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Review article

What does best evidence tell us about robotic gait rehabilitation in stroke patients: A systematic review and meta-analysis

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ABSTRACT

Background: Studies about electromechanical-assisted devices proved the validity and effectiveness of these tools in gait rehabilitation, especially if used in association with conventional physiotherapy in stroke patients.
Objective: The aim of this study was to compare the effects of different robotic devices in improving post-stroke gait abnormalities.
Methods: A computerized literature research of articles was conducted in the databases MEDLINE, PEDro, COCHRANE, besides a search for the same items in the Library System of the University of Parma (Italy). We selected 13 randomized controlled trials, and the results were divided into sub-acute stroke patients and chronic stroke patients. We selected studies including at least one of the following test: 10-Meter Walking Test, 6-Minute Walk Test, Timed-Up-and-Go, 5-Meter Walk Test, and Functional Ambulation Categories.
Results: Stroke patients who received physiotherapy treatment in combination with robotic devices, such as Lokomat or Gait Trainer, were more likely to reach better results, compared to patients who receive conventional gait training alone. Moreover, electromechanical-assisted gait training in association with Functional Electrical Stimulations produced more benefits than the only robotic treatment (−0.80 [−1.14; −0.46], $p > .05$).
Conclusions: The evaluation of the results confirm that the use of robotics can positively affect the outcome of a gait rehabilitation in patients with stroke. The effects of different devices seems to be similar on the most commonly outcome evaluated by this review.

1. Introduction

The World Health Organization (WHO) defines stroke as a "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 h or longer or leading to death, with no apparent cause other than of vascular origin" [1].

Stroke is the most frequent cause of disability in adults in the industrialized world, and the cost of stroke-related care is increasing rapidly [2]. The Global Burden of Disease 2013 Study has shown that, although stroke incidence, prevalence, mortality, and disability-adjusted life-years rates tended to decline from 1990 to 2013, the overall stroke burden in terms of absolute number of people affected by, or who remained disabled from, stroke, has increased across the globe in both men and women of all ages [3]. Indeed, the annual stroke incidence is approximately 180 patients per 100,000 inhabitants in the industrialized world.

Post-stroke disability may involve mobility and stability of joints, muscle power, tone and reflexes, muscle endurance, control of movement, and gait pattern functions. These impairments lead to problems with transferring, maintaining body position, mobility, balance, and walking. In the first 6 months post stroke, almost all patients experience at least some predictable degree of functional recovery. Although the majority of stroke patients learn to walk independently by 6 months after stroke, gait and balance problems persist through the chronic stage of the condition and have a significant impact on patients' quality life [4].

Recovery of walking function to obtain independence in daily life is one of the main goals of patients after stroke [5] and in gait rehabilitation, and no conventional treatment approach has so far

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proven to be superior [6]. Recovery of walking function mainly occurs within the first 11 weeks after stroke [7]; indeed, patients who experience functional recovery after that time are few [8]. Modern concepts favor a task-specific repetitive approach [9]. Electromechanical-assisted gait training and treadmill training, with and without partial body weight support, are used in combination with over-ground gait training to improve function of patients after stroke. The main difference between electromechanical-assisted and treadmill training is that the process of gait training is automated and supported by an electromechanical solution. Treadmill training with partial body weight support (BWS) enables wheelchair-bound subjects to repetitively practice complete gait cycles. The major limitation of treadmill therapy as a daily routine is the effort required by two or even three therapists in assisting the gait of severely affected subjects, setting the paretic limb, and controlling the trunk movements [8]. Electromechanical devices can be used to give patients intensive practice (in terms of high repetition) of complex gait cycles with a reduced effort for therapist, as they no longer need to set the paretic limbs or assist trunk movements [10].

Electromechanical devices for automated-assistive walking training can be differentiated into end-effector and exoskeleton devices [11]. The definition of an end-effector principle is that patient's feet are placed on footplates, whose trajectories simulate the stance and swing phases during gait training whereas exoskeleton devices are outfitted with programmable drives or passive elements, which move the knees and hips during the phases of gait [12]. Examples of exoskeleton type of devices are the "LOPES" (Lower Extremity Powered Exoskeleton) [13] and the "Lokomat" [14]. Example of end-effector devices are the "G-EO-system" [12], the "Lokohelp" [15] the "Haptik Walker" [16] and the "Gait Trainer GT1" [17].

The main objective of the present review was to compare the effects of different devices used in gait rehabilitation after stroke and provide information about the main differences.

2. Material and methods

2.1. Study selection

We included only randomized controlled trials (RCTs) written in English aimed to study the effects of robotic devices in improving walking in stroke patients. In particular, we selected articles including the comparison between electromechanical devices, such as exoskeleton and end-effector devices. Thus, we selected studies meeting the following criteria: (i) use of robotic treatment versus conventional physiotherapy treatment; (ii) use of electromechanical devices, with and without functional electric stimulation versus conventional physiotherapy treatment; (iii) use of exoskeleton robots versus end-effector robots. On the contrary, we excluded studies met the following criteria: (i) heterogeneity in the groups; (ii) lack of differentiation of subacute patients from chronic patients; (iii) inappropriate randomization. All case-report studies and case-control studies were excluded for lack of sustainability of results, as well as works concerning the development of new technologies. Reviews that evaluated effects of electromechanical and robotic-assisted gait training plus and versus conventional physiotherapy for regaining and improving walking after stroke were also excluded.

2.2. Outcomes

Our primary outcome was the efficacy of exoskeleton robot devices and of end-effector robot devices in stroke patients, measured through the walking speed (m/s) at the end of the intervention. Therefore, we selected studies including one of the following test: 10-Meter Walking Test (10-MWT) [18], 6-Minute Walk Test (6MWT) [19], Timed-Up-and-Go (TUG) [20], and 5-Meter Walk Test (5MWT) [21]. The secondary outcome was the efficacy of robotic treatment in comparison with robotic treatment in combination with the Functional Electrical Stimulation (FES), measured by the Functional Ambulation Categories (FAC) scale, a functional walking test that evaluates ambulation ability [22].

2.3. Search strategy

In order to identify studies that potentially fulfill the inclusion criteria, a research was conducted in the electronic bibliographic Cochrane Library, Medline and PEDro databases, besides in the Library System of the University of Parma (Italy), up to June 2015 without language restrictions for relevant articles. Terms used in the search of the articles were "Lokomat"; "Gait Trainer"; "Lokohelp"; "G-EO system"; "Lokomat stroke"; "Stroke AND robotics"; "Gait AND robotics AND stroke"; "Gait AND electromechanical AND stroke"; "Gait Trainer AND robotics AND stroke"; "Gait Trainer AND electromechanical AND stroke".

At first, the titles of the identified publications were read, and the studies having connection with post-stroke robotic rehabilitation were selected. Then, the abstracts of the articles were read, in order to discard the ones that did not meet the inclusion criteria. In case of uncertainty, or when the abstract was not available, the entire article was read.

2.4. Data analysis

The main analysis concerned the comparison of robotic rehabilitation versus conventional rehabilitation, subdividing the studies by type of electromechanical device used (exoskeleton or end-effector). We also performed a subgroup analysis by subdividing the studies according to the elapsed time from stroke: patients in the sub-acute phase (within six months), and patients in the chronic phase (more than six months). Finally, the comparison between robotic treatment alone and robotic treatment in combination with FES was performed.

Since many studies used different outcome scales, the treatment effect of an intervention was estimated by pooling the standardized mean difference (SMD) with 95% confidence interval (CI). Heterogeneity was quantified by the estimated between-study variance τ^2 and I^2. When the level of heterogeneity was higher than 75%, we considered the results obtained by the application of the random effects model. All data were analyzed using Comprehensive Meta-analysis 3 (Biostat, Englewood, USA). P-values lower than 0.05 were considered statistically significant.

3. Results

Fig. 1 represents our study selection process. A total of 3881 records were identified after having searched by using the aforementioned keywords, and 3 additional records identified through other sources. After reading title and removing duplicates, 60 articles were identified. Twenty-seven articles were further excluded during the phase of abstract reading. All case-report studies and case-control studies were excluded for lack of sustainability of results. Eight articles were not available in full text and journals were not present in the catalogs of our library. Four of the 17 remaining studies were excluded, given that they were systematic reviews. Thus, only 13 randomized controlled trials were selected for our work, with a total of 673 participants (mean age at baseline: 61.8 ± 5.6 years), as reported in Table 1. The mean ± SD trial duration was 4.6 ± 1.9 weeks, and it was significantly longer in

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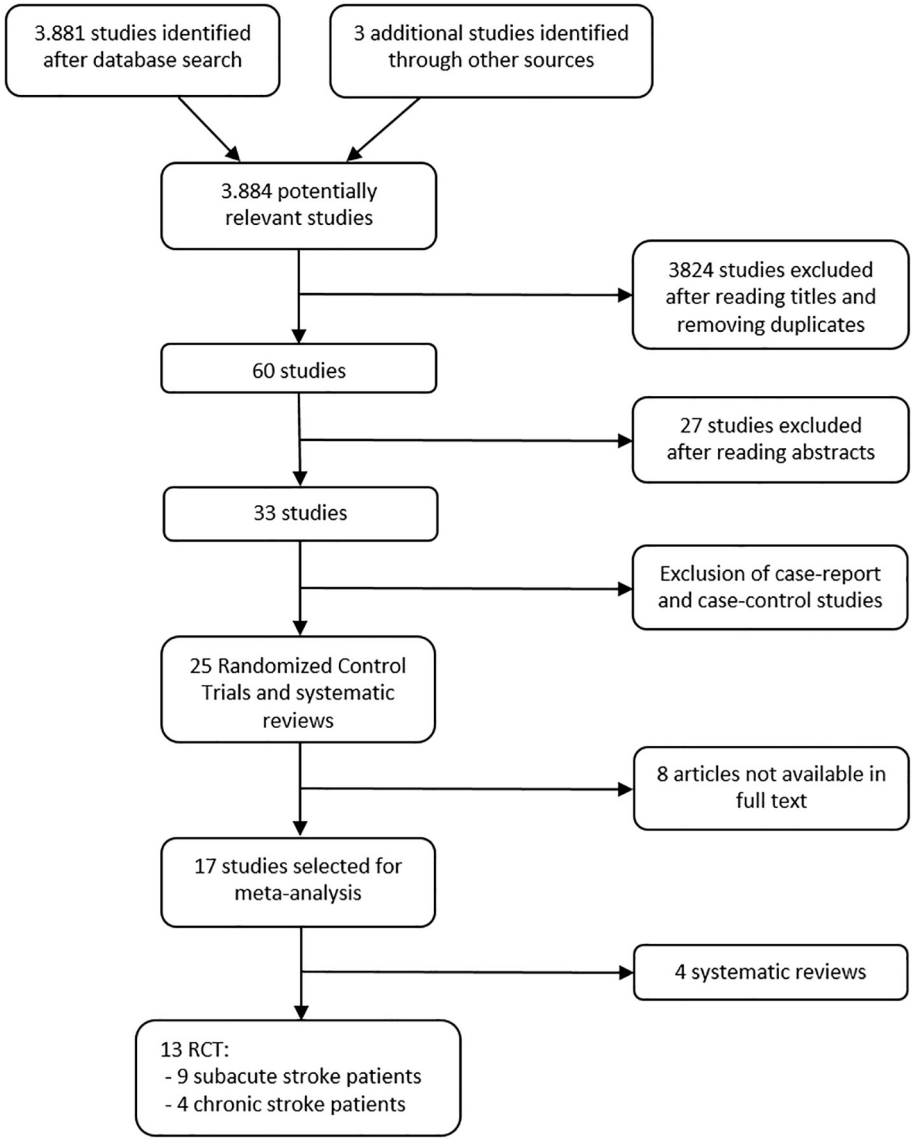

Fig. 1. Flow diagram of the study selection process.

Table 1
Overview of the RCTs included in the meta-analysis.

Study, year [Ref]	Device	Subjects	Age, years	Time onset	Outcome for walking speed	Duration	FES
End-effector studies							
Werner, 2002 [8]	Gait Trainer	30	60	7 weeks	FAC; 10-MWT	2 weeks	No
Peurala, 2005 [30]	Gait Trainer	90	52	3 years	10-MWT; 6 MWT	3 weeks	Yes
Tong, 2006 [32]	Gait Trainer	54	68	3 weeks	FAC; 5 MWT	4 weeks	Yes
Ng, 2008 [33]	Gait Trainer	44	67	3 weeks	FAC; 5 MWT	4 weeks	Yes
Pohl, 2007 [34]	Gait Trainer	155	63	4 weeks	FAC; 10-MWT; 6 MWT	4 weeks	No
Dias, 2007 [35]	Gait Trainer	40	69	47 weeks	10-MWT	5 weeks	No
Peurala, 2009 [5]	Gait Trainer	56	68	8 days	FAC; 10-MWT; 6 MWT	3 weeks	No
Exoskeleton studies							
Husemann, 2007 [36]	Lokomat	30	59	≤200 days	FAC; 10-MWT	4 weeks	No
Schwartz, 2009 [37]	Lokomat	58	63	22 days	FAC; TUG	6 weeks	No
Hidler, 2009 [38]	Lokomat	63	57	4 months	FAC; 6 MWT	24 sessions	No
Westlake, 2009 [39]	Lokomat	16	57	40 months	6 MWT	4 weeks	No
Kelley, 2013 [40]	Lokomat	21	66	2,6 years	10-MWT; 6 MWT	8 weeks	No
van Nunen, 2014 [41]	Lokomat	30	55	63 days	FAC; 10-MWT	8 weeks	No

10-MWT = 10-Meter Walking Test; 6 MWT = 6-Minute Walk Test; TUG = Timed-Up-and-Go; 5 MWT = 5-Meter Walk Test; EMS = Elderly Mobility Scale; FAC = Functional Ambulation Categories.

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studies involving exoskeletons (6.0 ± 2.0 weeks) than in those with end-effectors (3.6 ± 1.0 weeks). The mean age of participants at baseline was 61.8 ± 5.6 years.

In two studies neither the patients nor the research physical therapist were blinded to the treatment. In nine studies, there was no blinding of participants, while in only one study there was no blinding of personnel. One study did not report any information about blindness of participants or personnel. Eleven trials reported dropouts at post-training or at follow-up for death or outbreaks of disease.

For the primary outcome, the trials used different assessment scales in order to measure the walking speed (m/s) at the end of the intervention: 10-MWT was used in 8 studies, 6 MWT in 2 studies, 5 MWT in 2 studies, and TUG test in one study.

Since there was no significant heterogeneity for any analyses, a fixed effects analysis was used.

Fig. 2 shows meta-analyses of robot-assisted therapy (treatment) versus conventional rehabilitation (control), subdivided by type of electromechanical device used. Overall, there were 469 participants in seven end-effector robot studies (mean age 63.9 ± 6.1), and 218 participant in six exoskeleton robot studies (mean age 58.0 ± 4.2). We found that the end-effector device was significantly effective in improving walking speed compared to control (0.38 [0.21; 0.55], $p < .05$). On the contrary, we found no evidence that the exoskeleton robot was more effective than conventional therapy (−0.12 [−0.38; 0.14], $p > .05$).

Nine trials included 520 participants in the sub-acute phase: 339 in 5 end-effector robot studies, and 181 in 4 exoskeleton robot studies. We found that end-effector device was significantly effective in improving walking speed compared to control (0.48 [0.23; 0.71], $p < .05$), as well as the exoskeleton robot, although it did not reach the statistical significance (0.12 [−0.18; 0.42], $p > .05$) (Fig. 3). Four trials involved 167 participants in the chronic phase: 130 in two end-effector robot studies, and 37 in two exoskeleton robot studies. Overall, we found no significant difference between the robotic treatment and conventional therapy concerning their effectiveness on post-stroke gait impairment, neither for end-effector devises (−0.05 [−0.44; 0.34], $p > .05$) nor for exoskeleton devices (−0.13 [−0.74; 0.48], $p > .05$) (Fig. 4).

Notably, 9 studies measured the ambulation ability by means of FAC. Among these, 6 trials included patients who could not walk independently at study onset (FAC < 3), and 3 included 3 groups of treatment: (i) robotic treatment, (ii) conventional treatment, and (iii) robotic treatment in combination with the Functional Electrical Stimulation (Table 1). We compared FAC scores of participants who underwent the robotic treatment with the participants who underwent the robotic treatment + FES, to assess what kind of therapy provides the best result. Since only two studies used the FAC scale, the RCT by Peurala et al. was not included in this part of the meta-analysis. As showed in Fig. 5, the comparison between these two groups provides evidence that electromechanical–assisted gait training in association with Functional Electrical Stimulations produces more benefits than the only robotic treatment (−0.80 [−1.14; −0.46], $p > .05$).

4. Discussion

This systematic review further supports the use of robot-assisted therapy to improve motor function in stroke patients, but when this is coupled to conventional physical therapy. Moreover, our work shows that the earlier the training starts, the better the gait recovery. One main hypothesis for the better patient's improvement with mechanically assisted walking could be that the intervention provides the opportunity to perform a more intensive, repetitive, and task-oriented training than would be possible with the conventional over-ground walking alone.

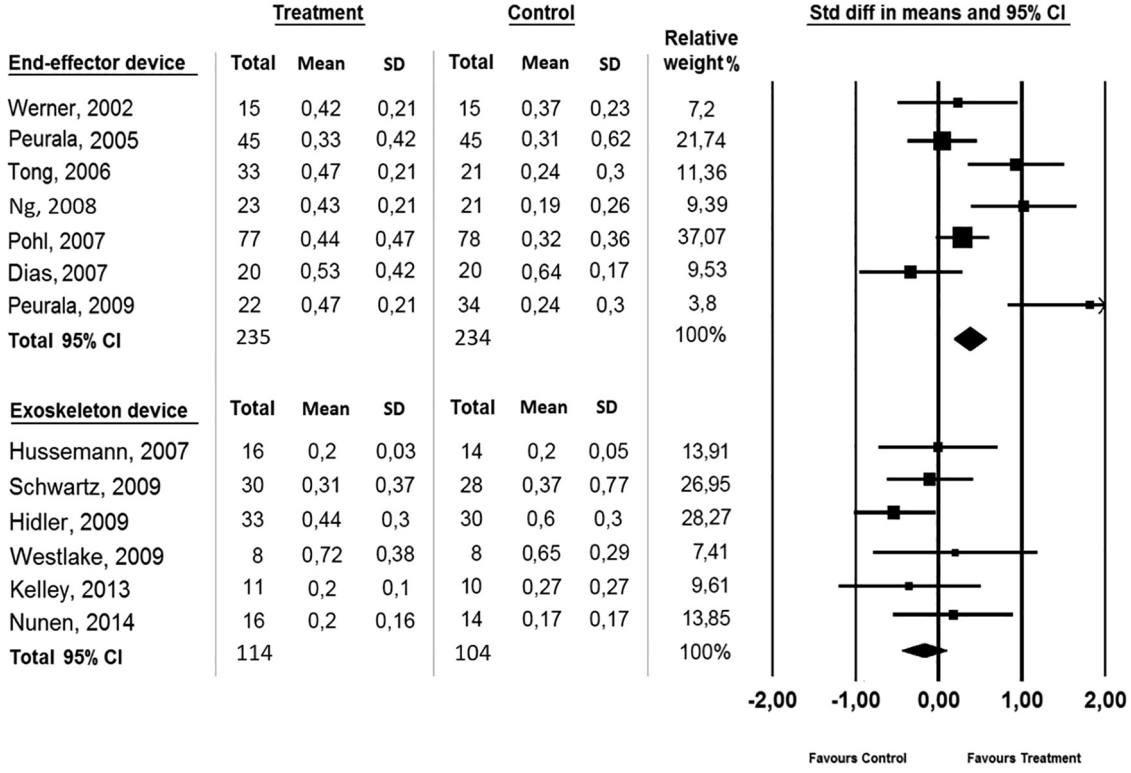

Fig. 2. Comparison of robot-assisted therapy (treatment) versus conventional rehabilitation (control) on end-effector and exoskeleton devices. Number of participants, with mean and standard deviation (SD) of walking speed (m/s) at the end of the rehabilitative treatment are presented for each study in any group. The point estimates and the overall effects, with 95% confidence intervals, are indicated by a diamond in the forest plots.

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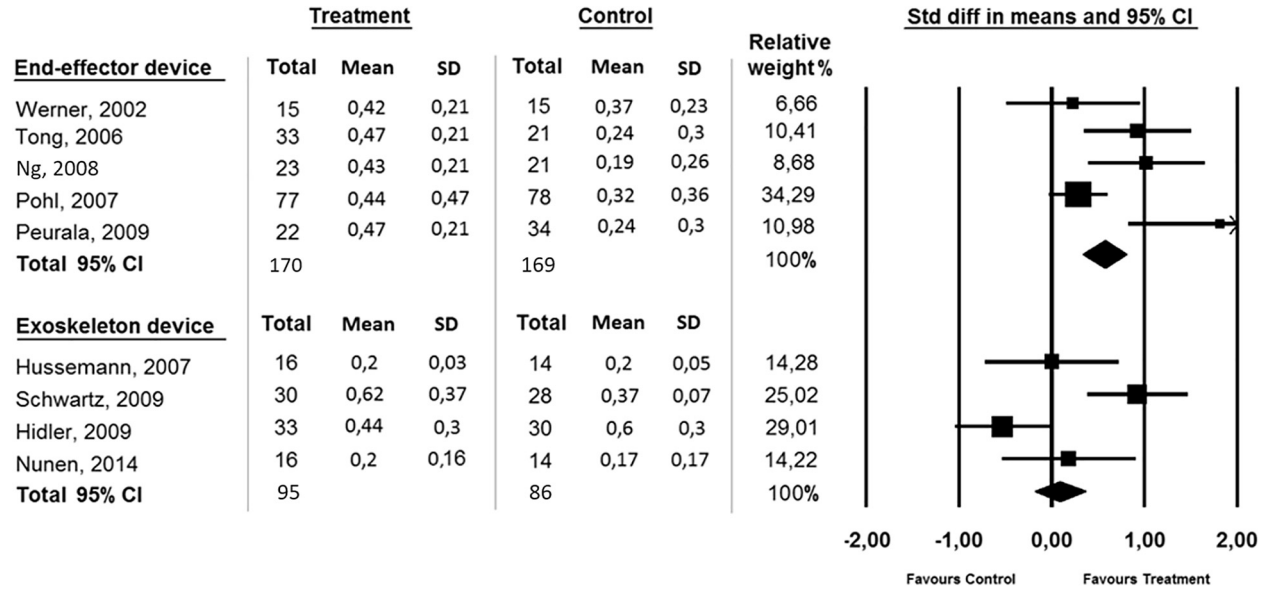

Fig. 3. Comparison of robot-assisted therapy (treatment) versus conventional rehabilitation (control) on end-effector and exoskeleton devices in sub-acute stroke patients. Number of participants, with mean and standard deviation (SD) of walking speed (m/s) at the end of the rehabilitative treatment are presented for each study in each group. The point estimates and the overall effects, with 95% confidence intervals, are indicated by a diamond in the forest plots.

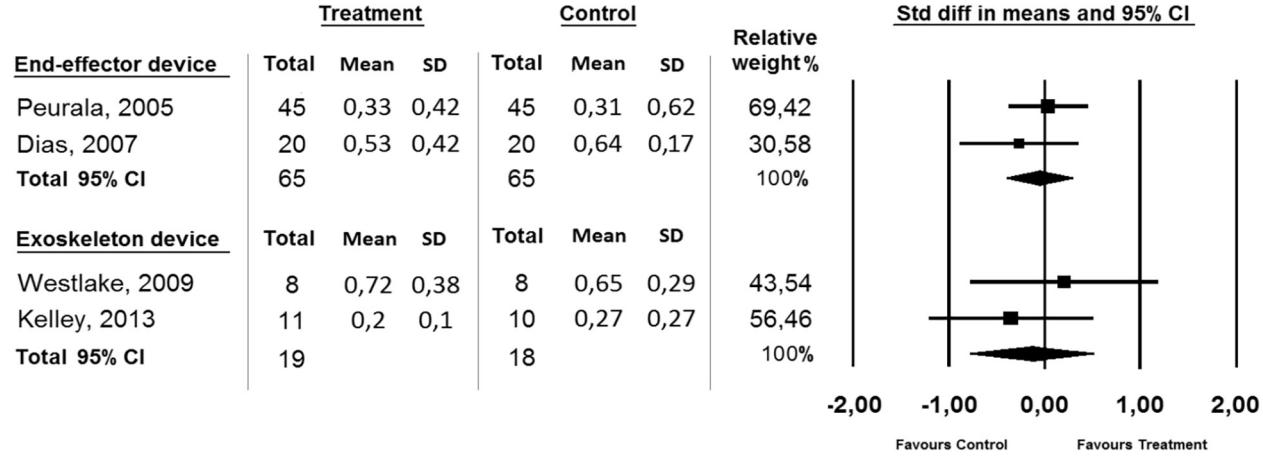

Fig. 4. Comparison of robot-assisted therapy (treatment) versus conventional rehabilitation (control) on end-effector and exoskeleton devices in chronic stroke patients. Number of participants, with mean and standard deviation (SD) of walking speed (m/s) at the end of the rehabilitative treatment are presented for each study in each group. The point estimates and the overall effects, with 95% confidence intervals, are indicated by a diamond in the forest plots.

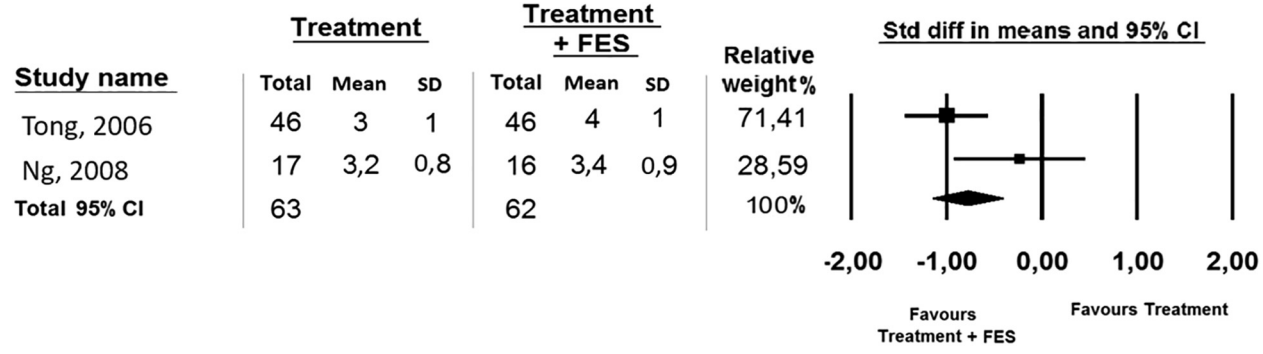

Fig. 5. Comparison of robot-assisted therapy (treatment) versus robotic treatment in combination with the Functional Electrical Stimulation. Number of participants, with mean and standard deviation (SD) of FAC scale at the end of the rehabilitative treatment are presented for each study in each group. The point estimates and the overall effects, with 95% confidence intervals, are indicated by a diamond in the forest plots.

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In this work, we firstly subdivided the selected articles by the electromechanical devices used in the trial (i.e. end-effectors and exoskeletons), and then by the elapsed time from stroke (i.e. subacute and chronic phase).

Exoskeletons are wearable devices that operate mechanically and simultaneously to the human body, with possible interference and friction with the limb natural movement. Thus, several critical biomechanics factors have to be considered in the design of limb exoskeletons, such as degree of freedom (DoF), ranges of motion (RoM) and joint torque. Indeed, the limb exoskeletons should have sufficient DoF as compared to human's limb in order to reproduce the human natural motions and minimize the user's discomforts [23]. Whilst, end-effector stationary robots use footplates to guide the feet and thereby reproduce gait trajectories, and represent an alternative to the treadmill-centered devices. Such tools are able to apply mechanical force to the distal segments of the lower limbs, allowing imitating the stance and swinging phases of gait while the patient is on the devices, without friction and interference. In both the device types, the BWS mechanism is used to off-load a part of the weight of the patient during the stance phase, reducing the load that needs to be overcome by the patient and ensuring safety and stability during walking.

We are not completely able to state the reason why patients undergoing end-effector training had better outcomes than those submitted to exoskeleton devices. However, our findings are in agreement with a previous review demonstrating the efficacy of the end effector Gait Trainer, only in patients affected by stroke in the post-acute phase, whereas exoskeletons had controversial results both in the acute and subacute phases [24]. Moreover, a Cochrane systematic review showed that the greatest benefits, with regard to independence in walking and walking speed, can be achieved in individuals who are non-ambulatory at the start of the study and in those for whom the intervention is applied early post-stroke [25]. According to this, our review demonstrates that sub-acute stroke patients trained with electromechanical devices in combination with conventional physiotherapy treatment reached better results (with regard to an increase change to achieve independent walking) than those undergoing conventional physical therapy.

In chronic stroke patients, we did not find a significant evidence that the robotic treatment provided better effects than the conventional therapy. The patients who received conventional therapy also improved their motor ability, but the functional gain remained poor. Thus, it would seem that robotic rehabilitation is a valuable post-stroke treatment, leading to the best results in the subacute phase.

Recovery from a stroke event is a complex process that occurs through a combination of spontaneous and mediated processes. Partial structural and functional impairment likely recovers through a potentiation and extension of residual brain areas, whereas complete lesions of specific brain areas require a substitution by functionally related systems [26,27].

Although it is widely recognized that most spontaneous behavioral recovery tends to occur within the first 3 months after stroke onset, different patterns of recovery may then emerge depending on many complex factors, and therefore, neuroplasticity phenomena with functional recovery may be present also in the chronic phase.

Such processes and related outcomes should be taken into consideration to better understand when to expect recovery, plan the most appropriate treatment, and determine the timing of rehabilitation, including the robotic one.

Another interesting finding by the present review is that subacute stroke patients undergoing electromechanical devices in combination with functional electrical stimulation reached the best results. Indeed, it has been found that FES may improve motor function compared with both no intervention and training alone, suggesting that FES should be used in stroke rehabilitation to improve the ability to perform activities [28]. However, the best therapeutic effects of FES on the body function and activity levels occur when it is used as a training modality [29].

A big limitation of the studies included in this systematic review is that patients are not clearly classified on the basis of FAC scale. Only one study [30] divided patients in respect of their ambulation ability. Moreover, another important factor influencing the effects of the therapy is the duration of training, and unfortunately, either the number of trained steps during the rehabilitation and the precise training intensities were not often clearly reported in the studies. Finally, we did not evaluate whether or not the robotic training was associated to an augmented feedback, given that the use of virtual reality may have played a pivotal role in post-stroke motor recovery [31].

In conclusion, robot-assisted gait rehabilitation can increase the length, intensity, and the number of physiotherapy sessions, reducing both therapist burden and healthcare costs. Based on our findings, we may argue that patients with different levels of post-stroke impairment have a different answer to the two main types of robot devices (i.e. end-effectors and exoskeletons), although for both the device types the better results were obtained in the sub-acute phase. Thus, robotic neurorehabilitation may be considered a valuable tool in improving gait abnormalities and reducing disability with a consequent betterment of post-stroke patients' quality of life. Further studies should be fostered to assess whether this robotic training may be effective also in the chronic phase, and to evaluate the long-term after-effects.

Declaration of interest

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

References

[1] World Health Organization. The World Health Report: 2002: Reducing Risks, Promoting Healthy Life. World Health Organization; 2002.
[2] Dobkin BH. Clinical practice. Rehabilitation after stroke. N Engl J Med 2005;352:1677–84.
[3] Feigin VL, Norrving B, Mensah GA. Global burden of stroke. Circ Res 2017;120:439–48.
[4] Eng JJ, Tang PF. Gait training strategies to optimize walking ability in people with stroke: a synthesis of the evidence. Expert Rev Neurother 2007;7(10):1417–36.
[5] Peurala SH, Airaksinen O, Huuskonen P, Jäkälä P, Juhakoski M, Sandell K, Tarkka IM, Sivenius J. Effects of intensive therapy using gait trainer or floor walking excercise early after stroke. J Rehab Med 2009;41:166–73.
[6] Gresham GE, Duncan PW, Stason WB, et al. Post-stroke Rehabilitation. Clinical Practice Guidelines, No. 16. US Department of Health and Human Services. Public Health Service, Agency for Health Care Policy and Research; 1995. AHCPR Publication No. 95-0662.
[7] Jørgensen HS, Nakayama H, Raaschou HO, Olsen TS. Recovery of walking function in stroke patients: the copenhagen stroke study. Arch Phys Med Rehabil 1995;76(1):27–32.
[8] C. Werner, S. Von Frankenberg, T. Treig, M. Konrad, S. Hesse. Treadmill training with partial body weight support and an electromechanical gait trainer for restoration of gait in subacute stroke patients, a randomized crossover study. 33 June 2002, pp. 2895–2901.
[9] Pohl M, Werner C. Repetitive locomotor training and physiotherapy improve walking and basic activities of daily living after stroke: a single-blind, randomized multicenter trial. Clin Rehabil 2007;21:17–27.
[10] Mehrholz J, Pohl M. Electromechanical-assisted gait training after stroke: a systematic review comparing end-effector and exoskeleton devices. J Rehabil Med 2012;44:193–9.
[11] Mehrholz J, Elsner B, Werner C, Kugler J, Pohl M. Electromechanical-assisted training for walking after stroke (Review). Cochrane Database Syst Rev 2013(7):CD006185.
[12] Hesse S, Waldner A, Tomelleri C. Innovative gait robot for the repetitive practice of floor walking and stair climbing up and down in stroke patients. J Neuroeng Rehabil 2010;7:30.
[13] J. Veneman, R. Kruidhof, F.C.T. van der Helm, H. van der Kooy, Design of a series elastic- and bowden cable-based actuation system for use as torque-actuator

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in exoskeleton-type training robots. In: Proceeding of the ICOOR 2005, June 28-30, Chicago, USA.
[14] Colombo G, Joerg M, Schreier R, Dietz V. Treadmill training of paraplegic patients using a robotic orthosis. J Rehabil Res Dev 2000;37:693–700.
[15] Freivogel S, Schmalohr D, Mehrholz J. Improved walking ability and reduced therapeutic stress with an electromechanical gait device. J Rehabil Med 2009;41(9):734–9.
[16] Schmidt H, Hesse S, Bernhardt R, Krüger J. Haptik walker – a novel haptik foot device. ACM Trans Appl Percept 2005;2:166–80.
[17] Hesse S, Sarkodie-Gyan T, Uhlenbrock D. Development of an advanced mechanised gait trainer, controlling movement of the centre of mass, for restoring gait in non-ambulant subjects. Biomed Tech (Berl) 1999;44(7–8):194–201.
[18] Wade DT, Wood VA, Heller A, Maggs J, Langton Hewer R. Walking after stroke. Measurement and recovery over the first 3 months. Scand J Rehabil Med 1987;19(1):25–30.
[19] Sciurba FC, Slivka WA. Six-minute walk-testing. Semin Resp Crit Care Med 1998;9:383–91.
[20] Mathias S, Nayak US, Isaacs B. Balance in elderly patients: the "get-up and go" test. Arch Phys Med Rehabil 1986;67:387–9.
[21] Salbach NM, Mayo NE, Higgins J, Ahmed S, Finch LE, Richards CL. Responsiveness and predictability of gait speed and other disability measures in acute stroke. Arch Phys Med Rehabil 2001;82:1204–12.
[22] Holden MK, Gill KM, Magliozzi MR, Nathan J, Piehl-Baker L. Clinical gait assessment in the neurologically impaired reliability meaningfulness. Phys Ther 1984;64(1):35–40.
[23] Calabrò RS, Cacciola A, Bertè F, Manuli A, Leo A, Bramanti A, Naro A, Milardi D, Bramanti P. Robotic gait rehabilitation and substitution devices in neurological disorders: where are we now? Neurol Sci 2016;37(4):503–14.
[24] Schwartz I, Meiner Z. Robotic-assisted gait training in neurological patients: who may benefit? Ann Biomed Eng 2015;43(5):1260–9.
[25] Mehrholz J, Elsner B, Werner C, Kugler J, Pohl M. Electromechanical-assisted training for walking after stroke. Cochrane Database Syst Rev. 2013;7. CD006185.
[26] Jones TA, Adkins DL. Motor system reorganization after stroke: stimulating and training toward perfection. Physiology (Bethesda) 2015;30(5):358–70.
[27] Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: a systematic review. Lancet Neurol 2009;8(8):741–54.
[28] Howlett OA, Lannin NA, Ada L, McKinstry C. Functional electrical stimulation improves activity after stroke: a systematic review with meta-analysis. Arch Phys Med Rehabil 2015;96(5):934–43.
[29] Kafri M, Laufer Y. Therapeutic effects of functional electrical stimulation on gait in individuals post-stroke. Ann Biomed Eng 2015;43(2):451–66.
[30] Peurala SH, Tarkka IM, Pitkänen K, Sivenius J. The effectiveness of body weight-supported gait training and floor walking in patients with chronic stroke. Arch Phys Med Rehabil 2005;86(8):1557–64.
[31] Moreira MC, de Amorim Lima AM, Ferraz KM, Benedetti Rodrigues MA. Use of virtual reality in gait recovery among post stroke patients – a systematic literature review. Disabil Rehabil Assist Technol 2013;8(5):357–62.
[32] Tong RK, Ng MF, Li LS. Effectiveness of gait training using an electromechanical gait trainer, with and without functional electric stimulation, in subacute stroke: a randomized controlled trial. Arch Phys Med Rehabil 2006;87(10):1298–304.
[33] Ng MF, Tong RK, Li LS. A pilot study of randomized clinical controlled trial of gait training in subacute stroke patients with partial body-weight support electromechanical gait trainer and functional electrical stimulation: six-month follow-up. Stroke 2008;39(1):154–60.
[34] Pohl M, Werner C, Holzgraefe M, Kroczek G, Mehrholz J, Wingendorf I, Hoölig G, Koch R, Hesse S. Repetitive locomotor training and physiotherapy improve walking and basic activities of daily living after stroke: a single-blind, randomized multicentre trial (DEutsche GAngtrainerStudie, DEGAS). Clin Rehabil 2007;21(1):17–27.
[35] Dias D, Laíns J, Pereira A, Nunes R, Caldas J, Amaral C, Pires S, Costa A, Alves P, Moreira M, Garrido N, Loureiro L. Can we improve gait skills in chronic hemiplegics? A randomised control trial with gait trainer. Eura Medicophys 2007;43(4):499–504.
[36] Husemann B, Müller F, Krewer C, Heller S, Koenig E. Effects of locomotion training with assistance of a robot-driven gait orthosis in hemiparetic patients after stroke: a randomized controlled pilot study. Stroke 2007;38(2):349–54.
[37] Schwartz I, Sajin A, Fisher I, Neeb M, Shochina M, Katz-Leurer M, Meiner ZPMR. The effectiveness of locomotor therapy using robotic-assisted gait training in subacute stroke patients: a randomized controlled trial.. PM R 2009;1(6):516–23.
[38] Hidler J, Nichols D, Pelliccio M, Brady K, Campbell DD, Kahn JH, Hornby TG. Multicenter randomized clinical trial evaluating the effectiveness of the Lokomat in subacute stroke. Neurorehabil Neural Repair 2009;23(1):5–13.
[39] Westlake KP, Patten C. Pilot study of Lokomat versus manual-assisted treadmill training for locomotor recovery post-stroke. J Neuroeng Rehabil 2009;6:18.
[40] Kelley CP, Childress J, Boake C, Noser EA. Over-ground and robotic-assisted locomotor training in adults with chronic stroke: a blinded randomized clinical trial. Disabil Rehabil Assist Technol 2013;8(2):161–8.
[41] van Nunen MP, Gerrits KH, Konijnenbelt M, Janssen TW, de Haan A. Recovery of walking ability using a robotic device in subacute stroke patients: a randomized controlled study. Disabil Rehabil Assist Technol 2015;10(2):141–8.

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