

Conflicting results of robot-assisted versus usual gait training during postacute rehabilitation of stroke patients: a randomized clinical trial

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Robot gait training has the potential to increase the effectiveness of walking therapy. Clinical outcomes after robotic training are often not superior to conventional therapy. We evaluated the effectiveness of a robot training compared with a usual gait training physiotherapy during a standardized rehabilitation protocol in inpatient participants with poststroke hemiparesis. This was a randomized double-blind clinical trial in a postacute physical and rehabilitation medicine hospital. Twenty-eight patients, 39.3% women (72 ± 6 years), with hemiparesis (< 6 months after stroke) receiving a conventional treatment according to the Bobath approach were assigned randomly to an experimental or a control intervention of robot gait training to improve walking (five sessions a week for 5 weeks). Outcome measures included the 6-min walk test, the 10 m walk test, Functional Independence Measure, SF-36 physical functioning and the Tinetti scale. Outcomes were collected at baseline, immediately following the intervention period and 3 months following the end of the intervention. The experimental group showed a significant increase in functional independence and gait speed (10 m walk test) at the end of the treatment and follow-up, higher than the

minimal detectable change. The control group showed a significant increase in the gait endurance (6-min walk test) at the follow-up, higher than the minimal detectable change. Both treatments were effective in the improvement of gait performances, although the statistical analysis of functional independence showed a significant improvement in the experimental group, indicating possible advantages during generic activities of daily living compared with overground treatment. *International Journal of Rehabilitation Research* 39:29–35 Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

Stroke is the leading cause of death and of serious long-term disability in adults; 3 months after stroke, 20% of individuals remain wheelchair bound and 70% walk at reduced velocity (Sakuma *et al.*, 2014). Improvement in walking after stroke is a priority for many patients and is one of the most frequently demanded goals of rehabilitation, and interventions that effectively enhance locomotor function are essential to improve quality of life of many stroke survivors and their families (Maclean *et al.*, 2000).

Stroke patients, when they regain ambulatory function, walk with a typically asymmetrical gait pattern, slow and metabolically inefficient. These characteristics are associated with difficulty advancing the paretic limb and bearing weight through the more affected limb, leading to instability and increased risk of falls. Muscle weakness,

muscle tonus, muscle disuse, balance and reduced cardiorespiratory capacity contribute towards decrease walking velocity and endurance and finally worsen the disability (Perry *et al.*, 1995).

To restore gait, modern concepts of rehabilitation favour a repetitive task-specific approach (French *et al.*, 2007). In the past 10 years, it has also been shown that higher intensities of walking practice result in better outcomes for individuals after stroke (Van Peppen *et al.*, 2004).

For gait training, it is important to walk repetitively in a natural gait similar to overground gait (Dobkin, 2004), and with proprioceptive and exteroceptive feedback (Barbeau, 2003), which recreates conditions favourable to motor learning.

In recent years, as an adjunct to overground gait training, treadmill training has been introduced for the rehabilitation of individuals after stroke (Moseley *et al.*, 2005). Treadmill training with and without body-weight support enables the repetitive practice of a generic gait cycle (Taveggia *et al.*, 2014). Manually assisted Body-Weight

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Supported Treadmill Training is a contemporary approach to gait rehabilitation after stroke, whereas when a patient walks on a treadmill, the therapists manually facilitate hemiparetic limb and trunk control in an effort to normalize upright and reciprocal walk and dynamic postural control. The advantages of this approach are that reduced motion ability is required to start locomotion; thus, early poststroke training effects can be observed in overground gait, that is, gait symmetry, speed and endurance as well as motor impairment and balance scores (McCain *et al.*, 2008).

A disadvantage of Body-Weight Supported Treadmill Training might be the effort required by therapists to set the paretic limbs and to control weight shift, thereby possibly limiting the duration of the active therapy, especially in more impaired patients. Automated electro-mechanical gait machines for automated assistive walking training were developed to reduce dependence on therapists and can be differentiated into end-effector and exoskeleton devices.

Selection of patients and an early application of robot-aided rehabilitation are considered a prerequisite to achieve the best results. However, the impact of other factors such as the type of technology in relationship to the patient's selection as well as the duration/intensity of the robot-aided treatment has not received more attention (Mehrholtz *et al.*, 2013). The main aim of the present study is to compare the effects of electromechanical-assisted gait training after stroke and overground conventional physical therapy in a double-blind research for functional gait recovery of individuals unable to walk independently.

Methods

Design

We conducted a double-blind (evaluator and statistician) randomized-controlled trial. Informed consent was obtained from all participants and procedures were performed according to the Declaration of Helsinki. Before participation in the study, all patients signed an informed consent form. The protocol (N° U0074917/11110) was approved by the Local Ethical Committee. The study has been registered at the Trial registration Current Controlled Trials website.

Setting

Postacute physical and rehabilitation medicine.

Participants

Sample size and power calculations were performed before carrying out the study to determine the number of participants needed in each group with the ENE 3.0 software (GlaxoSmithKline, Universidad Autónoma, Barcelona, Spain). The calculations were based on detecting a mean difference of 0.32 m/s minimally clinically important difference on a 6MWT (Westlake and

Patten, 2009), a two-tailed test, an α level of 0.05 and a desired power of 80%. The estimated desired sample size was 12 individuals per group.

Thirty-two participants, aged 18 to 85 years, were recruited for the study from March 2012 to July 2013. All inpatients had hemiparesis resulting from a single stroke (confirmed by computed tomography or MRI) less than 6 months before the study. Diagnosis was made on the basis of a clinical evaluation, in compliance with gold criteria (Curfman *et al.*, 2014), by an expert neurologist physician (R.L.) with 10 years of experience in this exam. Each patient underwent a subjective and physical examination performed by a Physical Therapist experienced in neurology problems and rehabilitation to evaluate inclusion and exclusion criteria. All patients were diagnosed with poststroke hemiparesis (<6 months from onset) and were unable to walk independently (Functional Ambulation Classification scores < 4) (Masiero *et al.*, 2007). Exclusion criteria were as follows: severe cardiovascular disease; degenerative neurological or psychiatric diseases; and severe visual or auditory impairments. Patients with multiple cerebrovascular lesions or infratentorial lesions were not recruited.

Outcome measures

Primary outcomes: gait performances

Different assessment tools were used to determine the motor abilities of the participants. All evaluation procedures were performed by the same examiner, who was blinded to the aims of the study and to which group the participants were allocated. The 6-min walk test (6MWT) (Grecco *et al.*, 2013; ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002) and the 10 m walking test (TWT) (Dean *et al.*, 2001) were used to assess endurance and speed, respectively.

The 6MWT (ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002) quantifies functional mobility on the basis of the distance in metres travelled in 6 min. This outcome is a measure of endurance and is particularly significant to evaluate the possibility to perform continuative tasks, which are particularly important for the rehabilitation of poststroke patients and are relevant for an independent life (Chisari *et al.*, 2014).

The speed was quantified using the TWT over the ground (Dean *et al.*, 2001). The gait speed measurement is performed over the middle 6 m of the TWT and patients are asked to walk at a comfortable speed (Nascimento *et al.*, 2012). TWT can overestimate the speed over long distances in patients with impaired aerobic capacity; thus, the combination of 6MWT and TWT was considered to evaluate the gait performances of the patients. Patients were instructed to walk at a comfortable speed to use assistive devices (Hornby *et al.*, 2005).

Secondary outcomes: functional and balance

Afterwards, patients underwent the following functional tests.

- (1) Functional Independence Measure (FIM): it evaluates the assistance required by the patient to perform some everyday tasks (White *et al.*, 2011).
- (2) The Item Short-Form Health Survey (SF-36) physical functioning questionnaire is often used as a tool to assess the quality of life in various medical fields, where it is valued especially for its ability to capture the social dimensions of life (Vellone *et al.*, 2010).
- (3) The Tinetti scale, which includes subscores for balance and gait features (Tinetti, 1986). Fourteen items on this clinical test measure balance characteristics (scored out of 24) and 10 items examine gait features (scored out of 16), for a total score of 40, with higher scores indicating greater balance.

All outcomes measures were captured at baseline (pre), immediately after intervention (post), and at 3 months after intervention by an assessor blinded to group assignment. The sequence of testing for the outcome measures was randomized among the participants. The trial was designed according to the CONSORT publishing guidelines (Johnson and Green, 2009).

Protocol

The inpatient participants in both groups were treated by a clinician with postgraduate physiotherapist training and more than 10 years of clinical experience in the management of neurological disease. The physical therapist was blinded to all data that were collected for the study. The participants were assigned to experimental and control treatment groups by simple randomization. After the completion of all baseline measurements, using a computer program (GraphPad Software Inc., La Jolla, California, USA), patients were randomly assigned by an external assistant into one of two groups: an experimental group or a control group. All participants received 25 treatment sessions scheduled on separate days, at least 24 h apart and at the same time of day, 5 days per week, for 5 weeks. All outcomes were collected by an external assessor blinded to the treatment allocation of the participants. The variables were measured at baseline, after intervention, and follow-up.

Experimental treatment intervention

Patients in the experimental group received a multimodal treatment intervention consisting of 60 min of conventional treatment according to the Bobath approach and 30 min of robotic gait training on the Lokomat robotic system. Patients started the first session with 50% weight unload and 0.4 m/s gait speed; performance increments were allowed only in the following sessions. Participants were provided verbal encouragement to actively step in

conjunction with the movement presented by the Lokomat training.

Our patients were treated for a total dosage of 12:30 h with the Lokomat robotic system with programs of increasing difficulty on the basis of individual functional evolution.

Control intervention

Patients in the control group, in addition to the multimodal treatment intervention consisting of 60 min of conventional treatment according to the Bobath approach, received 30 min activities targeted at improvement in walking in substitution of the Lokomat (i.e. strengthening exercises of the knee extensors, hip lateral rotators and abductors, standing posture, reconditioning exercises).

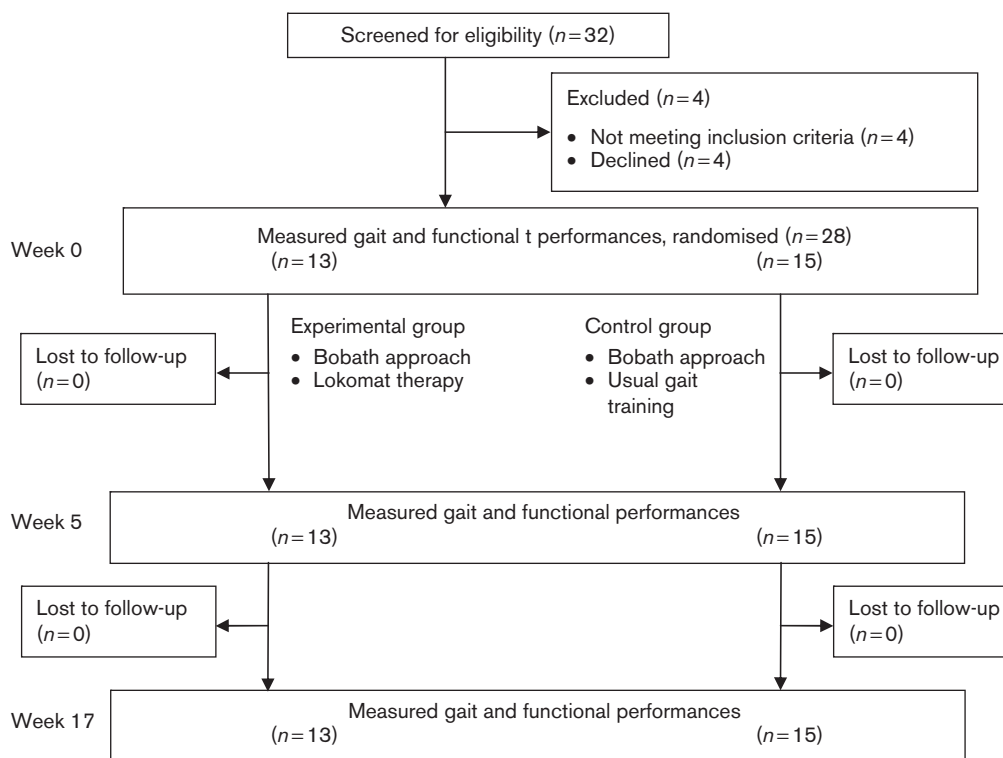
Statistical analysis

Data were analysed using SPSS, version 20.0 (SPSS Inc., Chicago, Illinois, USA) following an intention-to-treat analysis using the last value forward method. Group data were summarized using means and SDs. The Kolmogorov–Smirnov test confirmed the normality of the distribution of the data; thus, a repeated-measures analysis of variance (ANOVA) was used to determine the differences in 6MWT and TWT with time (pre-intervention, postintervention, and follow-up) as the within-patients factor and group (experimental or control) as the between-patients factor. The main hypothesis of interest was group-by-time interaction. Between-group differences were expressed as mean differences with 95% confidence intervals (CIs). Spearman's rank correlation coefficient (R_s) was used to evaluate the relationship between the 6MWT distance and the other parameters evaluated. The R_s values were interpreted according to Domholdt's recommendations. Finally, between-groups effect sizes were calculated using Cohen's d coefficient. An effect size greater than 0.8 was considered large, around 0.5 moderate, and less than 0.2 small. The statistical analysis was carried out at a 95% CI and a P -value less than 0.05 was considered statistically significant.

Results

Thirty-two consecutive patients ($n=32$) with poststroke hemiparesis, were screened for eligibility criteria. Twenty-eight patients (72 ± 6 years; 39.3% women) fulfilled all eligibility criteria, agreed to participate and were randomized to the experimental ($n=13$) or the control ($n=15$) group. The reasons for ineligibility were not independent gait ($n=2$) and medically unstable (no uncontrolled hypertension) ($n=2$). Figure 1 shows a flow diagram of patient recruitment and retention through the study. Baseline features of both groups were similar for all variables (Table 1). No adverse effects were detected during or after the application of the treatment, and none of the patients started drug therapy during the study.

Fig. 1



Flow diagram of criteria in the study.

Table 1 Baseline demographics for both groups

	Experimental (n=13)	Control (n=15)	P-value
Age (years)	71 ± 5	73 ± 7	0.76
Female sex [n (%)]	6 (46.2)	5 (33.3)	
Height	166 ± 0.07	167 ± 0.09	0.91
Weight	68.2 ± 14.0	67.4 ± 11.4	0.91
FAC	2.2 ± 1.3	1.1 ± 0.7	0.96
It-NIHSS	6.6 ± 3.0	7.6 ± 4.0	0.3
Days between stroke and preintervention	60.1 ± 49.5	39.4 ± 31.7	0.09

Data are expressed as mean ± SD.

FAC, Functional Ambulation Classification scores; It-NIHSS, Italian version of the National Institutes of Health Stroke Scale.

Primary outcomes: gait performances

10 m walking test

For speed measured over the TWT, there was significance for time [$F_{(2,0)}=11.009$; $P<0.001$; partial $\eta=0.52$], but not for group-by-time interaction [$F_{(2,0)}=0.298$; $P=0.75$; partial $\eta=0.03$].

Post-hoc analysis indicated that the patients receiving the experimental intervention experienced a significantly greater improvement in speed compared with those receiving the control intervention immediately after intervention and follow-up [mean and 95% CI; experimental group, 0.28 (0.51–0.06), $P=0.014$; control group, 0.21 (0.52–0.11), $P=0.3$ as well as at the 3-month follow-

up; experimental group, 0.25 (0.44–0.07), $P<0.01$; control group, 0.26 (0.52–0.003), $P=0.05$]. Between-groups effect sizes were small during all periods ($d<0.2$). The data are summarized in Table 2.

6-min walk test

In terms of the results of the 6MWT, the ANOVA showed a significant effect of time [$F_{(2,0)}=10.925$; $P<0.001$; partial $\eta=0.5$], but not for group-by-time interaction [$F_{(2,0)}=1.101$; $P=0.3$; partial $\eta=0.08$] for walking capacity (endurance).

Post-hoc analysis indicated that the patients in the control group had improved endurance, with a significant increase the 6MWT compared with those receiving the experimental intervention at the follow-up (control group, 124.2; 95% CI: 226.6–21.8; $P=0.017$). Between-groups effect sizes were small for all periods ($d<0.2$). The data are summarized in Table 2.

Secondary outcomes: functional

Outcomes for the Tinetti gait scale showed a significant effect of time [$F_{(2,0)}=24.562$; $P<0.001$; partial $\eta=0.7$], but not significant main effects of group [$F_{(2,0)}=1.02$; $P=0.4$; partial $\eta=0.8$] interactions.

Post-hoc analysis indicated that with both treatments, patients experienced a significant improvement in

Table 2 Mean (SD) for gait and functional performances at all study visits for each group, mean (SD) difference within groups and mean (95% confidence interval) difference between groups

Outcome	Groups						Difference within groups						Effect size		Difference between groups		
	Week 0		Week 5		Week 17		Week 5 minus week 0		Week 17 minus week 0		Week 5 minus week 0		Week 17 minus week 0		Cohen's <i>d</i>	Exp minus Con	Exp minus Con
	Exp (n = 13)	Con (n = 15)	Exp (n = 13)	Con (n = 15)	Exp (n = 13)	Con (n = 15)	Exp	Con	Exp	Con	Exp	Con	Exp	Con			
6MWT (min)	124.8 (117.6)	171.4 (130.0)	191.6 (178.4)	272.8 (155.6)	184.9 (139.8)	295.6 (183.9)	66.8 (30.3)	101.4 (40.6)	59.6 (27.5)	124.2* (36.9)	111.3 (-78.2 to 300.7)	81.2 (-126.7 to 289.2)	-0.49	111.3 (-78.2 to 300.7)	81.2 (-126.7 to 289.2)		
TWT (m)	0.27 (0.25)	0.46 (0.26)	0.56 (0.44)	0.66 (0.19)	0.53 (0.37)	0.72 (0.38)	0.28* (0.08)	0.21 (0.1)	0.25* (0.07)	0.26 (0.09)	0.19 (-0.31 to 0.7)	0.11 (-0.42 to 0.63)	-0.3	0.19 (-0.31 to 0.7)	0.11 (-0.42 to 0.63)		
Tinetti gait scale	3.3 (2.9)	5.2 (1.9)	5.4 (2.7)	8.6 (3.8)	5.8 (2.9)	8.6 (1.9)	2.1* (0.6)	3.4* (0.8)	2.4* (0.4)	3.4* (0.6)	2.8 (-0.4 to 0.4)	3.2 (-0.6 to 7.0)	-0.97	2.8 (-0.4 to 0.4)	3.2 (-0.6 to 7.0)		
FIM	75.6 (22.8)	90.8 (15.3)	89.4 (24.3)	100.2 (11.0)	100.1 (21.8)	100.6 (9.9)	13.8* (3.3)	9.4 (4.6)	24.5* (4.4)	12.8 (6.2)	3.5 (-19.0 to 26.0)	10.8 (-14.1 to 35.7)	-0.57	3.5 (-19.0 to 26.0)	10.8 (-14.1 to 35.7)		
SF-36 PF	20.8 (31.1)	26.0 (30.5)	28.4 (30.3)	21.0 (25.1)	36.5 (28.9)	19.0 (19.0)	8.5 (7.4)	5.0 (8.5)	16.2 (7.0)	-7.0 (8.0)	7.8 (-16.8 to 32.5)	17.5 (-5.9 to 41.0)	0.27	7.8 (-16.8 to 32.5)	17.5 (-5.9 to 41.0)		

6MWT, 6-min walk test; Con, control group; Exp, experimental group; FIM, Functional Independence Measure; SF-36 PF, 36-Item Short-Form Health Survey Physical Functioning; TWT, 10 m walking test.

*Significantly different within group, $P < 0.05$ (95% confidence interval).

*Significant difference between group, $P < 0.05$ (95% confidence interval).

balance immediately after intervention and follow-up (all, $P < 0.01$, Table 2).

Outcomes for FIM indicated a significant time factor [$F_{(2,0)} = 17.371$; $P < 0.001$; partial $\eta = 0.57$]. The group-by-time interaction was not significant [$F_{(2,0)} = 1.71$; $P = 0.2$; partial $\eta = 0.12$]. The post-hoc analysis showed significant differences between the 25 sessions and follow-up for the experimental group (all, $P < 0.003$).

For SF-36 physical functioning, the ANOVA showed no significant effect of time [$F_{(2,0)} = 1.455$; $P = 0.3$; partial $\eta = 0.2$] and for group-by-time [$F_{(2,0)} = 0.854$; $P = 0.4$; partial $\eta = 0.07$] interactions.

Spearman's rank correlation coefficients showed a strong, significant and positive relationship between the 6MWT distance and the TWT and Tinetti gait scale ($R_s = 0.792$ and 0.603 , respectively, all $P < 0.001$). No significant correlation was found between the 6MWT distance and weight, height and FIM. Finally, a strong, significant and positive correlation was found between the TWT and the Tinetti gait scale ($R_s = 0.578$, $P = 0.003$).

Discussion

Lokomat intervention with conventional therapy has been used in neurorehabilitation for the purpose of recreating conditions favourable to motor learning by facilitating active and intensive performance in important tasks. Functional recovery is achieved through use-dependent cortical reorganization, and active participation increases levels of physiological reorganization and provides more clinical benefits. Evidence shows that the addition of a robotic intervention to usual care result in improvements in gait function and generic activities of daily living.

This randomized-controlled trial examined the effects of an additional intervention with Lokomat gait rehabilitation on subacute patients with poststroke hemiparesis versus conventional physical therapy without this device. Low-level performances are measured as gait speed and gait endurance. Gait speed is a predictor of adverse outcomes (Abellan van Kan *et al.*, 2009) and the experimental group showed a significant increase in this parameter at the end of the treatment and at the follow-up. The change in speed detected is higher than the MDC, which is in the range 0.07–0.36 m/s (Fulk and Echtermach, 2008); thus, the improvement is also clinically significant. However, the control group showed a significant increase in gait endurance at the follow-up that was also higher than the MDC (Abellan van Kan *et al.*, 2009). A more synthetic measure of gait functional performances is introduced with the Tinetti gait scale, which confirmed the previous results: both treatments are effective and neither of them can be preferred in terms of pure gait performances (Hidler *et al.*, 2009). An interesting result emerged when higher functional level performances were measured, that is, with FIM, which

shows how the experimental treatment produced functional improvements at the end of the treatment period and also at the follow-up. These positive data on functional performances after the end of the treatment in the experimental group suggest that improvements in motor skills and functional gait, in poststroke patients, continue over time and do not lose their effectiveness even after many months of the end of the robotic training, pointing to a long-lasting motor recovery on the basis of functional relearning induced by intense and repetitive stimulations. Although this phenomenon of persistence is of great interest in neurorehabilitation, it is still relatively unknown and deserves further investigation to design better rehabilitation programmes and maintenance therapy (Pollock *et al.*, 2014).

Recovery walking capacity is closely related to life quality in poststroke patients (Pohl *et al.*, 2007): this characteristic is measured using the SF-36 (only with the Physical Function component) and both are comparable, with no preference. These functional improvements are not reflected in improvement in the quality of life, probably because of the reduced number of patients or the low sensitivity of the SF-36 scale, which produces high SD, or patient selection, which does not exclude depressed individuals.

The recovery of walking after stroke is a major goal in gait rehabilitation priority of many patients, and our patients showed an improvement in walking speed after the experimental treatment in combination with physical and rehabilitation therapy.

A recent systematic review (Mehrholtz *et al.*, 2013) provided evidence that the use of electromechanical-assisted gait training devices in combination with physiotherapy increases the chance of regaining independent walking ability for individuals after stroke.

Specifically, this type of intervention seems to be suitable for early subacute patients unable to walk. Probably repetitive robot-assisted training of locomotion intensified patient training, increasing the number of gait cycles and improving step accuracy with reduced trainer effort.

In the second analysis, we focused on the importance of determining a training intervention sufficiently intense in duration and type of rehabilitation programme.

Our patients were treated for a total duration of 12:30 h with robot-assisted training with programmes of increasing difficulty on the basis of individual functional evolution.

This dose effect in the literature is a determining factor of the efficacy of an intervention.

We believe that the increased effectiveness of gait training could be caused by motivational support associated to virtual reality tasks.

After a stroke event, a secondary reduction of cardiorespiratory capacity emerges, due to reduced physical activity. Thus intensive training may be effective on these patients, due to aerobic effects associated with the high metabolic cost of the training. These improvements are indicative of a potential aerobic conditioning effect of treatments in patients with lower walking capacity.

This work has many limitations; first, the reduced number of patients and second, the number of sessions and the duration of the treatment were selected on the basis of experience without specific clinical trials.

Conclusion

Both treatments are effective in the improvement of gait performances, although only experimental treatment produced functional improvements. Further analyses should be carried out to understand why functional gait improvements are not reflected in the patients.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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