Efficacy of Electromechanical-Assisted Gait Training on Walking Ability and Symmetry After Brain Injury: A Multicenter Randomized Controlled Trial

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Abstract

Background: Electromechanical-assisted gait training might be one of the most effective interventions to promote motor recovery after brain injury. But many studies still have difficulties to clarify the difference with conventional gait training.

Objective: To evaluate the effectiveness of electromechanical-assisted gait training compared to conventional gait training on walking ability and symmetry in stroke patients.

Methods: Patients with stroke (n = 144) were randomly assigned to control (physical therapist-assisted gait training) and experimental groups (electromechanical gait training). Both types of gait training were performed for 30 minutes each day, 5 days a week for 4 weeks. Main outcome measures are changes in functional ambulatory category (FAC). Secondary outcomes were walking abilities and walking symmetries of swing time and step length.

Results: FAC showed significant improvement after 4 weeks intervention in both groups. Walking abilities showed significant improvement after intervention, but, walking symmetries did not in both groups. According to sub-group analysis of stroke duration of 90 days, FAC and walking abilities in both groups showed significant improvement in subacute group compared to chronic group. However, walking symmetries did not show any significant changes in subacute and chronic group. Swing time asymmetry in the experimental group showed significant improvement in chronic group while it did not in the control group.

Conclusion: Electromechanical-assisted gait training by Exowalk® was shown to be as effective as conventional gait training with a physiotherapist. Electromechanical-assisted gait training for four weeks can change gait patterns close to normal by reducing swing time asymmetry in chronic stroke patients.

Trial registration: KCT0003411 Clinical Research Information Service (CRIS), Republic of Korea.

Introduction

There are a number of people with disabilities whose total or partial motor functions of the lower limbs have significantly decreased due to brain lesions. Rehabilitation following brain injury of stroke has the potential to improve their walking efficiency and functional independence for activities of daily living.[1] For gait rehabilitation, highly repetitive practice can restore gait function.[2] Automated electromechanical gait training devices have been developed to assist people with brain lesions for walking training, mainly in Europe and the United States.[3] Some of them have been commercialized.

Electromechanical-assisted gait training that requires repetitive tasks can improve the neuro-plasticity for motor learning with a focus on reorganization of brain tissue, resulting in better balance and faster gait speed.[4] In the 2017 Cochran review, seven papers showed that walking rehabilitation robot treatment was more effective than conventional gait rehabilitation treatment, while six papers did not.[5] Accumulating evidence suggests that high-intensity repetitive task-specific practice might be the most effective strategy to promote motor recovery after stroke. Electromechanical-assisted gait training represents such treatment option.[6]

Most of previous studies on electromechanical-assisted gait training were mainly based on clinical evaluations with 10-meter walking speed, distance walked in 6 minutes, and so on. Several studies have used some quantitative gait indices, and these are limited to spatiotemporal parameters.[7,8] It is currently unknown if spatiotemporal gait asymmetries are in fact related to the effect of electro-mechanical gait training.[9] The resulting spatiotemporal gait asymmetries (i.e., stance time, swing time, and step length asymmetries) are well documented in many individuals post stroke. They have been purported to be related to impairments in balance.[9] Recent review indicated that there is still a need for well-designed, large-scale, multicenter studies to evaluate the benefits of electromechanical-assisted gait training for walking after stroke.[5] Comparisons between different devices and conventional training are also currently lacking. [5]

Exowalk® (HMH Co., HR-01, A67020.02, Grade2, South Korea) is an electromechanical-assisted gait trainer that can provide a stable and firm standing ability with little chance of falling (Fig. 1). It obviates the need for an additional cane or walker compared with currently popular exoskeletons. Such designs are user-friendly without needing a harness for weight support. However, many studies investigated the effectiveness by clinical evaluation and still have difficulties to clarify the difference between conventional and electromechanically assisted gait training. One reason for such difficulties was due to insufficient subjects[10–12] and, the other reason was lack of spatiotemporal analysis. The purpose of this prospective study was to investigate the effect of an electromechanical-assisted gait training using Exowalk® known to provide repetitive training with normal gait motion on walking ability and symmetry of stroke patients with a multi-center randomized design.

Methods

This was a multicenter, randomized, prospective and parallel-group study on the efficacy and safety of electromechanical -assisted gait trainer Exowalk®. All enrolled subjects were patients with stroke. Three clinical research centers participated in this trial as follows: Dongguk University Ilsan Hospital, Chungnam National University Hospital and Seoul National University Bundang Hospital. This research protocol was approved by each hospital as follows: Dongguk University Ilsan Hospital's Institutional Review board (IRB No. DUIH 2018-08-026-001), Chungnam National University Hospital's IRB (IRB No. CNUH 2018-09-033) and Seoul National University Bundang Hospital's IRB (IRB No. B-1810/497-001). And this study was registered at Clinical Research Information Service (CRIS, KCT0003411, Date of registration: 03/01/2019).

The screening was conducted based on data of patients who agreed to participate in this study, patients who met the inclusion and exclusion criteria. The target sample size was 144 subjects. Inclusion criteria were 1) those who had a stroke, 2) those who had a score of 10 or more in the Mini-Mental State Examination (MMSE), 3) those who had a Modified Ashworth Scale (MAS) Grade 2 or lower, and 4) those who could stand alone. Exclusion criteria were 1) those with poor cognition that made it difficult to carry out instructions, 2) those with ataxia that made unstable standing balance, 3) those with spasticity MAS Grade 3 or above, 4) those with severe leg arthritis, and 5) those with difficulty walking due to joint problems of the lower leg.

This was a randomized controlled trial and single blind trial. Subjects were assigned into an experimental group or a control group in accordance with a randomized allocation table for subjects who met both the inclusion/exclusion criteria and agreed to participate in this study. Randomization tables were created for each research organization. Randomization was conducted using a random number generator computerized with a block randomization method in SAS version 9.4 (SAS institute Inc., Cary, NC, USA). The single-blind methodology was that the outcome assessors were blind. Intervention and evaluation were performed by different physiotherapists with 5 years or more of experience, in order to increase reliability by minimizing the measurement error. At enrollment, patients were instructed not to reveal their allocation arm to the outcome assessor. The researcher who performed the randomization and data analyses was not involved in any assessment and training.

All patients in both groups were given 30 minutes of training per session, five times per week for four weeks. In addition, both groups performed basic rehabilitation (neurodevelopmental treatment, exercise for range of motion and strengthening). The experimental group received electromechanical-assisted gait training with Exowalk® and the control group received conventional gait rehabilitation treatment by therapists. Because patient's tolerance and safety of electromechanical gait training compared to physiotherapy need to be considered, Exowalk® facilitates less than 1000 steps in 30 min with a velocity of 1.8 km/h according to initial evaluation, although its maximum velocity is 2.3 km/h. Patients in this study were recommended to receive the electromechanical exoskeleton-assisted gait training at a comfortable speed. For subjects in the control group, the physiotherapist guided and walked the patient while assisting the subject on the side or the back

Analysis of data

In this study, demographic and clinical characteristics of subjects were measured and documented after screening. Demographic information included gender, date of birth, height, weight, and joint problems (or not). Clinical characteristics included the name of the diagnosis, the cause of the disability (brain infarction, cerebral hemorrhage), the paralysis side (Rt., Lt), the possibility of expressing intention (standard: MMSE 10 or higher), and the lower limb spasticity score (standard: MAS grade 2 or lower).

The change in functional ambulatory category (FAC) before and after gait training were primary outcomes to evaluate the efficacy of electromechanical exoskeleton-assisted gait training. FAC was determined the existence of independent walking through a concise level assessment. Primary endpoints were evaluated once at baseline (pre-intervention) four weeks after the baseline (post-intervention), and four weeks after the last treatment (follow-up). FAC was evaluated by dividing the degree of needing for assistance when walking to 1 to 6. FAC level ranged from Level 1 for 'nonfunctional' to Level 6 for 'independent without help for non-level surfaces'.

Secondary outcomes were the changes in Rivermead mobility index (RMI), 10-meter walk test (10mWT), 6-minute walk test (6MWT), Motricity Index (MI), Berg balance scale (BBS) and the changes in spatiotemporal parameters of swing time asymmetry and step length asymmetry. These evaluations were conducted once at baseline (pre- intervention), four weeks after the baseline (post- intervention), and four weeks after the last intervention (follow-up).

Second endpoints had a total of 7 assessments. First, RMI was used to evaluate motor skills. It consisted of 15 questions step by step, depending on the level ranging from bed rotation to running. A total of 15 questions were scored. Each was scored 1 point if yes or 0 if no. The total sum was used as a result of the evaluation. Second, walking velocity as a 10mWT was used to measure the speed during a 10-meter walking. The unit was m/sec (meter per second). Similarly, walking capacity was evaluated with a 6MWT to measure the distance that one could walk for 6 minutes. The unit was m (meter). The fourth item was MI. It was evaluated as 1 to 99 points by measuring the lower leg force level from the ankle to the knee. Assessment items consisted of three questions, each with a score of 0/9/14/19/25/33. The total sum of scores was used as the result of the evaluation. The fifth item was BBS to evaluate the balance ability with 0 to 56 points. There were 14 questions in total. Each question was scored from 0 to 4 points. The total sum of scores was used as the result of the evaluation. The last two evaluation items were measured with motion analysis devices for those who could walk stable without aids. Swing time asymmetry and step length asymmetry were analyzed by HumanTrack (Rbiotech, 1806A_DA004_H1FS, South Korea) a gait analysis system which is capable of performing walking analysis at a distance of 5-7 m without space restriction. The swing time was calculated based on phase of gait begins when the foot first leaves the ground and ends when the same foot touches the ground again. The step length was calculated as the distance between the heel of the foot and the heel of the other foot. Each asymmetry value was calculated as the absolute value difference between the paretic side and the non-paretic side. The physical content of the clinical alteration was reported by auditors, practitioners, and patients at each visit. All indication, data of onset, and period were recorded.

Sample size estimation

Based on results of a previous trial,[13] the mean change was 0.54 in the control group and 1 in the test group. Medical devices used in this work were expected to achieve approximately 25% better performance results than the test group, assuming a variation of 1.25. Thus, it was assumed that the difference in the change between the test medical device and the control device was 0.71. The largest value, 1.4, was assumed for conservative access to the standard deviation. Thus, 65 participants were needed for each group to achieve 80% power at a significant level of 0.05. Considering a possible dropout rate of 10%, 144 participants (72 participants per group) were determined to be the sample size.

Analysis

For demographic and clinical characteristics, categorical variables such as gender, joint problems, disability cause, paralysis side, and lower extremity MAS scores are presented as frequency and percentage. They were analyzed for pre-homogeneity with Chi-squired tests. Continuous variables are presented as mean, standard deviation (SD), and range of minimum and maximum (Min, Max). In case of height and weight satisfying normality, pre-homogeneity was analyzed using student's t-test. For age not satisfying normality, Wilcoxon rank sum test was used.

All values of primary and secondary outcomes are presented as mean and SD (Mean ± SD). Although basic results of FAC were scored 1, 2, 3, 4, 5, and 6 on an ordinal scale, FAC are presented as mean and SD because it was one of the most popular tools for measuring the ambulatory function. Within each group, values of pre and post-intervention changes were analyzed using paired t-test if normality was satisfied or Wilcoxon's signed rank test if normality was not satisfied. In addition, for comparison between pre and post-intervention values of test and control groups, student's t-test and Wilcoxon's rank sum test were performed (Table 2). Stroke duration was the most important factor that affected results. Subgroup analysis compared variations between subjects with stroke durations of 90 days or less (below 90 days) and those with 91 days or more (over 91 days) in the experimental group. For all results, values of pre and post-intervention changes were analyzed using paired t-test if normality was satisfied and Wilcoxon's signed rank test if normality was not satisfied. In order to compare pre-post changes between groups, the analysis was performed using student's t-test and Wilcoxon's rank sum test, depending on whether the normality was satisfied (Table 4). All statistical analyses were performed using SAS version 9.4 or later. All statistical tests were two-sided and the level of significance was set at 0.05.

Results

A total of 144 subjects were included in this study, 104 of whom completed the gait training and outcome measures at 4 weeks after the initiation of the intervention. Withdrawal before first evaluation due to personal reasons (n = 2), withdrawal before the first treatment due to personal reasons (n = 2), withdrawal after the first treatment due to personal reasons (n = 4), and incomplete second evaluation (n = 9) occurred in the experimental group (Fig. 2). Withdrawal before first evaluation due to personal reasons (n = 4), withdrawal before the first treatment due to personal reasons (n = 2), withdrawal after the first treatment due to personal reasons (n = 7), and incomplete second evaluation (n = 5) occurred in the control group. There were no significant differences in baseline characteristics between the control and experimental groups. All subjects could control their gait direction and speed and their mean MMSE was 24.81 ± 4.65 in experimental group and 23.69 ± 5.17 in control group. All subjects could ambulate with or without the assistance of another person (Table 1).

The mean FAC in the experimental group was 3.15 ± 1.39 before intervention (pre-intervention) and 4.22 ± 1.37 after the intervention (post-intervention) (Table 2). The mean FAC in the control group was 3.11 ± 1.29 pre-intervention and 4.20 ± 1.03 post-intervention. Between pre and post-intervention, the change in FAC showed significant improvement in both groups (Table 2). However, the change in FAC did not differ between the two groups. All secondary outcomes of walking abilities by clinical measures showed significant improvements after the intervention (Fig. 3), but all secondary outcomes of walking symmetries by spatiotemporal analysis did not in the control group. While all secondary outcomes of walking abilities by clinical measures also showed significant improvements after the intervention in the experimental group (Fig. 3), only swing time asymmetry among walking symmetries by spatiotemporal analysis showed significant improvement (Table 2). However, the changes in secondary outcomes of both walking abilities and symmetries did not differ between two groups (Table 2).

Of 104 total patients, 87 participated follow-up evaluation. Baseline characteristics of follow-up evaluation showed no significant differences between the control and experimental group. Most outcomes showed significant improvements and maintained at follow-up evaluation (Fig. 2).

When each group was divided into two groups according to stroke duration of 90 days, the changes in the gait abilities was greater in the below 90 days group than those in the over 91 days group in both the control group (Table 3) and the experimental group (Table 4). However, the changes in the gait symmetries did not show any difference between two groups. Only swing time asymmetry in the experimental group was improved significantly in the over 91 days group (p=0.0156) and the change in swing time asymmetry of the over 91 days showed more improvement than that in the below 90 days group although it did not reach the statistical significance (p=0.0991) (Table 4). No adverse events were found during gait training in either group.

Discussion

Electromechanical gait training devices have been developed and their effectiveness has been proven by the clinical studies for stroke patients.[14,15] Regarding clinical effects of electromechanical-assisted gait training, Mehrholz et al.[5] have demonstrated that it could improve post-stroke independent walking recovery when combined with physical therapy in patients suffering from a stroke. And it was effective for the patients in the first three months after stroke and those who are not able to walk.[5] In fact, there is growing evidence that the motor system is plastic following stroke and that motor training can be of aid, particularly in the first 3 months.[16–18] Considering that electromechanical-assisted gait training can provide unlimited, repetitive, and accurate motion, it could be also applied to stroke patients who could walk with or without another's assistance, especially for those who wish to walk better.[19–21] Exowalk® is an electromechanical exoskeleton-assisted gait-training device. It has a unique design which applies the exoskeleton in front of a robotic body and actualizes walking using motorized wheel controlled by the patient. There were two randomized controlled trials (RCTs) by Exowalk® which conducted to investigate the effect of electromechanical-assisted gait training for stroke patients. The first study revealed that gait training of 30 minutes with Exowalk® was effective, and stroke patients could have confidence in their gait and desire to continue gait training. However, the effect declined with increase of stroke duration.[22] The second study was conducted for chronic stroke patients of over 91 days and it revealed that it was not superior to conventional physiotherapy.[23] This study also revealed that electromechanical-assisted gait training was as effective as conventional gait training in the clinical measures, but the effect was superior in the below 90 days of stroke duration group. It was the same results as our previous studies.

Although our previous results showed the same effect of Exowalk® as conventional gait training, they did not show superiority assistant to conventional physiotherapy with subacute and chronic stroke patients for improving walking ability when it was used as a gait trainer. Recent documents showed similar or

superior effects of robot-assisted therapy in combination with conventional physiotherapy versus conventional therapy alone on gait recovery, especially for patients with a sub-acute stroke.[24–26] Most of these analyses were mainly based on clinical evaluations,[7,8] and our previous RCTs with Exowalk® were lack of spatiotemporal parameters, either. In addition, our previous RCTs were insufficient to clarify the effects of electromechanical-assisted gait training on stroke patients with the limitation of sample size estimation with unpredicted dropout rate. In systematic reviews of electromechanical-assisted gait training plus physiotherapy versus physiotherapy, there is still a need for large-scale and multicenter study with well design after stroke.[5] Therefore, we need the large-scale research of multicenter with conservative sample size estimation and need to evaluate the spatiotemporal analysis. Thus, the aim of this study was to evaluate the effectiveness of electromechanical-assisted gait training compared to conventional gait training in improving both walking ability by clinical measures and walking symmetry by spatiotemporal analysis. This study revealed that the walking abilities were improved after electromechanical gait training by clinical measures, but, the walking symmetries were not improved by spatiotemporal analysis. The previous study revealed that the chronic stroke patients have a desire to walk well,[23] and we measured the spatiotemporal parameter for those who could walk independently without aids in this study and found that swing time asymmetry reduced.

The difference in FAC change between pre and post intervention was 1.09 ± 1.01 in the control group and 1.07 ± 0.82 in the experimental group. When various interventions of gait training including conventional treatments are performed for stroke patients, FAC shows an improvement in a range of 0.3 to 1.0.[27–29] In this study, the change in FAC and secondary outcomes was significant enough clinically, but those declined in the over 91 days group. The Cochrane review by Mehrholz et al. revealed that electromechanical-assisted training for walking after stroke did not improve the walking capacity or velocity.[5] In this study, the walking capacity and velocity also improved after intervention in the below 90 days group, and those were not related to walking symmetry. Swing time asymmetry was improved significantly in the over 91 days in the experimental group, it did not affect walking capacity and velocity.

Electromechanically assisted gait training has been shown to be effective in patients with acute and sub-acute stroke, but not in those with chronic stroke, according to subgroup analysis of 461 participants in the chronic phase, defined as more than 90 days after stroke.[5] When the experimental group was divided into two groups according to the stroke duration of 90 days, most outcomes in the subacute patients showed improvements more than those in chronic patients in both control and experimental groups. The improvement of walking symmetry did not differ between control and experimental groups. However, swing time asymmetry showed different patterns from other outcomes. Swing time asymmetry showed significant improvement after intervention in the chronic patients in the experimental group. Because the chronic stroke patients had fixed paralysis, the step length asymmetry is also fixed. But, the swing time asymmetry was correctable by repetitive symmetric motion of gait training because the patients could control the swing speed and reduce limping. The extensive repetition of gait pattern, which is effective in establishing a robust pattern.[30] As motor impairment occurs over time, there is an adapted gait pattern.[31] Electromechanical gait training provides a large number of repetitive training with the normal gait pattern, which can be more effective in leading to pattern changes in chronic stroke patients who had an established gait patterns than in acute patients who had no fixed neurologic pattern which might be changeable over time.

Limitation

In this study, spatiotemporal parameters were important secondary outcomes to evaluate the effectiveness of electromechanical-assisted gait training. Since the inclusion criteria were stroke patient who could stand alone, many patients who needed walking aids or assistance were registered and we did not evaluate their gait analysis at the time of pre-intervention. Some of them became to walk independently without need of walking aids or assistance, but their spatiotemporal parameters could not be evaluated in this study. Thus, the number of spatiotemporal parameters were small when we divided the group according to stroke duration.

Conclusions

Electromechanical-assisted gait training by Exowalk® (HMH Co., Ltd, Incheon, Korea) was shown to be as effective as conventional gait training with a physiotherapist. The walking ability by clinical measures improved significantly after gait training, but the walking symmetry did not improve. These effects in both electromechanical-assisted gait training and conventional gait training groups maintained 4 weeks after intervention. According the results of sub analysis by stroke duration, the walking ability of the patients with subacute patients improved more than chronic patients in both groups. However, swing time asymmetry improved more in chronic patients than subacute patients. Electromechanical-assisted gait training could provide the repetitive normal gait cycle for four weeks and it could change gait patterns close to normal by reducing swing time asymmetry in chronic stroke patients.

Declarations

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

YGN and BSK made substantial contributions to the experimental design, data analysis, and drafting the manuscript. SKB, NJB, CYL and MJK made substantial contributions to the data collection, data analysis, and drafting the manuscript. LJW made substantial contributions to the development of the device, device maintenance during the clinical trial, and drafting of the manuscript. All authors read and approved the final manuscript.

References

1. Reisman DS, Rudolph KS, Farquhar WB. Influence of speed on walking economy poststroke. Neurorehabilitation and neural repair. Jul-Aug 2009;23(6):529-534.
2. Kidwell CS, Saver JL, Schubert GB, Eckstein M, Starkman S. Design and retrospective analysis of the Los Angeles Prehospital Stroke Screen (LAPSS). Prehospital emergency care : official journal of the National Association of EMS Physicians and the National Association of State EMS Directors. Oct-Dec 1998;2(4):267-273.
3. Bortole M, Venkatakrishnan A, Zhu F, et al. The H2 robotic exoskeleton for gait rehabilitation after stroke: early findings from a clinical study. Journal of neuroengineering and rehabilitation. Jun 17 2015;12:54.
4. Kwakkel G, Kollen B, Lindeman E. Understanding the pattern of functional recovery after stroke: facts and theories. Restorative neurology and neuroscience. 2004;22(3-5):281-299.
5. Mehrholz J, Thomas S, Kugler J, Pohl M, Elsner B. Electromechanical-assisted training for walking after stroke. The Cochrane database of systematic reviews. Oct 22 2020;10:CD006185.
6. Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: a systematic review. The Lancet. Neurology. Aug 2009;8(8):741-754.
7. Lo AC, Chang VC, Gianfrancesco MA, Friedman JH, Patterson TS, Benedicto DF. Reduction of freezing of gait in Parkinson's disease by repetitive robot-assisted treadmill training: a pilot study. Journal of neuroengineering and rehabilitation. Oct 14 2010;7:51.
8. Sale P, De Pandis MF, Le Pera D, et al. Robot-assisted walking training for individuals with Parkinson's disease: a pilot randomized controlled trial. BMC neurology. May 24 2013;13:50.
9. Patterson KK, Gage WH, Brooks D, Black SE, McIlroy WE. Evaluation of gait symmetry after stroke: a comparison of current methods and recommendations for standardization. Gait & posture. Feb 2010;31(2):241-246.
10. Conesa L, Costa U, Morales E, et al. An observational report of intensive robotic and manual gait training in sub-acute stroke. Journal of neuroengineering and rehabilitation. Feb 13 2012;9:13.
11. Taveggia G, Borboni A, Mule C, Villafane JH, Negrini S. Conflicting results of robot-assisted versus usual gait training during postacute rehabilitation of stroke patients: a randomized clinical trial. International journal of rehabilitation research. Internationale Zeitschrift fur Rehabilitationsforschung. Revue internationale de recherches de readaptation. Mar 2016;39(1):29-35.
12. Kim J, Kim DY, Chun MH, et al. Effects of robot-(Morning Walk((R))) assisted gait training for patients after stroke: a randomized controlled trial. Clinical rehabilitation. Mar 2019;33(3):516-523.
13. Watanabe H, Tanaka N, Inuta T, Saitou H, Yanagi H. Locomotion improvement using a hybrid assistive limb in recovery phase stroke patients: a randomized controlled pilot study. Archives of physical medicine and rehabilitation. Nov 2014;95(11):2006-2012.
14. Peurala SH, Airaksinen O, Huuskonen P, et al. Effects of intensive therapy using gait trainer or floor walking exercises early after stroke. Journal of rehabilitation medicine. Feb 2009;41(3):166-173.
15. Swinnen E, Duerinck S, Baeyens JP, Meeusen R, Kerckhofs E. Effectiveness of robot-assisted gait training in persons with spinal cord injury: a systematic review. Journal of rehabilitation medicine. Jun 2010;42(6):520-526.
16. Wolpert DM, Diedrichsen J, Flanagan JR. Principles of sensorimotor learning. Nature reviews. Neuroscience. Oct 27 2011;12(12):739-751.
17. Mossberg KA. Reliability of a timed walk test in persons with acquired brain injury. American journal of physical medicine & rehabilitation. May 2003;82(5):385-390; quiz 391-382.
18. Marque P, Gasq D, Castel-Lacanal E, De Boissezon X, Loubinoux I. Post-stroke hemiplegia rehabilitation: evolution of the concepts. Annals of physical and rehabilitation medicine. Nov 2014;57(8):520-529.
19. Kwakkel G, Kollen B, Lindeman E. Understanding the pattern of functional recovery after stroke: facts and theories. Restorative neurology and neuroscience. 2004;22(3-5):281-299.
20. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. Lancet. May 14 2011;377(9778):1693-1702.
21. Peurala SH, Karttunen AH, Sjogren T, Paltamaa J, Heinonen A. Evidence for the effectiveness of walking training on walking and self-care after stroke: a systematic review and meta-analysis of randomized controlled trials. Journal of rehabilitation medicine. May 2014;46(5):387-399.
22. Nam YG, Lee JW, Park JW, et al. Effects of Electromechanical Exoskeleton-Assisted Gait Training on Walking Ability of Stroke Patients: A Randomized Controlled Trial. Archives of physical medicine and rehabilitation. Jan 2019;100(1):26-31.
23. Nam YG, Park JW, Lee HJ, et al. Further effects of electromechanically assisted gait trainer (Exowalk(R)) in patients with chronic stroke: A randomized controlled trial. Journal of rehabilitation medicine. Sep 8 2020;52(9):jrm00097.
24. Chang WH, Kim MS, Huh JP, Lee PK, Kim YH. Effects of robot-assisted gait training on cardiopulmonary fitness in subacute stroke patients: a randomized controlled study. Neurorehabilitation and neural repair. May 2012;26(4):318-324.
25. Westlake KP, Patten C. Pilot study of Lokomat versus manual-assisted treadmill training for locomotor recovery post-stroke. Journal of neuroengineering and rehabilitation. Jun 12 2009;6:18.

26. Schwartz I, Meiner Z. Robotic-assisted gait training in neurological patients: who may benefit? Annals of biomedical engineering. May 2015;43(5):1260-1269.
27. Pohl M, Werner C, Holzgraefe M, et al. Repetitive locomotor training and physiotherapy improve walking and basic activities of daily living after stroke: a single-blind, randomized multicentre trial (DEutsche GAngtrainerStudie, DEGAS). Clinical rehabilitation. Jan 2007;21(1):17-27.
28. Hidler J, Nichols D, Pelliccio M, et al. Multicenter randomized clinical trial evaluating the effectiveness of the Lokomat in subacute stroke. Neurorehabilitation and neural repair. Jan 2009;23(1):5-13.
29. Yoshikawa K, Mizukami M, Kawamoto H, et al. Gait training with Hybrid Assistive Limb enhances the gait functions in subacute stroke patients: A pilot study. NeuroRehabilitation. 2017;40(1):87-97.
30. Wallard L, Dietrich G, Kerlirzin Y, Bredin J. Effects of robotic gait rehabilitation on biomechanical parameters in the chronic hemiplegic patients. Neurophysiologie clinique = Clinical neurophysiology. Sep 2015;45(3):215-219.
31. Wang Y, Mukaino M, Hirano S, et al. Persistent Effect of Gait Exercise Assist Robot Training on Gait Ability and Lower Limb Function of Patients With Subacute Stroke: A Matched Case-Control Study With Three-Dimensional Gait Analysis. Frontiers in neurorobotics. 2020;14:42.

Tables

Table 1. The baseline characteristic of the experimental and control group

Variables	Control group n=55	Experimental group n=54	p-value
Sex, n (%)			
Male	35(63.64%)	34(62.96%)	0.942*
Female	20(36.36%)	20(37.04%)	
Age			
Mean±SD	62.42±15.04	60.63±15.61	0.728##
Range(Min, Max)	22, 89	23, 86	
Height, cm			
Mean±SD	163.23±9.70	164.07±7.12	0.605#
Range(Min, Max)	146.4, 185.0	148.0, 177.8	
Weight, kg			
Mean±SD	64.24±11.21	64.22±10.70	0.990#
Range(Min, Max)	39.4, 95.1	38.7, 98.1	
Type, n(%)			
Infarction	34(61.82%)	33(61.11%)	0.939*
Hemorrhage	21(38.18%)	21(38.89%)	
Paretic side, n(%)			
Rt.	28(50.91%)	25(46.3%)	0.630*
Lt.	27(49.09%)	29(53.70%)	
MMSE			
Mean±SD	23.69±5.17	24.81±4.65	0.3063##
Range(Min, Max)	13, 30	10, 30	
MAS			
0	43(78.18%)	43(79.63%)	0.9362*
1	8(14.55%)	6(11.11%)	
1.5	1(1.82%)	1(1.85%)	
2	3(5.45%)	4(7.41%)	
Onset duration, day			
Mean±SD	522.40±1220.70	767.17±1435.78	0.1139##
Range(Min, Max)	3, 7529	1, 8435	

NOTE: MMSE Mini-mental state examination, MAS Modified Ashworth Scale

*:p-value obtained from Chi-square test

#:p-value obtained from Student's t-test

##:p-value obtained from Wilcoxon rank sum test

Table2. The difference of outcome changes in the experimental and control group

Variables	Control group					Experimental group				
	N	Pre	Post	Post-Pre	p-value	N	Pre	Post	Post-Pre	p-valu
FAC	55	3.11±1.29	4.2±1.03	1.09±1.01	<0.0001##	54	3.15±1.39	4.22±1.37	1.07±0.82	<0.00
RMI	55	6.51±3.82	8.56±3.68	2.055±3.21	<0.0001##	54	6.69±3.42	8.31±3.99	1.63±2.52	<0.00
10mWT (m/s)	55	0.45±0.29	0.57±0.33	0.17±0.23	<0.0001##	54	0.50±0.52	0.58±0.55	0.12±0.55	<0.00
6MWT	55	131.09±101.40	184.58±123.83	55.30±106.98	<0.0001##	54	115.95±105.03	180.93±127.58	61.48±91.08	<0.00
MI	55	55.24±16.48	66.69±17.23	11.45±13.87	<0.0001##	54	50.07±19.78	61.56±20.42	11.19±12.79	<0.00
BBS	55	26.22±17.17	38.67±13.48	12.45±13.91	<0.0001##	54	26.33±17.23	37.13±15.30	10.80±11.92	<0.00
Swing Time Asymmetry	19	200.58±144.33	201±154.40	0.42±169.79	0.7381##	16	205.19±122.78	134.75±104.73	-70.44±102.36	0.013
Step length Asymmetry	19	11.32±8.37	8.63±6.42	-2.68±7.41	0.1782##	16	6.31±7.95	7.75±8.80	1.44±5.95	0.461

NOTE: FAC Functional Ambulation Categories, RMI Rivermead Mobility Index, 10mWT 10-Meter Walk Test, 6MWT 6-Minute Walk Test, MI Motricity Index, BBS Scale

#:p-value obtained from Paired t-test

##:p-value obtained from Wilcoxon signed rank test

*:p-value obtained from Student's t-test

**:p-value obtained from Wilcoxon's rank sum test

Table 3. The difference of outcome changes with stroke duration in the control group

Variables	Stroke duration ≤ 90 days					Stroke duration ≥ 91 days				
	N	Pre	Post	Post-Pre	p-value	N	Pre	Post	Post-Pre	p-value
FAC	31	2.94±1.18	4.35±0.91	1.42±0.99	<0.0001##	24	3.33±1.40	4.00±1.14	0.67±0.87	<0.000
RMI	31	6.35±3.94	9.06±3.70	2.71±3.80	0.0004#	24	6.71±3.75	7.92±3.62	1.21±2.00	0.007#
10mWT	31	0.37±0.30	0.61±0.34	0.24±0.20	<0.0001##	24	0.38±0.35	0.53±0.31	0.15±0.29	0.0011
6MWT	31	132.61±110.32	204.39±119.48	71.77±85.11	0.0011##	24	107.27±94.17	159.00±127.16	51.73±143.37	0.0233
MI	31	55.65±16.41	72.97±15.96	17.32±13.74	<0.0001#	24	54.71±16.92	58.58±15.59	3.88±9.97	0.0694
BBS	31	24.52±17.67	39.13±13.69	14.61±13.78	<0.0001##	24	28.42±16.63	38.08±13.48	9.67±13.87	<0.000
Swing Time Asymmetry	9	203.78±142.10	165.33±162.19	-38.44±136.10	0.4214#	10	197.7±153.93	233.1±147.92	35.4±195.77	0.5814
Step length Asymmetry	9	8.72±7.80	6.44±3.68	-2.28±5.83	0.2734##	10	13.65±8.57	10.6±7.82	-3.05±8.91	0.3073

NOTE: FAC Functional Ambulation Categories, RMI Rivermead Mobility Index, 10mWT 10-Meter Walk Test, 6MWT 6-Minute Walk Test, MI Motricity Index, BBS Scale

#:p-value obtained from Paired t-test

##:p-value obtained from Wilcoxon signed rank test

*:p-value obtained from Student's t-test

**:p-value obtained from Wilcoxon rank sum test

Figures

Table 4. The difference of outcome changes with stroke duration in the experimental group

Variables	Stroke duration ≤ 90 days					Stroke duration ≥ 91 days				
	N	Pre	Post	Post-Pre	p-value	N	Pre	Post	Post-Pre	p-valu
FAC	21	2.95±1.16	4.52±1.25	1.57±1.08	<0.0001##	33	3.27±1.53	4.03±1.42	0.76±0.79	<0.000
RMI	21	6.43±4.24	9.19±4.76	2.76±3.45	0.0013##	33	6.85±3.03	7.76±3.38	0.91±1.31	0.0003
10mWT (m/s)	21	0.38±0.28	0.70±0.67	0.33±0.51	<0.0001##	33	0.50±0.63	0.49±0.45	-0.01±0.51	0.0115
6MWT	21	126.19±85.71	205.14±115.51	78.95±94.75	0.0011#	33	98.89±116.34	160.05±135.28	61.15±115.16	0.0001
MI	21	51.14±16.44	70.10±18.66	18.95±13.61	<0.0001#	33	49.39±21.86	55.64±19.73	6.24±9.50	0.0007
BBS	21	23.38±17.65	39.71±14.29	16.33±12.76	<0.0001##	33	28.21±16.96	35.48±15.91	7.27±10.03	<0.000
Swing Time Asymmetry	8	142.25±113.02	114.13±104.90	-28.13±96.97	0.439#	8	268.13±102.35	155.38±107.36	-112.75±94.65	0.0156
Step length Asymmetry	8	2.63±2.39	4.75±4.37	2.13±5.06	0.25##	8	10±9.92	10.75±11.23	0.75±7.02	0.9688

NOTE: FAC Functional Ambulation Categories, RMI Rivermead Mobility Index, 10mWT 10-Meter Walk Test, 6MWT 6-Minute Walk Test, MI Motricity Index, BBS Scale

#:p-value obtained from Paired t-test

##:p-value obtained from Wilcoxon signed rank test

*:p-value obtained from Student's t-test

**:p-value obtained from Wilcoxon rank sum test

Figure 1

Exowalk® (HMH Co. Ltd, South Korea)

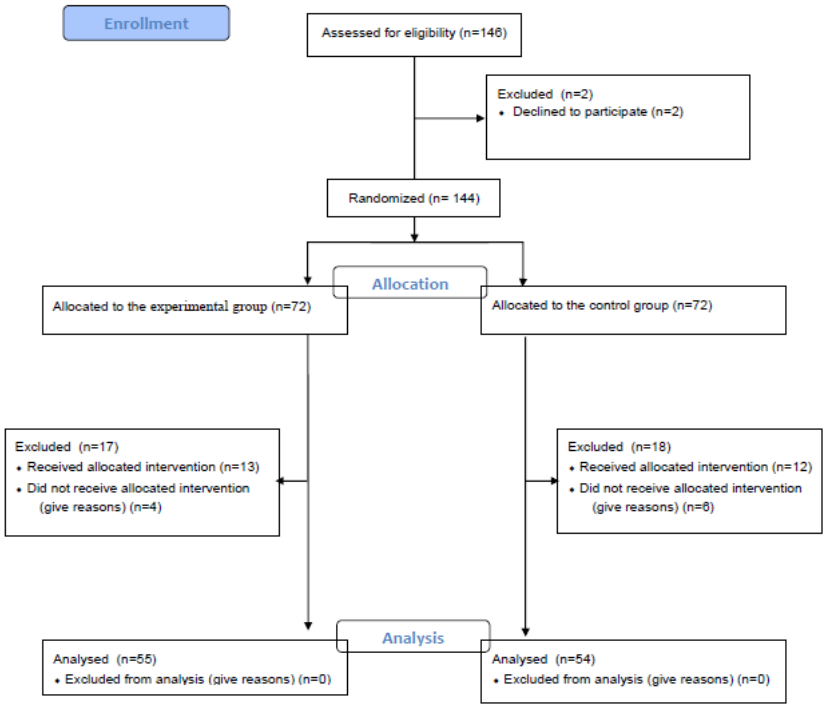

Figure 2

CONSORT flow diagram

Figure 3

The changes of outcome measures pre-intervention (0 week), immediate post-intervention (4 weeks) and 4 weeks after intervention (follow up) of the control group (solid line) and experimental group (dotted line).