spasticity, pain, cardiovascular, bladder dysfunction, neurogenic bowel and osteopenia), activities (walking tests, balance) and participation (quality of life). Regarding secondary outcomes, we only extracted data reported as a difference, subtracting pre-test score from the post-test score.

Data and statistical analysis

All collected data were structured in tables for qualitative synthesis and analysis. When applicable, subgroups were expressed in terms of percentage of total. Also, when possible, percentages in PP and TP populations were compared using a Fisher's exact test. Statistical level of significance was set at 0.05 for all analyses.

Results

Study selection

Database search retrieved 6471 references. After removal of duplicates and initial title and abstract screening, 226 articles were selected for full-text analysis. Finally, 41 studies were included in this review. Details of the selection process are illustrated in the study PRISMA flowchart (Fig. 1).

Study characteristics

In this review, we retained 6 randomized trials, 23 cohorts and 12 cases series. Except for 6 case series and 2 randomized trials, all studies concerned mixed populations including both PP and TP.

Patient characteristics

A total of 570 patients with SCI were included in this review among which 166 (29%) TP. Among 166 TP, 26 (16%) presented with complete tetraplegia (AIS A), 71 (43%) were classified as high NLI and 17 (10%) were in the acute or subacute phase post-SCI (less than 6 months since SCI) [5, 10, 18–20]. Table 2 displays detailed information for each included study regarding severity of lesion, NLI and time post-SCI.

Gait training using WPE

Eight types of WPE used for gait training after SCI injury were identified (Table 2). Ekso® (all models combined) was the most frequently used WPE (over 56% of the studies) for gait training after SCI and the most studied in the TP population (78 among 166 TP in total). HAL® is the second most used WPE and was used in 24% of the studies including 72 TP. Other WPE including ReWalk®, H-Mex®, Rex®,

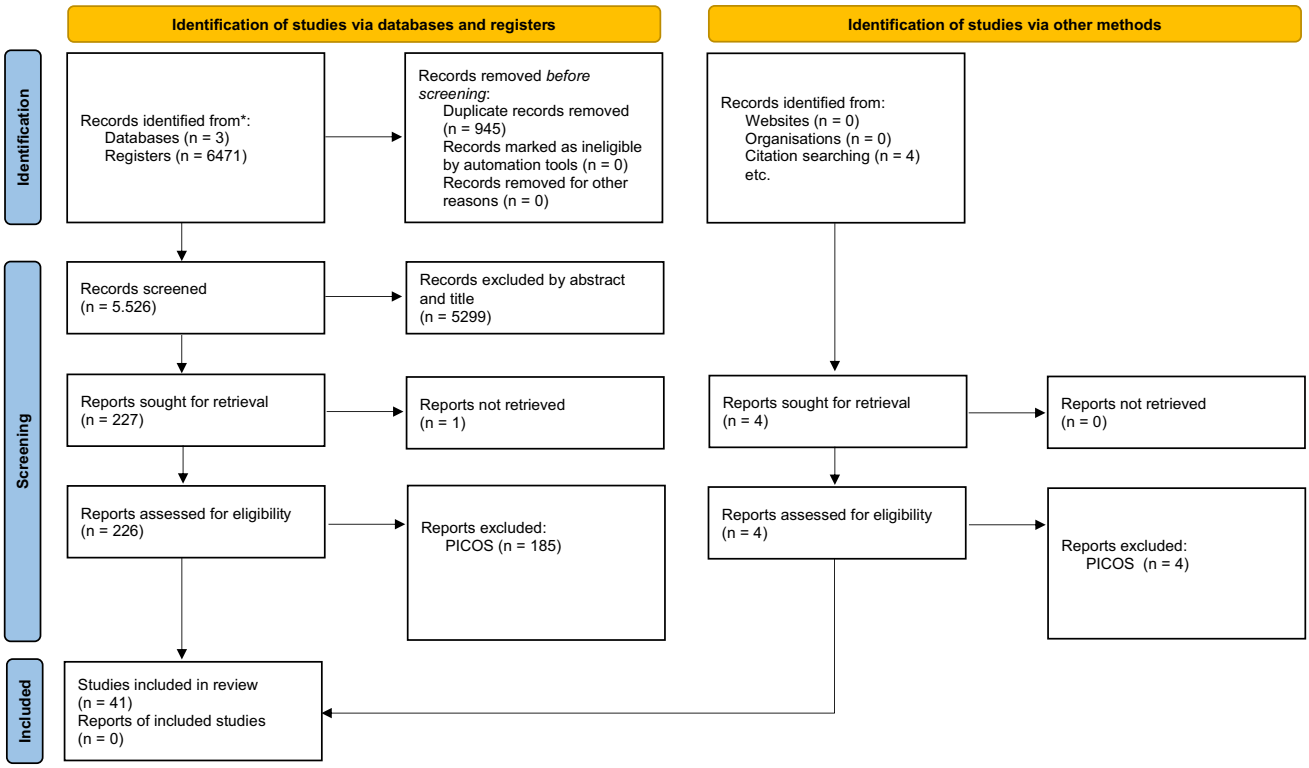


Fig. 1 Flow diagram (PRISMA) of the selection process

Indego®, Angelegs® and exo-H2® were used in one-to-two studies for a total of 16 TP.

Rehabilitation protocols present considerable heterogeneity among included studies (Table 3). Differences can be represented by the total number of sessions, ranging from 1 to 100. In most programs, session duration was set between 60 and 90 min at a frequency of 2–3 sessions per week.

Regarding design characteristics, among the eight types of WPE, the differences are small in terms of machine weight (except for Rex® which is heavier), contact points and set up procedures. Control mechanisms during gait training were not explicitly described among clinical studies using these types of WPE. Most common control mechanisms consist of two types: complete and partial assistance. Complete assistance mechanisms allow automatic gait activation, without any patient movement, according to a predefined set of parameters regarding position and velocity. Partial assistance mechanisms enable movement-triggered gait, through trunk inclination or muscle activation in the upper or lower. In both cases, gait training characteristics can be modified in real time during sessions.

In 73% of studies, the training protocol included overground gait training without BWSS. In all studies using HAL®, a BWSS or treadmill training were used in 100% and in 80% of studies, respectively (Table 3). Only one study combined a BWSS with Ekso® [4]. Close supervision by one therapist is the common rule. In three cases, up to three therapists were required for assistance during transfers to fit into the exoskeleton and supervision during gait training.

Primary outcomes

This review retrieved a total of 174 AE (Table 4). Occurrence of AE (both minor and major) is significantly higher ($p = 0.001$) in a PP population ($n = 157$, 90%) compared to TP ($n = 17$, 10%). Only one serious AE concerned a TP (stress fracture of tibia) [21, 22]. The 16 minor AE assigned to TP are characterized as follows: 8 cardiovascular [23–25], 5 pressure sores [5, 26–28], and 3 musculoskeletal [29].

In addition, 32 cases of mechanical and/or software issue or a manipulation error were reported, without any consequences for the participant.

Finally, 34 dropouts were reported in total concerning both PP and TP: 12 for an incomplete assessment [9, 30–32], 4 with no reason communicated [8, 10, 32], 2 linked to major anxiety diagnosed before the intervention [10], 7 due to patient withdrawal for personal reasons [8, 9, 28, 31, 33, 34], 5 caused by time restrains [23, 33–35], 1 surgery not related to the intervention [23], and 3 concomitant medical issues/unrelated injuries [23, 28].

Table 2 Characteristics of included studies and tetraplegic participants grouped by type of exoskeleton used in each series

Type of WPE	Author, year	Study design	Participants (total) (*n*)	Participants (tetraplegic) (*n*)	Mean age (tetraplegic) year ± SD	NLI		AIS score		Stage		D&B
						High	Low	A-B	C-D	Acute	Chronic	
Ekso©												
	Baunsgaard 2018 Bach Baunsgaard 2018	Cohort	52	14			3	3	11			Fair
	Chang 2018	RT	4	2	47 ± 24	1	1		2		2	Fair
	Chang 2020	Case-report	1	1	66		1	1			1	NA
	Chisholm 2017	Case-series	3	1	42		1	1			1	NA
	Delgado 2020	Cohort	12	6		6			6	6		Fair
	Edwards 2022	RT	12	6	46 ± 7.2	5	1		6		6	Good
	Escalona 2018	Cohort	13	1	42	1		1			1	Fair
	Escalona 2020	Case-series	3	1	51	1			1		1	NA
	Evans 2021 Schackleton 2021	RT	8	8	40 ± 11.2	7	1		8		8	Fair Fair
	Gagnon 2018	Cohort	14	1	42	1		1		1		Good
	Gorgey 2017	Case-series	4	2	37 ± 23.3	2		1	1		2	Good
	Hong 2020* Gorman 2021*	RT	50	14				4	10		14	Fair Fair
	Kozlowski 2015	Cohort	7	2		1	1	1	1		2	Poor
	Kressler 2018	Case-series	4	1	24	1			1		1	NA
	Lester 2018	Case-series	1	1	21	1		1			1	NA
	McIntosh 2020	Cohort	11	2	27 ± 15.6	2		1	1	2		Fair
	Ramanujam 2017*	Cohort	5	2	53 ± 1.4	2			2		2	Poor
	Ramanujam 2019*	Cohort	14	5	49 ± 9.7	3	2		5		5	Poor
	Stampacchia 2016	Cohort	21	4	53 ± 14.3		4	1	3		4	Poor
	Tsai 2020	Cohort	10	4					4	4		Fair
	Total		249	78		34	15	16	62	13	51	
Hal©												
	Brinkemper 2021	Cohort	15	4	43 ± 14.9	4			4	2	2	Fair
	Fisahn 2016	Case-series	1	1	29	1			1	1		NA
	Grasmücke 2017	Cohort	55	13		10	3		13		13	Fair
	Ikumi 2017	Case-series	1	1	19	1		1			1	NA
	Jansen 2018	Cohort	21	3	28 ± 11	2	1		3		3	Fair
	Okawara 2020	Cohort	20	10							10	Fair
	Okawara 2022	Cohort	9	6	44 ± 17.5	5	4	3	3		6	Fair
	Shimizu 2017	Case-series	4	1	20	1		1			1	NA
	Soma 2021	Case-series	1	1	47		1		1		1	NA
	Zieriacks 2021	Cohort	121	32							32	Fair

Table 2 (continued)

	Total		248	72		24	9	5	25	3	69	
Rewalk®												
	Benson 2016	Cohort	10	2	26 ± 4.2		2	1	1		2	Fair
	Khan 2019	Cohort	12	3		2	1		3		3	Good
	Total		22	5		2	3	1	4		5	
H-Mex©												
	Kim 2021	Cohort	11	1	58	1			1		1	Fair
	Park 2021											Fair
Rex©												
	Birch 2017	Cohort	20	5		5			5		5	Fair
Indego©												
	Hartigan 2015	Cohort	16	3		3		3			3	Poor
Angelegs®												
	Jang 2019	Case-series	1	1	57	1			1		1	NA
Exo-H2©												
	Pérez-Nombela 2017	Case-series	3	1		1			1	1		NA

WPE wearable powered exoskeleton, *Type of series* according to equator network website; *High* C2–C6;, *Low* C7–T1, *NLI* Neurological level of injury, *AIS* ASIA impairment scale; *Acute* < 6 months; *Chronic* ≥ 6 months; *D&B* Downs and Blacks checklist, *RT* randomized trial, *NA* not applicable

*Studies using Rewalk® and Ekso®

Table 3 Characteristics of gait training rehabilitation programs grouped by type of exoskeleton used in each study

Type of WPE	Author, year	Participants (tetraplegic) (*n*)	sessions (*n*)	Frequency (sessions per week)	Time per session (minutes)	BWSS	Assistive devices	Therapists (*n*)	Treadmill
Ekso©									
	Baunsgaard 2018	14	24	3	60		✓		
	Bach Baunsgaard 2018								
	Chang 2018	2	15	5	60		✓		
	Chang 2020	1	9	2–5	60	✓	✓	2	
	Chisholm 2017*	1	10	3–4	45				
	Delgado 2020*	6	1–4	3	90		✓	1	
	Edwards 2022	6	36	3	30		✓	1	
	Escalona 2018*	1	4	2–3			✓	1	
	Escalona 2020	1	4	5	45–60		✓	1	
	Evans 2021 Shackleton 2021	8	72	3	60				
	Gagnon 2018	1	18	3	60		✓	1	
	Gorgey 2017	2	10–15	1	60		✓	1	
	Hong 2020	14	36	3	60–90		✓	1	
	Gorman 2021								
	Kozlowski 2015	2	24	1	120		✓	1	
	Kressler 2018*	1	26	1–2	60–90		✓	1	
	Lester 2018	1	3	1	< 60		✓	2	
	McIntosh 2020	2	25	3	60			1	
	Ramanujam 2017	2	60–100					1	
	Ramanujam 2019	5	60–80	3–4	70–100		✓	3	
	Stampacchia 2016	4	1		60		✓	1	
	Tsai 2020	4	2–7	3	60–90		✓	1	
Hal©									
	Brinkemper 2021	4	60	5	30	✓		1	✓
	Fisahn 2016	1	60	5		✓		1	✓
	Grasmücke 2017	13	60	5	90	✓		1	✓
	Ikumi 2017	1	10	2	60	✓		3	✓
	Jansen 2018	3	60	5	90	✓		1	✓
	Okawara 2020	10	20	2–5	60	✓		1	✓
	Okawara 2022	6	20	2–5	60	✓		1	✓
	Shimizu 2017*	1	10	2	60–90	✓	✓	4	
	Soma 2021	1	13	4	40	✓	✓	1–2	
	Zieriacks 2021	32	60	5	90–120	✓		1	✓
ReWalk®									
	Benson 2016	2	20				✓	1	
	Khan 2019	3	45	3–4	60		✓	1	
H-Mex©									
	Kim 2021	1	30	3	60		✓	1–2	
	Park 2021								
Rex©									
	Birch 2017	5	1		180–240			1–2	
Indego©									
	Hartigan 2015	3	5		90		✓	1	
Angelegs©									
	Jang 2019	1	30	5	20		✓	1	
Exo-H2©									
	Pérez-Nombela 2017	1	1		< 60			1	

Data reported according to the FITT principle (Hafidz 2014): Frequency, Intensity, Time, Type; *WPE* = wearable powered exoskeleton; # total number; *BWSS:* Bodyweight support system; @ condition respected or device used; * reported data concern tetraplegic participants on a mixed population

Table 4 Minor and serious reported adverse events regarding tetraplegic patients and mixed populations

Author, year	Participants (*n*)	Minor adverse events								Serious adverse events	
		Cutaneous			Cardiovascular		Musculo-skeletal	Pain	Fall	Cutaneous	Musculoskel-etal or factures
		G1	G2	OH	BPC	HT					
Tetraplegic patients											
Bach Baunsgaard 2018*	14			1							
Benson 2016*	2										
Chang 2020	1										
Chang 2018	2						1				
Delgado 2020	6	1									
Evans 2021 Schakleton 2021	8										1
Fisahn 2016	1										
Gagnon 2018*	1			1							
Ikumi 2017	1				6						
Jang 2019	1										
Khan 2019	3	1					1				
Lester 2018	1	1									
Shimizu 2017	1	1									
Soma 2021	1						1				
Tsai 2020	4	1									
Total	47	5		2	6		3				1
Mixed paraplegic and tetraplegic population											
Bach Baunsgaard 2018* Baunsgaard 2018	52	5	4	9				9			3
Benson 2016*	10	5	8					1		2	1
Birch 2017	20										
Brinkemper 2021	15										
Chisholm 2017	3										
Edwards 2022	12	5					7	2			2
Escalona 2020	3	–	–	–	–	–	–	–	–	–	–
Escalona 2018	13	–	–	–	–	–	–	–	–	–	–
Gagnon 2018*	14			6			1	5			1
Gorgey 2017	4										
Grasmücke 2017	55										
Hartigan 2015	16	2									
Hong 2020 Gorman 2021	50	39					8		2		
Jansen 2018	21	4									
Kim 2021 Park 2021	11	2							1		
Kozlowski 2015	7	1									
Kressler 2018	4										
McIntosh 2020	11	2		2					1		1
Okawara 2022	9										
Okawara 2020	20										
Pérez-Nombela 2017	3	–	–	–	–	–	–	–	–	–	–
Ramanujam 2019	14	–	–	–	–	–	–	–	–	–	–
Ramanujam 2017	5	–	–	–	–	–	–	–	–	–	–
Stampacchia 2016	21										
Zieriacks 2021	121										
Total	514	65	12	17			16	17	4	2	8

G1 grade 1, *G2*: grade 2 (Schanck 2015), *OH* orthostatic hypotension, *BPC* blood pressure changes, *HT* hypertension

*Studies where specific adverse events for tetraplegic patients are specified, but serious adverse events occurred on a mixed population

– Data not available

Secondary outcomes

Walking parameters and walking functional tests

In total, 20 studies reported outcomes separately for TP: 12 concerning walking parameters and 13 concerning walking functional tests (Table 5). Among them, 4 studies focusing on walking parameters showed statistically significant improvements regarding walking speed, walking distance, walking time, 6MWT, 10 m walking test (10MWT) and Time Up and Go [18, 21, 36, 37]. In one randomized trial, including eight tetraplegic patients in the intervention group, a statistically significant improvement of approximately 60% was reported [24]. Interestingly, one TP improved his ASIA score [18] and another one become a walker without the exoskeleton after the WPE rehabilitation program [28]. Finally, one randomized trial showed similar improvements in walking functional tests between incomplete TP and PP after a gait training program using two types of exoskeletons (Ekso® & ReWalk®). However, the same study reported greater improvement in PP than in TP with complete lesions [37].

Additional health benefits

In total, 12 studies examined potential AHB of gait training using WPE specifically for TP. These potential AHB concerned various aspects of health: functional status, balance, cardiovascular health, pain, spasticity, bowel and lower urinary function, bone mineral density and quality of life. In each case, different scales or measures have been used for each outcome. In total, 2 studies, including a total of 9 TP, have reported a statistically significant improvement in at least one AHB: a case report reported improvement of spasticity measured with the modified Ashworth scale and a randomized trial showed improvements in cardiovascular efficiency measured with the Total Heart Beat Index [21, 27].

Finally, in 7 studies concerning TP, gait rehabilitation using WPE constituted a way to perform physical activity at light-to-moderate intensity [20, 35, 38–42]. One of these studies showed that TP have a higher cardiorespiratory demand during WPE gait training than PP [40].

Discussion

Main findings

This systematic review shows that gait training using WPE for patients with tetraplegia is a feasible and safe intervention with no distinction in terms of NLI and severity of the lesion. These results are in line with previous findings regarding paraplegia [6, 13, 43]. Additionally, some studies, with an overall low level of evidence, including a small number of TP, suggest that gait training using WPE could lead to a reduction of spasticity and an improvement of cardiovascular efficiency [21, 27].

Gait training using WPE in tetraplegia compared to paraplegia

To this date, gait rehabilitation using WPE in tetraplegia is poorly studied which is probably due to greater requirements of TP during rehabilitation. TP often present with trunk and upper limb impairments which lead to higher needs in terms of time and therapist supervision, thus higher treatment costs. Indeed, TP require more assistance during transfers or for fitting into the WPE [12, 44, 45]. Also, a more meticulous patient selection [26] and a closer medical supervision were deemed necessary, since the risk of medical concerns, such as cardiovascular autonomic dysfunction (autonomic dysreflexia or orthostatic hypotension), is theoretically higher than for PP [20, 46, 47]. Additionally, reduction in bone mineral density (BMD) seems to occur rapidly after SCI, leading to an increase in risk of fragility fractures [48, 49]. According to some authors, up to 46% of people with SCI will develop a fragility fracture in the sublesional areas within 5 years of initial injury [50, 51]. However, it has been suggested that the level of lesion does not seem to determine the severity of bone loss [52]. Concerns over these issues probably discouraged the use of WPE in patients with tetraplegia, especially when SCI is considered as “high” [11].

In some cases, special adaptations of the program intensity and content may be required. Individual adaptations can be scheduled depending on specific characteristics of each TP (mobility restrictions, upper and lower limb strength, autonomy during transfers, medical history) [26]. TP need more human assistance during gait training and choice of AD should be adapted depending on the NLI and the exoskeleton specificities [24]. Self-balancing exoskeletons such as Rex® or Atalante®, that do not need AD or other supplemental upper body support during gait training, offer new possibilities for rehabilitation after high and/or complete tetraplegia [12].

Special considerations before starting gait training using WPE in tetraplegia

Occurrence of AE did not qualitatively differ among the eight types of WPE identified in this review. However, to minimize occurrence of AE, it seems crucial to adequately select and prepare the candidate before starting the gait rehabilitation program. First, manufacturer recommendations concerning height, weight, spasticity, range of motion and NLI must be respected. These recommendations slightly

Table 5 Secondary outcomes: potential health benefits according to ICF-WHO model

Author, year	Body function and structure							Activities	Participation
	Walking parameters	Balance	Cardiovascular	Pain	Spasticity	Urinary tract and bowels	Bone mineral density	Functional walking tests	QOL
Tetraplegic population									
Benson 2016			●	●	●			●	●
Chang 2020	●								●
Delgado 2020								●	
Escalona 2020			●					●	
Evans 2021			✓					✓	
Fisahn 2016	✓							✓	
Gagnon 2018	●								
Gorgey 2017	●		●					●	
Grasmücke 2017	✓							✓	
Hartigan 2015								●	
Hong 2020								✓	
Ikumi 2017	●				●				
Jang 2019	●		●		●			●	
Kozlowski 2015	●	●	●					●	
Kressler 2018			●						
Lester 2018	●		●						
McIntosh 2020	●		●	●				●	
Shackleton 2021							=		
Shimizu 2017	●				✓				
Soma 2021	●	●						●	
Mixed paraplegic and tetraplegic population									
Baunsgaard 2018				=	✓	●		✓	✓
Bach Baunsgaard 2018	✓	●	✓					✓	
Birch 2017								●	
Brinkemper 2021	✓							✓	
Chang 2018	✓							✓	
Chisholm 2017		●							
Edwards 2022	✓							=	
Escalona 2018			●					●	
Gorman 2021						=			
Jansen 2018	✓				●			✓	
Khan 2019	●	✓	●	●	●			●	
Kim 2021							=	✓	=
Okawara 2022	✓							●	
Okawara 2020	=	✓						✓	
Park 2021			✓					✓	
Pérez-Nombela 2017			●	●					
Ramanujam 2019		✓							
Ramanujam 2017	✓	●							
Stampacchia 2016				=	✓				
Tsai 2020	✓								
Zieriacks 2021	✓							✓	

Walking parameters included path characteristics such as walking time, numbers of steps, walking speed, total standing up time, etc.

Functional walking tests included 2-Minute Walk Test, 6-Minute Walk Test, Timed Up & Go test, Walking Index for Spinal Cord Injury II, functional Ambulation Categories, Spinal Cord Independence measure III

QOL quality of life

●The study reported outcomes, but did not perform statistical analysis

✓Statistically significant difference between pre- and post-evaluation in favor of intervention using wearable powered exoskeleton for gait training

=No statistical difference between pre- and post-evaluation

vary for each device, but are in their vast majority similar [11]. Second, according to some authors, before starting gait training using WPE, patients should be able to stand in a standing bar to minimize occurrence of OH during walking sessions [20, 53]. Third, cutaneous inspection of skin areas in contact with the exoskeleton (typically the lower back and thighs) [28, 34] should be performed by a rehabilitation professional, usually the physiotherapist, before and after every session [54]. The majority of AE identified in our review could be minimized or at least quickly solved through vigilance and specific individualized adaptations. For example, using a cushion to avoid pression sores [27] or interrupting the training program until full recovery of minor skin injuries [20].

Concerning serious adverse events, previous work focusing on gait training using exoskeletons in paraplegia calculated an estimated incidence of fractures at 3.4% [6]. In one hand, fractures can be favorized by SCI-induced osteoporosis [55] and the elevated vertical ground reaction force which have been estimated at 36% (± 15%) of the total bodyweight of the patient when using a WPE [24, 56]. In our review, there was only one reported stress fracture of the tibia concerning a TP. Distal femur and proximal tibia appear to be the most frequently concerned areas for fragility fractures after SCI. On the other hand, one randomized controlled trial suggested that gait training using WPE potentially constitutes a secondary prevention treatment of progressive decline in BMD [22]. However, according to some authors, stress fracture occurrence may be underestimated [44] due to low sensitivity of conventional X-ray test and other imaging procedures, such as MRI or CT-scan, may be required for detection [23, 33]. Finally, some authors suggest that a BMD test should be performed before participation in gait rehabilitation programs using WPE [33, 57]. Nevertheless, in which case a BMD should be performed and how results should influence practice is still source of controversy [57, 58].

Characteristics and benefits of gait training programs using WPE in tetraplegia

In our review, most of the included studies used a training protocol similar to the one described by Asselin et al. [53]: 60 to 90 min per session at a frequency of two-to-three times per week. Total duration, in weeks, of gait training programs considerably varied among included studies. Generally, authors did not specify the control mechanism and how this was adapted to each patient during gait training. Whether WPE with different control mechanisms lead to differences in gait and functional recovery after SCI remains unclear. Also, there were no specifications regarding potential need of a familiarization period with the device and whether learning curves vary among participants [53].

According to recent literature findings, WPE rehabilitation could have similar benefits in terms of improvement in walking parameters between TP and PP [9, 20, 37]. Our findings are in line with recent studies concerning paraplegia regarding improvements in walking parameters such as walking speed and distance [6, 13]. Whether these improvements are more important for patients with acute and incomplete injuries, due to enhanced spinal neuroplasticity favoring motor relearning, needs to be further investigated in TP [13, 20, 28, 30, 37, 59–61].

In rehabilitation and research settings, gait training using exoskeletons allows TP to walk with a speed range from 0.11 to 0.4 m/s [32, 36, 45]. This speed may not be enough to consider the patient an outdoor walker [62], but constitutes a way to achieve indoor movements in standing position and could lead to better autonomy during activities of daily living, especially if the WPE is used in the home environment. Additionally, the use of WPE allows avoidance of prolonged sitting or decubitus. According to our findings, verticalization and movement in the WPE could lead to AHB such as reduction of spasticity and improved cardiovascular efficiency [21, 27]. Outcomes concerning bone mineral density, balance, urinary tract, bowel, quality of life and pain management are poorly studied and remain controversial [7, 22, 34, 63–65]. Future studies should further investigate these potential AHB.

Finally, interventions using WPE can be considered as a way to perform regular physical activity at light-to-moderate intensity [35] for TP, a population typically considered as sedentary [66]. New International Spinal Cord Society (ISCOS) recommendations suggest that, in accordance to the FITT principle of prescription (Frequency, Intensity, Time, Type) [67], patients with SCI need to perform 30 min of physical activity, of moderate-to-vigorous intensity, at a minimum frequency of three times per week to reduce risk of cardiovascular disease [6, 13, 66].

Strengths and limitations

This systematic review was conducted according to the PRISMA-S guidelines. Most selected studies were of moderate methodological quality and concerned mixed populations of both PP and TP. The level of evidence of the studies included in this review is low. No publication bias assessment was performed. Also, some AE specific to TP could have been missed due to impossibility to specifically assign all reported AE. Quantitative synthesis was not possible due to heterogeneity of reported outcomes.

Perspectives

This review encourages inclusion of TP in gait training programs using WPE. Future studies should investigate

efficacy of gait rehabilitation using WPE after SCI in terms of walking parameters and focus on potential AHB regarding cardiovascular and musculoskeletal systems. WPE should be considered as an alternative way to perform regular physical activity after SCI. Finally, the next generation of WPE opens new perspectives in terms of assistive robotics, as support and substitution technologies in ecological or outdoor environments, leading toward new ways of autonomy-enhancing compensation after SCI.

Conclusion

Gait training using WPE is a feasible and safe intervention after tetraplegia. Patient selection should be conducted according to safety recommendations. WPE and AD choice should be adapted to the patients' motor impairments. To this date, there are no specific rehabilitation protocols for TP and available protocols concern the entire SCI population. Some evidence suggests that gait training using WPE could lead to improvements in walking parameters, reduce spasticity and constitute a way to perform physical activity after tetraplegia. Other potential AHB concerning musculoskeletal, cardiovascular, urinary systems and quality of life should be further studied.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13760-022-02011-1.

Acknowledgements We would like to thank the FNRS for their support.

Author contributions GR and DI share co-first authorship. GR and DI conducted the study selection process, retrieved data, and performed analyses. TL and JGP contributed to data interpretation and manuscript revisions. All authors read and approved the final manuscript.

Funding FNRS Grant (F 5/4/130/5-CSD/CHU).

Availability of data and materials All data generated or analyzed during this study are included in this published article and its supplementary information files.

Declarations

Conflict of interest The authors declare that they have no competing interests.

Ethics approval Not applicable.

Informed consent Not applicable.

Consent for publication Not applicable.

References

1. WHO (2013) Spinal cord injury
2. Center (2020) NSCIS. The 2020 annual statistical report of the spinal cord injury model systems
3. Jansen O, Grasmuecke D, Meindl RC, Tegenthoff M, Schwenkreis P, Sczesny-Kaiser M et al (2018) Hybrid assistive limb exoskeleton HAL in the rehabilitation of chronic spinal cord injury: proof of concept; the results in 21 patients. World Neurosurg 110:e73–e78
4. Chang SH, Zhu F, Patel N, Afzal T, Kern M, Francisco GE (2020) Combining robotic exoskeleton and body weight unweighing technology to promote walking activity in tetraplegia following SCI: a case study. J Spinal Cord Med 43(1):126–129
5. Tsai CY, Delgado AD, Weinrauch WJ, Manente N, Levy I, Escalon MX et al (2020) Exoskeletal-assisted walking during acute inpatient rehabilitation leads to motor and functional improvement in persons with spinal cord injury: a pilot study. Arch Phys Med Rehabil 101(4):607–612
6. Miller LE, Zimmermann AK, Herbert WG (2016) Clinical effectiveness and safety of powered exoskeleton-assisted walking in patients with spinal cord injury: systematic review with meta-analysis. Med Dev (Auckl) 9:455–466
7. Chisholm AE, Alamro RA, Williams AM, Lam T (2017) Overground vs. treadmill-based robotic gait training to improve seated balance in people with motor-complete spinal cord injury: a case report. J Neuroeng Rehabil 14(1):27.
8. Okawara H, Tashiro S, Sawada T, Sugai K, Matsubayashi K, Kawakami M et al (2022) Neurorehabilitation using a voluntary driven exoskeletal robot improves trunk function in patients with chronic spinal cord injury: a single-Arm study. Neural Regen Res 17(2):427–432
9. Grasmücke D, Zieriacks A, Jansen O, Fisahn C, Sczesny-Kaiser M, Wessling M, et al (2017) Against the odds: what to expect in rehabilitation of chronic spinal cord injury with a neurologically controlled hybrid assistive limb exoskeleton. A subgroup analysis of 55 patients according to age and lesion level. Neurosurgical focus. 42(5):E15
10. Delgado AD, Escalon MX, Bryce TN, Weinrauch W, Suarez SJ, Kozlowski AJ (2020) Safety and feasibility of exoskeleton-assisted walking during acute/sub-acute SCI in an inpatient rehabilitation facility: a single-group preliminary study. J Spinal Cord Med 43(5):657–666
11. Palermo AE, Maher JL, Baunsgaard CB, Nash MS (2017) Clinician-focused overview of bionic exoskeleton use after spinal cord injury. Top Spinal Cord Inj Rehabil 23(3):234–244
12. Birch N, Graham J, Priestley T, Heywood C, Sakel M, Gall A, et al (2017) Results of the first interim analysis of the RAPPER II trial in patients with spinal cord injury: Ambulation and functional exercise programs in the REX powered walking aid. J NeuroEng Rehab 14(1).
13. Shackleton C, Evans R, Shamley D, West S, Albertus Y (2019) Effectiveness of over-ground robotic locomotor training in improving walking performance, cardiovascular demands, secondary complications and user-satisfaction in individuals with spinal cord injuries: a systematic review. J Rehabil Med 51(10):723–733
14. Dijkers MP, Akers KG, Dieffenbach S, Galen SS (2019) Systematic reviews of clinical benefits of exoskeleton use for gait and mobility in neurologic disorders: a tertiary study. Archi Phys Med Rehab
15. Federici S, Meloni F, Bracalenti M (2018) Gait rehabilitation with exoskeletons. In: Handbook of Human Motion. 2–3: Springer International Publishing, 1433–69
16. Gorgey AS, Wade R, Sumrell R, Villadelgado L, Khalil RE, Lavis T (2017) Exoskeleton training may improve level of

physical activity after spinal cord injury: a case series. Top Spinal Cord Inj Rehabil 23(3):245–255
17. Rethlefsen ML KS, Waffenschmidt S, Ayala AP, Moher D, Page MJ, Koffel JB; PRISMA-S Group (2021) PRISMA-S: an extension to the prisma statement for reporting literature searches in systematic reviews. Syst Rev 10(1):39.
18. Fisahn C, Aach M, Jansen O, Moisi M, Mayadev A, Pagarigan KT et al (2016) The effectiveness and safety of exoskeletons as assistive and rehabilitation devices in the treatment of neurologic gait disorders in patients with spinal cord injury: a systematic review. Global Spine J 6(8):822–841
19. Pérez-Nombela S, Del-Ama AJ, Asín-Prieto G, Piñuela-Martín E, Lozano-Berrio V, Serrano-Muñoz D et al (2017) Physiological evaluation of different control modes of lower limb robotic exoskeleton h2 in patients with incomplete spinal cord injury. Biosystems and Biorobotics. Springer International Publishing, pp 343–348
20. McIntosh K, Charbonneau R, Bensaada Y, Bhatiya U, Ho C (2020) The safety and feasibility of exoskeletal-assisted walking in acute rehabilitation after spinal cord injury. Arch Phys Med Rehabil 101(1):113–120
21. Evans RW, Shackleton CL, West S, Derman W, Laurie Rauch HG, Baalbergen E et al (2021) Robotic locomotor training leads to cardiovascular changes in individuals with incomplete spinal cord injury over a 24-week rehabilitation period: a randomized controlled pilot study. Arch Phys Med Rehabil 102(8):1447–1456
22. Shackleton C, Evans R, West S, Derman W, Albertus Y (2021) Robotic walking to mitigate bone mineral density decline and adverse body composition in individuals with incomplete spinal cord injury: a pilot randomized clinical trial. Am J Phys Med Rehabil.
23. Bach Baunsgaard C, Vig Nissen U, Katrin Brust A, Frotzler A, Ribeill C, Kalke YB et al (2018) Gait training after spinal cord injury: safety, feasibility and gait function following 8 weeks of training with the exoskeletons from Ekso Bionics. Spinal Cord 56(2):106–116
24. Gagnon DH, Escalona MJ, Vermette M, Carvalho LP, Karelis AD, Duclos C et al (2018) Locomotor training using an overground robotic exoskeleton in long-term manual wheelchair users with a chronic spinal cord injury living in the community: lessons learned from a feasibility study in terms of recruitment, attendance, learnability, performance and safety. J Neuroeng Rehabil 15(1):12
25. Ikumi A, Kubota S, Shimizu Y, Kadone H, Marushima A, Ueno T et al (2017) Decrease of spasticity after hybrid assistive limb(®) training for a patient with C4 quadriplegia due to chronic SCI. J Spinal Cord Med 40(5):573–578
26. Lester RM, Gorgey AS (2018) Feasibility of robotic exoskeleton ambulation in a C4 person with incomplete spinal cord injury: a case report. Spinal Cord Ser Cases 4:36
27. Shimizu Y, Kadone H, Kubota S, Suzuki K, Abe T, Ueno T, et al (2017) Voluntary ambulation by upper limb-triggered HAL® in patients with complete quadri/paraplegia due to chronic spinal cord injury. Front Neurosci 11(NOV)
28. Khan AS, Livingstone DC, Hurd CL, Duchcherer J, Misiaszek JE, Gorassini MA, et al (2019) Retraining walking over ground in a powered exoskeleton after spinal cord injury: a prospective cohort study to examine functional gains and neuroplasticity. J NeuroEng Rehab 16(1).
29. Chang SH, Afzal T, Berliner J, Francisco GE (2018) Exoskeleton-assisted gait training to improve gait in individuals with spinal cord injury: a pilot randomized study. Pilot Feasibility Stud 4:62
30. Zieriacks A, Aach M, Brinkemper A, Koller D, Schildhauer TA, Grasmücke D (2021) Rehabilitation of acute vs. chronic patients with spinal cord injury with a neurologically controlled hybrid assistive limb exoskeleton: is there a difference in outcome? Front Neurorobot 15
31. Chang SH, Afzal T, Berliner J, Francisco GE (2018) Exoskeleton-assisted gait training to improve gait in individuals with spinal cord injury: a pilot randomized study. Pilot Feasib Stud 4(1).
32. Edwards DJ, Forrest G, Cortes M, Weightman MM, Sadowsky C, Chang SH, et al (2022) Walking improvement in chronic incomplete spinal cord injury with exoskeleton robotic training (WISE): a randomized controlled trial. Spinal Cord
33. Benson I, Hart K, Tussler D, van Middendorp JJ (2016) Lower-limb exoskeletons for individuals with chronic spinal cord injury: findings from a feasibility study. Clin Rehabil 30(1):73–84
34. Kim HS, Park JH, Lee HS, Lee JY, Jung JW, Park SB et al (2021) Effects of wearable powered exoskeletal training on functional mobility, physiological health and quality of life in non-ambulatory spinal cord injury patients. J Korean Med Sci 36(12):e80
35. Park JH, Kim HS, Jang SH, Hyun DJ, Park SI, Yoon J, et al (2021) Cardiorespiratory responses to 10 weeks of exoskeleton-assisted overground walking training in chronic nonambulatory patients with spinal cord injury. Sens (Basel, Switzerl) 21(15)
36. Grasmücke D, Zieriacks A, Jansen O, Fisahn C, Sczesny-Kaiser M, Wessling M, et al (2017) Against the odds: what to expect in rehabilitation of chronic spinal cord injury with a neurologically controlled Hybrid Assistive Limb exoskeleton. A subgroup analysis of 55 patients according to age and lesion level. Neurosurg Focus 42(5):E15
37. Hong E, Gorman PH, Forrest GF, Asselin PK, Knezevic S, Scott W, et al (2020) Mobility skills with exoskeletal-assisted walking in persons With SCI: results from a three center randomized clinical trial. Front Robot AI. 7
38. Kozlowski AJ, Bryce TN, Dijkers MP (2015) Time and effort required by persons with spinal cord injury to learn to use a powered exoskeleton for assisted walking. Top Spinal Cord Inj Rehabil 21(2):110–121
39. Escalona MJ, Brosseau R, Vermette M, Comtois AS, Duclos C, Aubertin-Leheudre M et al (2018) Cardiorespiratory demand and rate of perceived exertion during overground walking with a robotic exoskeleton in long-term manual wheelchair users with chronic spinal cord injury: a cross-sectional study. Ann Phys Rehabil Med 61(4):215–223
40. Kressler J, Wymer T, Domingo A (2018) Respiratory, cardiovascular and metabolic responses during different modes of overground bionic ambulation in persons with motor-incomplete spinal cord injury: a case series. J Rehabil Med 50(2):173–180
41. Jang YC, Park HK, Han JY, Choi IS, Song MK (2019) Cardiopulmonary function after robotic exoskeleton-assisted over-ground walking training of a patient with an incomplete spinal cord injury: Case report. Med (Baltim) 98(50):e18286
42. Escalona MJ, Bourbonnais D, Goyette M, Duclos C, Gagnon DH (2020) Wearable exoskeleton control modes selected during overground walking affect muscle synergies in adults with a chronic incomplete spinal cord injury. Spinal Cord Series Cases 6(1)
43. Lajeunesse V, Vincent C, Routhier F, Careau E, Michaud F (2016) Exoskeletons' design and usefulness evidence according to a systematic review of lower limb exoskeletons used for functional mobility by people with spinal cord injury. Disabil Rehabil Assist Technol 11(7):535–547
44. Mekki M, Delgado AD, Fry A, Putrino D, Huang V (2018) Robotic rehabilitation and spinal cord injury: a narrative review. Neurotherapeutics 15(3):604–617
45. Hartigan C, Kandilakis C, Dalley S, Clausen M, Wilson E, Morrison S et al (2015) Mobility outcomes following five training sessions with a powered exoskeleton. Top Spinal Cord Inj Rehabil 21(2):93–99
46. Previnaire JG, Mathias CJ, El Masri W, Soler JM, Leclercq V, Denys P (2010) The isolated sympathetic spinal cord:

cardiovascular and sudomotor assessment in spinal cord injury patients: a literature survey. Ann Phys Rehabil Med 53(8):520–532
47. Bluvshtein V, Korczyn AD, Akselrod S, Pinhas I, Gelernter I, Catz A (2011) Hemodynamic responses to head-up tilt after spinal cord injury support a role for the mid-thoracic spinal cord in cardiovascular regulation. Spinal Cord 49(2):251–256
48. Dauty M, Perrouin Verbe B, Maugars Y, Dubois C, Mathe JF (2000) Supralesional and sublesional bone mineral density in spinal cord-injured patients. Bone 27(2):305–309
49. Morse LR, Biering-Soerensen F, Carbone LD, Cervinka T, Cirnigliaro CM, Johnston TE et al (2019) Bone mineral density testing in spinal cord injury: 2019 ISCD official position. J Clin Densitom 22(4):554–566
50. Vestergaard P, Krogh K, Rejnmark L, Mosekilde L (1998) Fracture rates and risk factors for fractures in patients with spinal cord injury. Spinal Cord 36(11):790–796
51. Garland DE, Adkins RH, Kushwaha V, Stewart C (2004) Risk factors for osteoporosis at the knee in the spinal cord injury population. J Spinal Cord Med 27(3):202–206
52. Kaya K, Aybay C, Ozel S, Kutay N, Gokkaya O (2006) Evaluation of bone mineral density in patients with spinal cord injury. J Spinal Cord Med 29(4):396–401
53. Asselin PK, Avedissian M, Knezevic S, Kornfeld S, Spungen AM (2016) Training persons with spinal cord injury to ambulate using a powered exoskeleton. J Vis Exp (112)
54. Esquenazi A, Talaty M, Jayaraman A (2017) Powered exoskeletons for walking assistance in persons with central nervous system injuries: a narrative review. PM R 9(1):46–62
55. Battaglino RA, Lazzari AA, Garshick E, Morse LR (2012) Spinal cord injury-induced osteoporosis: pathogenesis and emerging therapies. Curr Osteoporos Rep 10(4):278–285
56. Fineberg DB, Asselin P, Harel NY, Agranova-Breyter I, Kornfeld SD, Bauman WA et al (2013) Vertical ground reaction force-based analysis of powered exoskeleton-assisted walking in persons with motor-complete paraplegia. J Spinal Cord Med 36(4):313–321
57. Esquenazi A, Talaty M, Packel A, Saulino M (2012) The ReWalk powered exoskeleton to restore ambulatory function to individuals with thoracic-level motor-complete spinal cord injury. Am J Phys Med Rehabil 91(11):911–921
58. Bass A, Morin SN, Vermette M, Aubertin-Leheudre M, Gagnon DH (2020) Incidental bilateral calcaneal fractures following overground walking with a wearable robotic exoskeleton in a wheelchair user with a chronic spinal cord injury: is zero risk possible? Osteoporos Int 31(5):1007–1011
59. Aach M, Cruciger O, Sczesny-Kaiser M, Höffken O, Meindl RC, Tegenthoff M et al (2014) Voluntary driven exoskeleton as a new tool for rehabilitation in chronic spinal cord injury: a pilot study. Spine J 14(12):2847–2853
60. Soma Y, Kubota S, Kadone H, Shimizu Y, Takahashi H, Hada Y et al (2021) Hybrid assistive limb functional treatment for a patient with chronic incomplete cervical spinal cord injury. Int Med Case Rep J 14:413–420
61. Brinkemper A, Aach M, Grasmücke D, Jettkant B, Rosteius T, Dudda M, et al (2021) Improved physiological gait in acute and chronic sci patients after training with wearable cyborg hybrid assistive limb. Front Neurorobot 15
62. van Hedel HJA, Severini G, Scarton A, O'Brien A, Reed T, Gaebler-Spira D et al (2018) Advanced robotic therapy integrated centers (ARTIC): an international collaboration facilitating the application of rehabilitation technologies. J Neuroeng Rehabil 15(1):30
63. Chun A, Asselin PK, Knezevic S, Kornfeld S, Bauman WA, Korsten MA et al (2020) Changes in bowel function following exoskeletal-assisted walking in persons with spinal cord injury: an observational pilot study. Spinal Cord 58(4):459–466
64. Gorman PH, Forrest GF, Asselin PK, Scott W, Kornfeld S, Hong E et al (2021) The effect of exoskeletal-assisted walking on spinal cord injury bowel function: Results from a randomized trial and comparison to other physical interventions. J Clin Med 10(5):1–11
65. Okawara H, Sawada T, Matsubayashi K, Sugai K, Tsuji O, Nagoshi N et al (2020) Gait ability required to achieve therapeutic effect in gait and balance function with the voluntary driven exoskeleton in patients with chronic spinal cord injury: a clinical study. Spinal Cord 58(5):520–527
66. Martin Ginis KA, van der Scheer JW, Latimer-Cheung AE, Barrow A, Bourne C, Carruthers P et al (2018) Evidence-based scientific exercise guidelines for adults with spinal cord injury: an update and a new guideline. Spinal Cord 56(4):308–321
67. Hafidz A, Omar H, Latip HF, Latip M, Shahrom A (2014) Application of FITT principle in exercise rehabilitation focusing on common sports injury among Malaysian Athlete
68. Baunsgaard CB, Nissen UV, Brust AK, Frotzler A, Ribeill C, Kalke YB et al (2018) Exoskeleton gait training after spinal cord injury: an exploratory study on secondary health conditions. J Rehabil Med 50(9):806–813
69. Ramanujam A, Spungen A, Asselin P, Garbarini E, Augustine J, Canton S et al (2017) Training response to longitudinal powered exoskeleton training for SCI. Biosystems and Biorobotics. Springer International Publishing, pp 361–366
70. Ramanujam A, Momeni K, Ravi M, Augustine J, Garbarini E, Barrance P, et al., (eds) (2019) Center of mass adaptations and its interaction between the trunk and lower-extremity during exoskeleton walking. Institute of Electrical and Electronics Engineers Inc.

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