Can powered exoskeletons improve gait and balance in multiple sclerosis? A retrospective study

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Multiple sclerosis (MS) is a progressive neurologic disorder that can profoundly influence mobility, independence and quality of life. Gait dysfunction in MS is common, resulting in an increased risk of losing walking ability. Robotic exoskeletons have been developed to offer a new form of locomotor training. The aim of our study was to investigate the effectiveness of the powered exoskeleton (Ekso) in improving gait and balance in patients affected by MS. Twenty patients with MS (mean ± SD: age = 43.7 ± 10.3 years; 66.7% male) were enrolled in this retrospective study. They were divided into two groups, matched for demographic data (age and sex) and medical characteristics (disease duration and Expanded Disability Status Scale), but differing for the type of rehabilitation training performed. Group 1 [experimental group (EG)] received gait training with the Ekso device, whereas group 2 (control group) performed traditional gait training. Although both trainings led to a significant improvement in the ability to walk and balance, only in the EG a significant improvement in walking speed (10 Meter Walk test; $P = 0.002$), in person's mobility (Timed Up and Go test; $P = 0.002$), and in the perception of mental well-being (MSQoL-M; $P = 0.004$), with a good usability and acceptance of the device, was found. Powered exoskeletons could be considered a valuable tool to improve functional outcomes and get the therapeutic goal in patients with MS. *International Journal of Rehabilitation Research* XXX: 000–000 Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

Multiple sclerosis (MS) is a progressive neurologic disorder that can profoundly influence mobility, independence and quality of life [1]. Gait dysfunction in MS is common, resulting in an increased risk of losing walking ability, increasing the risk of secondary medical conditions. A large survey found that 40% of patients with MS reported some difficulty with ambulation, and 70% of them reported their walking issues to be the biggest challenge of their disease [1].

Assistive devices, such as canes, walkers and rollators, can help with ambulatory activity, but are only meant to assist and not to improve physical endurance of the user [2]. Robotic exoskeletons have been developed and recently approved for spinal cord injury and stroke rehabilitation [3,4], as they offer a relatively new form of locomotor training, with potential positive results also in MS [5]. These devices enable individuals with lower extremity weakness to stand up and walk over ground with a full weight-bearing and reciprocal gait. Nonetheless, people with MS are highly susceptible to fatigue and are at increased risk of falling [6]. Consequently, an exoskeleton that works well for SCI or stroke may not do so for MS, because of the variability in distribution and temporal presentation of motor and sensory impairments and symptoms, which could affect the safe device use. About this, Kozlowski *et al.* [7] tested the feasibility and safety of a powered exoskeleton for assisted walking in MS and the device appeared feasible and safe.

McGibbon showed that Keeogo (a lower body-powered knee exoskeleton) was able to deliver an exercise-mediated benefit to individuals with MS by improving unassisted gait endurance and stair-climbing ability [8]. The extent to which routine exoskeleton-assisted walking could provide secondary benefits [e.g. walking without the device, reductions to Expanded Disability Status Scale (EDSS) score, pain, depression, fatigue, or spasticity] is less clear.

The aim of our study was to investigate the effectiveness of the powered exoskeleton Ekso-GT in improving gait and balance in patients affected by MS.

Materials and methods

Study design and population

Patients with MS who attended the Robotic and Behavioral Neurorehabilitation Unit of the IRCCS Centro Neurolesi 'Bonino-Pulejo' from March 2018 to

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June 2019, were evaluated for inclusion in this retrospective case-control study, using an electronic recovery data system. Ten patients undergoing Ekso-GT (EG) were then compared to 10 patients (CG) receiving traditional gait training (TGT): the type of the training was normally assigned at the beginning of the rehabilitation by the rehab team. The evaluations, which we collected retrospectively, were carried out at the beginning and at the end of the training by the rehabilitation team (neurologist, physiatrist, nurse, physiotherapist, psychologist), as per research and clinical standards.

Inclusion criteria were as follows: (1) MS diagnosis according to the last revisions of the McDonald criteria [9]; (2) FIM [10] scale score >30; (3) EDSS between 4.5 and 6.5 [11]; (4) absence of disabling sensory alterations (i.e. auditory and visual loss) and cognitive deficits (Mini Mental State Examination and Quality of Life < 21) potentially interfering with the training [12]. Exclusion criteria were as follows: (1) age > 65 years; (2) severe spasticity (modified Ashworth Scale > 3) [13]; (3) MS relapse in the 6 months before enrollment; (4) EDSS > 6.5.

Data collection

Demographic and clinical information was collected from all the included patients. The MS development phase and the rehabilitation sessions were recorded. The data were collected retrospectively and then analyzed; patients had signed a general informed consensus on the use of data for research purposes.

Procedures and outcomes

The included patients were divided into two groups, having comparable demographic data (age and sex) and medical characteristics (disease duration and EDSS). The gait rehabilitation protocol consisted of 40 training sessions (i.e. five times a week for 8 weeks) lasting about 1 hour for each group. The patients received the same amount of treatment, but with two different gait training: the EG used the robotic device Ekso-GT whereas the CG received TGT. Patients in both groups were also provided with conventional physical therapy (i.e. stretching, muscle strength and occupational therapy).

All the patients were assessed at the beginning (T0) and at the end (T1) of the rehabilitation program, using 10 Meter Walk test (10MWT) to evaluate walking speed in meters per second over a short distance [14]; Timed Up and Go test (TUG) to assess a person's mobility and requires both static and dynamic balance [15]; Motricity Index to measure strength in upper and lower extremities [16]; Functional Ambulation Categories (FAC) that assesses the ability to walk [17]; Functional Independence Measure (FIM) and Berg Balance Scale (BBS) to measure balance ability (static and dynamic) [10,18]; Multiple Sclerosis Quality of Life-54 (MSQOL) to assess health-related quality of life [19]. Goal Attainment Scaling (GAS; for evaluating the extent to which the patient believes that individual goals during the intervention were achieved) and System Usability Scale (SUS; to investigate the usability of the Ekso-GT) were also administered [20,21].

Ekso-GT device

The Ekso-GT is a powered hip-knee medical rehabilitation exoskeleton developed by Ekso Bionics, and approved by the FDA for those recovering from a stroke and SCI. Ekso is an exoskeleton framework for the lower limbs, equipped with electric motors to power movement for the hip and knee joints, passive spring-loaded ankle joints, foot plates on which the user stands, a backpack that houses a computer, battery supply, and wired controller. Ekso-GT software includes three walk mode: (1) FirstStep-TM: aid to step is provided by the physiotherapist using the controller; such mode is used during the first training sessions; (2) ProStep-TM: aid to step depends on the patients' thanks to appropriate sideways and forward shifts of their weight whilst walking using Ekso-GT; (3) ProStep-Plus TM: the patient moves the device with appropriate sideways, forward movements and lifting of the foot by offloading the pressure of the sensors placed on the front of the foot. Different parameters (i.e. forward assistance, step length and height, swing and stand time, hip and knee flexion angle) are adjusted during the training in relation to patient's improvements and needs. Moreover, during the Ekso rehabilitation, it is also possible to set the different assistance modes, including the Adaptive (i.e. the device constantly monitors the amount of forward movement aid provided so as to receive the appropriate assistance needed) and the Fixed (100 to 0 value; the lower the value, the lower the assistance) ones.

Statistical analysis

Clinical records of 10 MS patients treated with Ekso and 10 patients with MS performed to TT were examined. We assigned them to one of two groups: EG and CG. To reduce the selection bias, we matched age, sex, duration of the disease and EDSS score. The data were analyzed using SPSS version 18.0, considering a $P < 0.05$ as statistically significant. Descriptive statistics were analyzed and expressed as mean ± SD or as median ± first-third quartile for continuous variables, as appropriate; frequencies (%) were used for categorical variables. Kolmogorov–Smirnov's Z test was used. Given the non-homogeneity of the distributions of continuous variables and the reduced number of data, a nonparametric approach was performed. For the data type, the Wilcoxon signed-rank test was applied, comparing the patient's result at different time points (two tails, if appropriate). Thus, we performed the analysis of covariance (ANCOVA) to test for group difference on scores at T1, controlling for scores at baseline. We used the score in the test at time T1 as the dependent variable; the independent variable was the categorical variable 'Group' (1 = experimental; 2 = control), and the covariate was the baseline test score (T0).

Results

All patients (12 male and eight female; mean age: 43.7 ± 8.07) completed the training, and both groups underwent the same amount of treatment. As the two groups were properly matched (Table 1), no significant differences were found in age (P = 1.00), disease duration, EDSS score (P = 1.00) and proportion of sex (P = 1.00). Moreover, at baseline, no significant differences emerged between the outcome scores of the two groups. The results of Wilcoxon's tests showed significant differences in all of the domains that we evaluated (Table 2), underlining that the scores of some tests were influenced by the type of treatment. The analysis results showed that both the training led to a significant improvement in the ability to walk (FAC), balance (BBS), functional capacity (FIM), perception of physical well-being (MSQOL-P), as well as in the perception of the achievement of the therapeutic goal. However, only in the EG, we observed a significant improvement in walking speed (10MWT; P = 0.002), and person's mobility (TUG; P = 0.002), in the perception of mental well-being (MSQOL-M; P = 0.004). Results showed that the type of treatment influenced many domains. Indeed, ANCOVA (Table 2), controlling for the covariates at T0, revealed a large-sized main effect on walking speed (10MWT), person's mobility (TUG) in the left body part, and in the ability to walk (FAC). However, a medium-sized main effect on mental QoL, person's mobility (TUG) in the right body part, balance (BBS), and in the perception of goal achievement (GAS). The assumption of homogeneity of the regression slopes was not satisfied in some covariate models: Motricity Index, FIM and e physical QoL. Therefore, ANCOVA could not be performed for these tests.

Table 1 **Demographic and clinical characteristics of the patients**

	EG	CG	All	*P*-value
Participant	10	10	20	
Sex				
Male	6	6	12	
Female	4	4	8	1.00
Age (years)	43.7 ± 10.3	43.7 ± 5.6	43.7 ± 8.07	1.00
Education				1.00
Primary	-	-	-	
Middle	2	2	4	
High	6	7	13	
University	2	1	3	
Disease duration	8.4 ± 3.5	8.4 ± 3.5	8.4 ± 3.5	1.00
Expanded Disability Status Scale (EDSS)	4.9	4.9	4.9	1.00

Mean ± SD was used to describe continuous variables; proportions (numbers and percents) were used to describe categorical variables.
CG, control group; EG, experimental group.

Notably, we observed that the majority of the sample indicated the main goal 'walking with a better balance' (77.7%) and 'acceptance of the disease' (33.3%). Finally, we observed that the EG perceived a high usability of the robotic device, which was well tolerated (SUS mean ± SD: 88.6 ± 5.6).

Discussion

This study supports the growing importance of robotics, with regard to powered exoskeleton, in improving functional outcomes in patients with MS. Indeed, a greater improvement in walking speed and walking distance (as per 10MWT) and subjects' mobility (as per TUG), as well as in balance, was more evident in the Ekso-GT group.

Earlier studies have indicated improvements in sitting, standing and walking postures, or endurance in gait after the use of recent powered exoskeletons, such as ReWalk and Keeogo [7,8]. In particular, it has been demonstrated that Keeogo exoskeleton, a device that assists only at the knee joints, lead to improvement in gait endurance and stair-climbing capacity in persons with MS having an EDSS ≤6.5 [7]. These data are in line with our findings,

Table 2 **Median and interquartile range of clinical scores at baseline (T0) and follow-up (T1), for both experimental and control groups**

	Experimental group			Control group			ANCOVA group variable		
Clinical assessment	T0	T1	*P*-value	T0	T1	*P*-value	*F* value	*P*-value	η^2
10MWT	8.14 (5.5–16.4)	7.32 (4.7–15.0)	**0.002**	9.32 (5.8–16.4)	10.00 (7.0–16.5)	0.250	13.41	0.002	0.44
TUG LEFT	13.6 (8.0–28.4)	8.5 (7.0–23.2)	**0.002**	13.2 (10.4–21.8)	12.4 (10.0–23.2)	0.064	2.62	0.002	0.13
TUG RIGHT	13.4 (8.1–25.6)	10.81 (7.4–23.1)	**0.002**	28.5 (22.5–32.0)	28.5 (22.5–32.0)	1.000	12.18	0.003	0.41
MI LL LEFT	66.0 (57.5–76.0)	75.0 (68.0–75.0)	0.063	64.0 (56.5–74.5)	68.0 (59.0–77.5)	**0.004**		NA	
MI LL RIGHT	77.0 (49.5–100.0)	83.0 (57.5–100.0)	0.062	84.0 (50.0–91.5)	86.0 (53.0–95.5)	**0.004**		NA	
MI UL LEFT	100.0 (85.5–100.0)	100.0 (92.0–100.0)	0.50	98.0 (85.0–100.0)	100.0 (87.0–100.0)	0.62		NA	
MI UL RIGHT	100.0 (100.0–100.0)	100.0 (100.0–100.0)	1.000	98.0 (99.0–100.0)	100.0 (98.5–100.0)	0.250		NA	
FAC	3.0 (2.5–4.0)	4.0 (3.0–5.0)	**0.016**	3.0 (2.5–4.0)	4.0 (3.5–4.0)	**0.031**	5.22	0.013	0.30
BBS	40.0 (39.0–44.0)	48.0 (46.0–53.5)	**0.004**	41.0 (39.0–43.0)	46.0 (44.0–49.0)	**0.004**	5.76	0.02	0.23
FIM	116.0 (101.0–119.0)	120.0 (112.0–122.0)	**0.004**	111.0 (105.0–118.5)	119.0 (112.5–120.5)	**0.004**		NA	
MSQOL-P	53.4 (38.0–61.0)	91.6 (71.6–132.0)	**0.004**	60.0 (36.0–83.0)	66.1 (48.0–84.5)	**0.008**		NA	
MSQOL-M	56.2 (42.9–64.4)	72.5 (68.8–95.8)	**0.004**	42.1 (41.6–57.1)	43.7 (41.5–60.5)	**0.078**	3.34	0.004	0.16
GAS	37.6 (31.3–37.7)	67.2 (50.0–71.7)	**0.004**	37.6 (37.6–37.6)	56.2 (43.1–60.5)	**0.012**	4.05	0.004	0.19

10MWT, 10 Meter Walking Test; ANCOVA, analysis of covariance; BBS, Berg Balance Scale; FAC, functional ambulation categories; FIM, functional independence measure; GAS, Goal Attainment Scaling; LL, lower limb; M, mental; MI, Motricity Index; MSQOL, multiple sclerosis - quality of life; P, physical; TUG, Timed Up and Go test; UL, upper limb.
Scores are in median (first-third quartile); significant differences are in bold.

potentially suggesting better results following robotic rehab only in individuals with higher disability scores [22–23].

Infact, Kozlowski *et al.* [7] showed the feasibility and safety, as well as effectiveness, of using the Rewalk exoskeleton in individuals with MS having an EDSS range 5.5–7.0. Moreover, considering the severity of the disorder, it has been shown long-term positive effects after over-ground robotic walking training especially in severe MS patients [22]. Azal *et al.* also demonstrated a significant negative correlation between self-selected gait speed (in terms of improvement) and metabolic expenditure (reduction) during short distance walks, in patients with EDSS between 6.0 and 7.5. This probably reflects improvement in neuromuscular efficiency without inducing fatigue and exhaustion [24].

Recovery of walking continues to be the primary goal for persons with neurologic deficits and a contributing factor to the quality of life. Therefore, (re)learning to walk is a major goal during rehabilitation. Although the optimal therapeutic intervention to achieve full recovery of gait remains unknown for many patients with neurologic injuries, any rehabilitation effort intended to drive changes toward motor recovery should incorporate principles of neuroplasticity [25–27].

RAGT fulfills two important elements of the task-specific training principle: relevant and repetitive training [28]. Relevant because of the opportunity to walk over ground in both indoor and outdoor environments, promoting a person's interest, motivation and active engagement. Then, the amount of time spent walking in the device demonstrates the repetitive nature of training. This could partly explain the reason why our patients receiving Ekso-GT training got better functional outcomes. Indeed, it has been shown that repetitive, high-intensity and task-oriented exercise could promote a better patient's recovery [35,44], also by stimulating awareness of movements' results and awareness of the quality of movements through a multisensory feedback [29–33].

Additionally, some studies have underlined the importance of robotic training (especially when coupled to virtual reality) in boosting both motor and cognitive outcomes and processing speed, with a positive perception of patients' performance, as compared to traditional training [5,34–37].

It is noteworthy that physical impairment should not be considered the only goal of the rehabilitation outcomes, as the potential impact on the psychologic well-being, self-esteem and confidence should be always considered, especially in severe disability [25].

The novelty of the study is that we have applied a patient-centered approach by using individualized health outcomes using the GAS, an accurate marker of success in relation to the intended goals of treatment, both by the patient and the clinician. We focused on the achievement of the rehabilitation outcomes based on the patients' evaluation of the use of the robotic device. In fact, our data showed as patients that performed the robotic training better improved in the GAS score, as compared to conventional therapy. Indeed, the patients had the perception of having reached the objectives set out at the beginning of the treatment, and found the Ekso-GT useful in gaining their goals and improving QoL.

To this aim, the MSQoL-54, a multidimensional health-related quality of life tool [19], showed a greater improvement in the EG, especially concerning mental health. In fact, the MSQoL-Mental health score showed that psychopathologic symptoms had more influence on the QoL of MS patients than physical impairment. Although MSQoL is a self-report tool, we believe that taking into consideration the patient's subjective evaluation on his/her impairment and the QoL should be highly recommended to optimize pharmacologic and nonpharmacologic therapy [38].

The main limitation of this study is the retrospective design and the absence of a follow-up, so it is not possible to define whether the results obtained by our sample are maintained over time. The sample size is relatively small for detecting valid effects on the outcomes. However, our results are in line with other studies evaluating the potential benefit of powered exoskeleton in MS.

Another limitation is the lack of assessment of the patient's mood and anxiety, which are believed to be major contributing factors of QoL, as well as the absence of a detailed neuropsychologic assessment. Further larger studies are needed to address these important issues.

In conclusion, our findings support the idea that over-ground robotic devices, by potentiating adherence and motivation during the rehabilitation training, may have positive impacts on functional and psychologic outcomes of patients with MS, potentially improving their well-being and quality of life.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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