applied sciences

MDPI

Article

Stroke Gait Rehabilitation: A Comparison of End-Effector, Overground Exoskeleton, and Conventional Gait Training

Michela Goffredo [1,*], Chiara Iacovelli [2], Emanuele Russo [3], Sanaz Pournajaf [1], Chiara Di Blasi [2], Daniele Galafate [1], Leonardo Pellicciari [1], Maurizio Agosti [4], Serena Filoni [3], Irene Aprile [2] and Marco Franceschini [1,5]

1 IRCCS San Raffaele Pisana, Department of Neurorehabilitation, Via della Pisana, 235, 00163 Rome, Italy
2 IRCCS Fondazione Don Carlo Gnocchi, 20121 Milan, Italy
3 Fondazione Centri di Riabilitazione Padre Pio Onlus, San Giovanni Rotondo, 71013 Foggia, Italy
4 Rehabilitation Medicine Service, Rehabilitation Geriatrics Department of the NHS-University Hospital of Parma, 43126 Parma, Italy
5 Department of motor science, San Raffaele University, 00163 Rome, Italy
* Correspondence: michela.goffredo@sanraffaele.it; Tel.: +39-06-52252319

Received: 28 May 2019; Accepted: 27 June 2019; Published: 28 June 2019

Featured Application: To introduce innovative rehabilitation strategies based on personalised Robot-Assisted Gait Training.

Abstract: Gait recovery is one of the main goals of post-stroke rehabilitation and Robot-Assisted Gait Training (RAGT) has shown positive outcomes. However, there is a lack of studies in the literature comparing the effects of different devices. This paper aims to study the effects, in terms of clinical and gait outcomes, of treadmill-based and overground RAGT, compared to conventional gait training in stroke subjects. The results showed a significant improvement of clinical outcomes in both robotic treatments and in conventional therapy. The performance of locomotor tasks was clinically significant in the robotic groups only. The spatio-temporal gait parameters did not reveal any significant difference. Results suggest future multicentre studies on a larger number of subjects.

Keywords: robot-assisted gait training; stroke; gait analysis

1. Introduction

Gait recovery is one of the primary aims of stroke rehabilitation, since almost one third of stroke survivors are unable to achieve an independent community ambulation at hospital discharge [1]. Successful approaches for gait recovery are based on intensive and repetitive task-oriented practice involving the subject's active participation [2]. In this scenario, Robot-Assisted Gait Training (RAGT) has been widely employed as a rehabilitation treatment for stroke survivors, as it lets subjects perform the gait task even if they are not able to walk [3]. Such treatments have positive practical consequences on motor and functional recovery, since robotic devices allow early lower limb mobilization [4]. Furthermore, the intensity (i.e., number of steps) and the quality of the movement executed with a robotic device are significantly higher than those performed during Conventional Gait Training (CGT) [5,6]. The efficacy of RAGT in subjects with neurological diseases is well-established in the literature, showing significant improvements in clinical outcomes in comparison with the CGT [7–18]. The robotic devices for gait training can be categorised into treadmill-based or overground, as recently defined by Calabrò et al. [19].

The treadmill-based Robot-Assisted Gait Training (t-RAGT) is performed with stationary robotic devices that help the subject execute the cyclic ambulatory motor task with a Body Weight Support (BWS). These devices are classified into end-effector and exoskeleton systems, when the considering the physical interface between the subject and the robot [20]. In end-effector t-RAGT (such as the G-EO System [7] and the Lokohelp [8]), the physical human–robot interaction occurs at the distal segments, i.e., the subject's feet are fixed on footplates which simulate stepping. In exoskeleton t-RAGT (such as the Lokomat [7] and the ALEX [10]), the physical human–robot interaction occurs at each of the main segments of the lower limb (calves, thighs), i.e., the device's actuators move each body segment through pre-programmed physiological gait patterns.

The overground Robot Assisted Gait Training (o-RAGT) is provided by wearable powered exoskeletons (such as the Ekso [11] and the Indego [21]) that allow the subject to walk overground on hard and flat surfaces by moving each lower limb with a pre-programmed physiological pattern. The main differences between o-RAGT and t-RAGT rely on the subject's participation and multisensory inputs. Indeed, the o-RAGT allows the subjects to walk overground and experience near-normal proprioceptive input during limb loading, and to explore the environment [12].

In the literature, most of the clinical studies on robotic gait rehabilitation have been carried out with t-RAGT [5,7,8,13–15]; such treatments, when combined with traditional therapy, led improvements in functional ambulation outcomes. Moreover, subjects who received t-RAGT were more likely to achieve independent walking than their peers who received CGT only [15]. Systematic reviews did not find any difference in gait speed and endurance when t-RAGT was administered with the same intensity and duration as CGT [3,6].

On the other hand, the literature on o-RAGT is limited, because wearable powered exoskeletons are a relatively new technology and have not been frequently employed in neurorehabilitation centres [11,16–18]. A review on o-RAGT declared that subacute stroke subjects might experience further benefits from such training compared to the chronic ones [16]. A pilot observational study confirmed this hypothesis, finding that subacute stroke subjects registered a significant change in the Trunk Control Test and Walking Handicap Scale at the end of o-RAGT [17]. Moreover, the recent observational study by Goffredo et al. [11] reported significant improvements in all the International Classification of Functioning, disability and health (ICF) domains [22].

Although the efficacy of t-RAGT and o-RAGT has been studied in stroke subjects, to our knowledge, literature comparing the effects of different devices is limited. In 2012, Mehrholz and Pohl published a systematic review that compared end-effector and exoskeleton devices for t-RAGT [15]; end-effector t-RAGT seemed to increase the rates of independent walking compared to exoskeleton t-RAGT. More recently, Esquenazi et al. [23] published an RCT comparing three different gait trainings in subjects with traumatic brain injury (BWS treadmill, end-effector t-RAGT, and exoskeleton t-RAGT). They found increased velocity in all three groups, no significant changes in gait symmetry, and no inter-group differences. However, studies on different effects of treadmill-based and overground robotic gait rehabilitation in stroke subjects seem to be rather limited in the literature.

This pilot study aims to investigate the effects of t-RAGT, o-RAGT, and CGT, in terms of clinical and gait outcomes, in stroke survivors.

2. Materials and Methods

2.1. Subjects

A pilot observational non-randomized controlled trial was carried out to satisfy the aim of the study in three Italian rehabilitation centres: IRCCS San Raffaele Pisana, Rome; Don Gnocchi Foundation, Rome; Padre Pio, Foundation, San Giovanni Rotondo (FG).

Twenty-six stroke subjects were screened and assessed for study eligibility by board-certified physiatrists, who were experienced in gait biomechanics and in the use of the robotic devices applied in the study.

Subjects were included if they met the following inclusion criteria: stroke (within 6 months from the first ever cerebral stroke event); age between 18 and 80 years; ability to fit into the robotic devices; no range of motion limitation of lower extremities joints; ability to tolerate upright standing for 60 s; ability to walk unassisted or with minimum assistance; ability to give written consent and comply with the study procedures. Subjects were excluded if they presented: contractures of the hip, knee, or ankle joints that might limit the range of motion during gait; medical issue that precludes full weight bearing and ambulation (e.g., orthopaedic injuries, pain, severe osteoporosis, or severe spasticity); cognitive and/or communicative deficit (e.g., due to brain injury) and inability to understand the instructions required for the study; cardiac pathologies, anxiety or psychosis that might interfere with the use of the equipment.

Written informed consent was obtained from each subject. Ethical approval of the treatments and study protocol was granted by our local Ethics Committee (date: 18/11/2015; code number: 09/15).

2.2. Procedures

Recruited subjects were divided into three groups, depending on the gait training protocol, as follows: 8 subjects underwent gait training with an end-effector t-RAGT (Geo-System, Reha Technology AG; Olten, CH)—Geo Group (GG); 8 subjects underwent gait training with an exoskeleton o-RAGT (Ekso™, Ekso Bionics, Richmond, California, USA)—Ekso Group (EG); 10 subjects underwent conventional gait training—Conventional Group (CG).

Subjects in GG conducted 15 ± 2 sessions (3 days/week for 6 weeks) of t-RAGT using the G-EO System (Reha Technology AG, Olten, Switzerland) device. The practice consisted of robot-assisted walking, at variable speeds, for 60 min, exploiting BWS. In the first session, all participants started with 30–40% BWS, at a speed of 1.5 km/h; afterwards, speed was progressively increased to reach 2.2–2.5 km/h maximum, while BWS was progressively decreased, up to 20%, according to subject's tolerance.

Subjects in EG conducted 15 ± 2 sessions (3 days/week for 6 weeks) of o-RAGT, using the Ekso™ (Ekso Bionics, Richmond, California, USA) wearable powered exoskeleton. Before starting the training period, a trained physiotherapist checked for correct alignment of the subject's joints with the robot and for areas of increased skin pressure, adjusting the fit accordingly. The exoskeleton gait parameters were fine-tuned using surface electromyography, as detailed in Gandolla et al. [24]. Each single session of gait training lasted 60 min. ProStep Plus™ and Bilateral Max Assist were used as device settings: i.e., each subject's step was triggered by the user's lateral weight shift, and the amount of power contribution to legs during walking was totally provided by the robot. No strength was required by the subject, only proper balance and weight shifts were required to walk.

Subjects in CG conducted 15 ± 2 sessions of CGT, including: muscle strengthening exercises of the lower limb; static and dynamic exercises for the recovery of balance in supine and standing positions using assistive devices; training gait exercises with parallel bars or in open spaces performed both with and without assistive devices; training to climb up and down stairs; exercises to improve proprioception in supine, sitting and standing positions, using a proprioceptive footboard; exercises to improve the trunk control.

In all groups, the gait training was combined with daily conventional therapy including physical therapy (e.g., upper limb rehabilitation, functional task practice, muscle strengthening), speech therapy, and occupational therapy.

2.3. Outcome Measures

Subjects were screened by board-certified rehabilitation operators, with a multimodal assessment schema including clinical measures and instrumental gait analysis. Before starting the study procedures, demographic and clinical variables were collected in order to describe the sample. Each subject was screened at the baseline (T0) and post treatment (T1).

A clinical evaluation based on the ICF [21] was carried out. For the body function and structure ICF domain, the Motricity Index of Affected lower Limb (MI-AlL) was used to measure limb muscle

strength [25], and the Modified Ashworth Scale of Affected lower Limb (MAS-AlL) to evaluate muscle spasticity [26]. The following scales were used to measure ICF activity participation: the modified Barthel Index (mBI) to assess independence during activities of daily living [27]; the Trunk Control Test (TCT) to assess the trunk stability and control [28]; the Functional Ambulation Classification (FAC) to evaluate basic locomotor skills necessary for functional ambulation [29]; the Time Up and Go test (TUG) to assess mobility, balance, and walking [30]; the 10-meter walking test (10mwt) to evaluate the walking speed over a short distance [31]; the 6-minute walking test (6mwt) as a sub-maximal test of aerobic capacity/endurance to assess the distance walked during 6 min [32]. For the participation ICF domain, the Walking Handicap Scale (WHS) was used to assess subject's customary level of walking ability at home and in the community [33].

Gait analysis was conducted by using the 8-camera SMART-DX motion capture system (BTS Bioengineering, Milano, Italy, 2014) sampling at 200 Hz. The Davis heel protocol, which includes 22 retro-reflective markers, was employed [34], and anthropometric data were collected. Each subject was asked to perform four linear walking trials, barefoot and at a self-selected speed, straight ahead along a level surface that was approximately 5 m long. 3D markers' trajectories were tracked using a frame-by-frame tracking system (Smart Tracker, BTS Bioengineering, Milan, Italy, 2014). Data were processed using 3D reconstruction software (SMART Analyzer, BTS, Milan, Italy, 2014). The mean value of the following spatio-temporal gait parameters were calculated: cadence (step/min)—number of steps in 60 s; gait cycle duration (s)—mean temporal duration of the gait cycle that begins with initial heel contact and ends with the subsequent heel contact of the same foot; mean velocity (m/s); stance time AL (% gait cycle)—percentage of the gait cycle that begins with initial contact and ends at toe off of the affected limb; stance time UL (% gait cycle)—percentage of the gait cycle that begins with initial contact and ends at toe off of the unaffected limb; swing time AL (% gait cycle)—percentage of the gait cycle that begins with the toe off and ends at heel strike of the affected limb; swing time UL (% gait cycle)—percentage of the gait cycle that begins with the toe off and ends at heel strike of the unaffected limb; step length AL (m)—mean longitudinal distance from one foot strike to the next one of the affected limb; step length UL (m)—mean longitudinal distance from one foot strike to the next one of the unaffected limb; and step width (m)—mediolateral distance between the two heels during the double support.

2.4. Statistical Analysis

Descriptive statistics were computed in order to appropriately explain clinical and demographic characteristics of the sample. Data are represented as frequency (with the relative percentage) and median value with Median Absolute Deviation (MAD) for the categorical and continuous variables, respectively. The Kruskal-Wallis test was applied to determine statistically significant differences between the groups at the baseline (T0) and post treatment (T1). Wilcoxon signed rank tests were used to find significant pre-post differences in each group. For all statistical analyses, the α value was set at p-value < 0.05 and the software was SPSS, Version 20.0 (SPSS Inc., Chicago, IL, USA, 2004).

3. Results

Twenty-six stroke subjects were enrolled in this study: 8 subjects were assigned to GG (median age = 59.00 years; 8 males; 5 ischemic; 3 left side; median distance from the acute event = 44 days); 8 subjects to EG (median age = 66.00 years; 4 males; 6 ischemic; 7 left side; median distance from the acute event = 112.50 days); and 10 subjects to CG (median age = 63.00 years; 7 males; 6 ischemic; 1 left side; median distance from the acute event = 111.00 days). Detailed demographic and clinical characteristics of the sample are depicted in Table 1. All participants completed the entire treatment without reporting any adverse event.

Table 2 shows the clinical outcomes registered at T0 and T1 for each group. The results of Kruskal-Wallis test revealed no significant difference at T0 and T1 ($p \geq 0.05$).

Table 1. Demographic and clinical characteristics of the sample.

Characteristics	GG (N = 8)	EG (N = 8)	CG (N = 10)
Age (years)	59.00 (15.57)	66.00 (14.83)	63.00 (6.67)
Gender (female/male)	2 (20%)/8 (80%)	4 (50%)/4 (50%)	3 (30%)/7 (70%)
Aetiology (ischemic/haemorrhagic)	5 (62.5%)/3 (37.5%)	6 (75%)/2 (25%)	6 (60%)/4 (40%)
Affected side (left/right)	3 (37.5%)/5 (62.5%)	7 (70%)/3 (30%)	1 (12.5%)/7 (87.5%)
Distance from the acute event (days)	44.00 (34.84)	112.50 (40.77)	111.00 (65.23)

N (%); median (median absolute deviation)

Within the GG, the Wilcoxon test showed significant pre-post variations in the following outcomes: mBI (p-value = 0.008), MI-AIL (p-value = 0.022) TCT (p-value = 0.036), FAC (p-value = 0.030), WHS (p-value = 0.032), TUG (p-value = 0.022), 6MWT (p-value = 0.008). The 10MWT (p-value = 0.272), and MAS-AIL (p-value = 0.242) did not reveal any significant temporal variations.

Within the EG, mBI (p-value = 0.022), MI-AIL (p-value = 0.022), FAC (p-value = 0.018), WHS (p-value = 0.012), and 10MWT (p-value = 0.050) significantly changed between T0 and T1. However, the TCT (p-value = 0.097), MAS-AIL (p-value = 0.097), TUG (p-value = 0.312), and 6MWT (p-value = 0.107) did not registered significant improvements.

Within the CG, significant differences between T0 and T1 were registered in mBI (p-value = 0.009), MI-AIL (p-value = 0.009), TCT (p-value = 0.033), FAC (p-value = 0.032), WHS (p-value = 0.010), TUG (p-value = 0.006), and 10MWT (p-value = 0.036). Data did not reveal any significant difference in MAS-AIL (p-value = 0.346) and 6MWT (p-value = 0.343).

The between-groups statistical significance was not achieved. However, the clinical significance was obtained in TUG, 10MWT, and 6MWT. Specifically, the mean pre-post differences in TUG were: GG = −6.86 s; EG = −6.80 s; CG = −2.98 s. Therefore, considering that the Minimal Clinical Important Difference (MCID) for TUG in stroke subjects is −2.9 s [16], all groups exceeded this value, with a higher pre-post difference in both robotic groups. Similarly, the mean pre-post differences in 6MWT (GG = 64.75 m; EG = 50.75 m; CG = 17.60 m) evidenced that only the GG and EG registered values higher than the MCID for 6MWT (34 m [16]). Conversely, in 10MWT, only the pre-post difference of EG (0.2 m/s) exceeded the MCID (0.16 m/s [16]), since the variations in velocity in GC (0.09 m/s) and CG (0.05 m/s) were lower indeed.

The spatio-temporal gait parameters at T0 and T1 are depicted in Table 3. The results of the Kruskal-Wallis and Wilcoxon tests revealed no significant differences ($p \geq 0.05$) for all gait outcomes.

Table 2. Clinical outcomes at the beginning (T0) and at the end (T1) of the gait treatment for all groups and the corresponding *p*-values obtained with the statistical analysis.

Outcomes	GG (N = 8)			EG (N = 8)			CG (N = 10)		
	T0	T1	*p*-Value	T0	T1	*p*-Value	T0	T1	*p*-Value
mBI (0–100)	42.00 (12.60)	81.00 (8.90)	**0.008**	63.50 (25.20)	83.00 (9.64)	**0.022**	63.00 (24.46)	82.00 (13.34)	**0.009**
MI-AlL (0–100)	54.00 (8.15)	73.00 (4.45)	**0.022**	59.00 (12.60)	70.00 (23.72)	**0.022**	64.00 (16.31)	76.00 (14.08)	**0.009**
MAS-AlL (0–12)	1.00 (1.48)	0.50 (0.74)	0.242	2.00 (1.85)	1.00 (0.74)	0.097	0.00 (0.00)	0.00 (0.00)	0.346
TCT (0–100)	80.50 (26.69)	100.00 (0.00)	**0.036**	74.00 (19.27)	100.00 (0.00)	0.097	80.50 (19.27)	100.00 (0.00)	**0.033**
FAC (0–5)	2.50 (1.48)	4.00 (0.00)	**0.030**	2.50 (0.74)	4.00 (0.00)	**0.018**	3.50 (0.74)	4.00 (1.48)	**0.032**
WHS (1–6)	3.50 (1.48)	4.00 (0.74)	**0.032**	3.00 (0.74)	4.00 (0.74)	**0.012**	3.00 (1.48)	4.00 (1.48)	**0.010**
TUG-time (s)	25.50 (20.85)	14.00 (8.90)	**0.022**	35.50 (24.46)	22.00 (12.85)	0.312	23.81 (13.40)	20.50 (13.11)	**0.006**
10MWT-velocity (m/s)	0.68 (0.37)	0.67 (0.60)	0.272	0.43 (0.05)	0.53 (0.19)	**0.050**	0.65 (0.29)	0.77 (0.29)	**0.036**
6MWT-distance (m)	152.00 (113.42)	234.00 (177.91)	**0.008**	121.50 (46.70)	145.50 (50.41)	0.107	193.00 (117.13)	231.00 (102.30)	0.343

median (median absolute deviation); *p*-value results of the Wilcoxon signed-rank test; Geo Group (GG); Ekso Group (EG); Conventional Group (CG); modified Barthel Index (mBI); Motricity Index Affected lower Limb (MI-AlL); Modified Ashworth Scale Affected lower Limb (MAS-AlL); Trunk Control Test (TCT); Functional Ambulation Classification (FAC); Walking Handicap Scale (WHS); Time Up and Go test (TUG); 10-Meter Walking Test (10MWT); 6-Minute Walking Test (6MWT).

Table 3. Spatio-temporal gait parameters at the beginning (T0) and at the end (T1) of the gait treatment for all groups and the corresponding *p*-values.

Parameters	GG (N = 8)			EG (N = 8)			CG (N = 10)		
	T0	T1	*p*-Value	T0	T1	*p*-Value	T0	T1	*p*-Value
Cadence (step/min)	71.50 (24.46)	75.00 (23.72)	0.14	62.85 (20.57)	62.33 (19.57)	0.46	80.43 (17.31)	83.91 (20.69)	0.19
Gait Cycle-GC (s)	1.69 (0.60)	1.60 (0.51)	0.38	1.68 (0.60)	1.60 (0.51)	0.38	1.49 (0.32)	1.45 (0.35)	0.26
Mean velocity (m/s)	0.39 (0.18)	0.46 (0.18)	0.64	0.33 (.19)	0.27 (0.12)	0.55	0.42 (0.09)	0.49 (0.24)	0.30
Stance time AL (% GC)	0.64 (0.04)	0.62 (0.04)	0.32	0.60 (0.03)	0.67 (0.10)	0.29	0.66 (0.04)	0.64 (0.07)	0.32
Stance time UL (% GC)	0.72 0(.09)	0.68 (0.10)	0.23	0.77 (0.02)	0.76 (0.05)	0.44	0.74 (0.04)	0.73 (0.06)	0.72
Swing time AL (% GC)	0.36 (0.04)	0.37 (0.05)	0.48	0.41 (0.04)	0.33 (0.10)	0.79	0.35 (0.04)	0.35 (0.08)	0.10
Swing time AL (% GC)	0.29 (0.09)	0.33 (0.10)	0.19	0.26 (0.07)	0.25 (0.04)	0.44	0.26 (0.04)	0.27 (0.06)	0.16
Step length AL (m)	0.42 (0.054)	0.41 (0.030)	0.67	0.31 (0.096)	0.32 (0.088)	0.72	0.32 (0.088)	0.30 (0.081)	0.63
Step length UL (m)	0.29 (0.115)	0.31 (0.128)	0.10	0.27 (0.133)	0.26 (0.111)	0.10	0.26 (0.096)	0.32 (0.111)	0.10
Step width (m)	0.19 (0.043)	0.18 (0.045)	0.72	0.14 (0.044)	0.15 (0.044)	0.80	0.18 (0.029)	0.18 (0.029)	0.09

median (median absolute deviation); *p*-value results of the Wilcoxon signed-rank test; Geo Group (GG); Ekso Group (EG); Conventional Group (CG); Affected Limb (AL); Unaffected Limb (UL).

4. Discussion

Gait recovery is a key factor for the restoration of satisfying levels of participation and quality of life in stroke subjects. In literature, many treatments have been proposed, but there is not a general consensus on their effects [2]. In this context, robotic technologies have been recently widespread in rehabilitation, and their efficacy has been demonstrated in clinical studies [3,5,6,12,16]. However, to our best knowledge, no evidence is available on which robotic technology is more effective for gait training in stroke subjects [15,19]. Therefore, the aim of this pilot study was to compare the effects of t-RAGT, o-RAGT, and CGT in stroke subjects by means of clinical and gait assessments.

Twenty-six stroke subjects were recruited for the study. Each treatment was well tolerated by all subjects and proved to be safe. We obtained a full complete adherence to the protocol, considering that all subjects completed the training sessions, without any drop-outs. No adverse event occurred.

Results on clinical outcomes showed significant pre-post differences in most ICF domains: each group registered improvements between the baseline and final assessments, but these differences were not significant among them. In TUG, 10MWT, and 6MWT, although the statistical significance was not obtained, pre-post differences on GG end EG were higher than the MDIC values reported in literature [16]. Such outcome was not found in CG. These results are encouraging and consistent with the literature on the effects of t-RAGT [13] and o-RAGT [11] with the same devices. Specifically, Aprile et al. [13] studied the efficacy of end-effector t-RAGT in 14 subjects with chronic stroke, and found significant higher pre-post differences in 6MWT in the robotic group, but no variations in spasticity. The recent observational study by Goffredo et al. [11] on o-RAGT in 48 stroke subjects found similar clinical outcomes: significant improvement in the majority of clinical assessments, in speed measured during 10MWT, and in the distance covered over a time of 6 min (6MWT).

Results on spatio-temporal gait parameters showed no significant pre-post and between-group differences. Data from gait analysis are consistent with findings reported in subjects after stroke [13,18,35] and traumatic brain injury [23] who conducted RAGT. Specifically, no within- and between-group differences were registered in spatio-temporal gait parameters after neither t-RAGT nor CGT in chronic stroke subjects [13]. Similarly, the study by Hidler et al. [35] on stroke subjects found that t-RAGT did not improve gait parameters. The study by Esquenazi et al. [23] that compared three different gait trainings (BWS treadmill, end-effector t-RAGT, and exoskeleton t-RAGT) in subjects with traumatic brain injury confirmed our findings, i.e., no inter-group differences occurred in gait parameters.

This study presented several limitations that deserve to be discussed. Firstly, the lack of the randomization may have maximised the selection bias. It was not possible to meet the need for randomisation because the clinical centres who participated to the study did not have both robotic devices available. Secondly, the sample size could be considered limited, and it could have influenced the statistical relevance and the power of this study. However, findings that came from this pilot study could provide the basis for a larger clinical trial. Finally, the study did not analyse the joint kinematics and kinetics: this choice in study design was purposed by the necessity to face our results with published studies on the topic [13,23,35]. Hence, the research agenda should include the implementation of future multicentre studies, the recruitment of more subjects, the analysis of joint biomechanics, and the inclusion of neurophysiological measurements (i.e., electromyography, electroencephalography).

5. Conclusions

This pilot study on stroke subjects suggested that robotic gait training produces significant improvement in clinical outcomes, as well as the conventional therapy. However, the performance in executing specific locomotor tasks (6MWT, 10MWT, and TUG) is clinically significant in the robotic groups only. The instrumental gait outcomes did not reveal any significant difference in spatio-temporal parameters and pave the way to a more detailed analysis of gait biomechanics and of neurophysiological signals.

The results obtained in this pilot study are encouraging and suggest future multicentre clinical trials that may help to reveal differences between different interventions. Moreover, studies with a larger sample size would help to identify demographic, clinical and functional characteristics of stroke subjects that could influence the effects of robotic gait training.

Author Contributions: Conceptualization, M.F., M.G.; methodology, M.F., M.A.; software, M.A., M.G., E.R.; investigation, S.P., C.I., C.D.B., D.G., E.R.; data curation, M.G., S.P.; writing—original draft preparation, M.G.; writing—review and editing, S.P., L.P., C.I., E.R.; supervision, M.F., I.A., S.F.

Funding: This project was partially funded by The Ministry of Health (Ricerca corrente).

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Nichols-Larsen, D.S.; Clark, P.; Zeringue, A.; Greenspan, A.; Blanton, S. Factors Influencing Stroke Survivors' Quality of Life During Subacute Recovery. *Stroke* **2005**, *36*, 1480–1484. [CrossRef] [PubMed]
2. European Stroke Organisation (ESO); Executive Committee; ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc. Dis.* **2008**, *25*, 457–507. [CrossRef] [PubMed]
3. Thomas, S.; Werner, C.; Kugler, J.; Pohl, M.; Elsner, B.; Mehrholz, J. Electromechanical-assisted training for walking after stroke. *Cochrane Database Syst. Rev.* **2017**, *5*, CD006185.
4. Cumming, T.B.; Thrift, A.; Collier, J.M.; Churilov, L.; Dewey, H.M.; Donnan, G.; Bernhardt, J. Very Early Mobilization After Stroke Fast-Tracks Return to Walking: Further Results From the Phase II AVERT Randomized Controlled Trial. *Stroke* **2011**, *42*, 153–158. [CrossRef] [PubMed]
5. Morone, G.; Paolucci, S.; Cherubini, A.; De Angelis, D.; Venturiero, V.; Coiro, P.; Iosa, M.; Iosa, V.A.P.B.M. Views: Robot-assisted gait training for stroke patients: Current state of the art and perspectives of robotics. *Neuropsychiatr. Dis. Treat.* **2017**, *13*, 1303–1311. [CrossRef] [PubMed]
6. Bruni, M.F.; Melegari, C.; De Cola, M.C.; Bramanti, A.; Bramanti, P.; Calabrò, R.S. What does best evidence tell us about robotic gait rehabilitation in stroke patients: A systematic review and meta-analysis. *J. Clin. Neurosci.* **2018**, *48*, 11–17. [CrossRef] [PubMed]
7. Hesse, S.; Tomelleri, C.; Bardeleben, A.; Werner, C.; Waldner, A. Robot-assisted practice of gait and stair climbing in nonambulatory stroke patients. *J. Rehabil. Res. Dev.* **2012**, *49*, 613–622. [CrossRef]
8. Freivogel, S.; Mehrholz, J.; Husak-Sotomayor, T.; Schmalohr, D. Gait training with the newly developed 'LokoHelp'-system is feasible for non-ambulatory patients after stroke, spinal cord and brain injury. A feasibility study. *Brain Inj.* **2008**, *22*, 625–632. [CrossRef]
9. Bonnyaud, C.; Pradon, D.; Boudarham, J.; Robertson, J.; Vuillerme, N.; Roche, N. Effects of gait training using a robotic constraint (LokomatÂ®) on gait kinematics and kinetics in chronic stroke patients. *J. Rehabil. Med.* **2014**, *46*, 132–138. [CrossRef]
10. Stroppa, F.; Loconsole, C.; Marcheschi, S.; Frisoli, A. A robot-assisted neuro-rehabilitation system for post-stroke patients' motor skill evaluation with ALEx exoskeleton. In *Converging Clinical and Engineering Research on Neurorehabilitation II*; Springer: Cham, Switzerland, 2017; pp. 501–505.
11. Goffredo, M.; Guanziroli, E.; Pournajaf, S.; Gaffuri, M.; Gasperini, G.; Filoni, S.; Molteni, F. Overground wearable powered exoskeleton for gait training in subacute stroke subjects: Clinical and gait assessments. *Eur. J. Phys. Rehabil. Med.* **2019**. [CrossRef]
12. Molteni, F.; Gasperini, G.; Cannaviello, G.; Guanziroli, E. Exoskeleton and end-effector robots for upper and lower limbs rehabilitation: Narrative review. *PMR* **2018**, *10*, S174–S188. [CrossRef] [PubMed]
13. Aprile, I.; Iacovelli, C.; Padua, L.; Galafate, D.; Criscuolo, S.; Gabbani, D.; Cruciani, A.; Germanotta, M.; Di Sipio, E.; De Pisi, F.; et al. Efficacy of Robotic-Assisted Gait Training in chronic stroke patients: Preliminary results of an Italian bi-centre study. *Neurorehabilitation* **2017**, *41*, 775–782. [CrossRef] [PubMed]
14. Mazzoleni, S.; Focacci, A.; Franceschini, M.; Waldner, A.; Spagnuolo, C.; Battini, E.; Bonaiuti, D. Robot-assisted end-effector-based gait training in chronic stroke patients: A multicentric uncontrolled observational retrospective clinical study. *Neurorehabilitation* **2017**, *40*, 483–492. [CrossRef] [PubMed]
15. Mehrholz, J.; Pohl, M. Electromechanical-assisted gait training after stroke: A systematic review comparing end-effector and exoskeleton devices. *J. Rehabil. Med.* **2012**, *44*, 193–199. [CrossRef] [PubMed]

16. Louie, D.R.; Eng, J.J. Powered robotic exoskeletons in post-stroke rehabilitation of gait: A scoping review. *J. Neuroeng. Rehabil.* **2016**, *13*, 53. [CrossRef] [PubMed]
17. Molteni, F.; Gasperini, G.; Gaffuri, M.; Colombo, M.; Giovanzana, C.; Lorenzon, C.; Farina, N.; Cannaviello, G.; Scarano, S.; Proserpio, D.; et al. Wearable robotic exoskeleton for over-ground gait training in sub-acute and chronic hemiparetic stroke patients: Preliminary results. *Eur. J. Phys. Rehabil. Med.* **2017**, *53*, 676–684. [PubMed]
18. Calabrò, R.S.; Naro, A.; Russo, M.; Bramanti, P.; Carioti, L.; Balletta, T.; Bramanti, A. Shaping neuroplasticity by using powered exoskeletons in patients with stroke: a randomized clinical trial. *J. Neuroeng. Rehabil.* **2018**, *15*, 35. [CrossRef] [PubMed]
19. Calabrò, R.S.; 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*, 503–514. [CrossRef]
20. Pons, J.L. *Wearable Robots: Biomechatronic Exoskeletons*; John Wiley & Sons: Hoboken, NJ, USA, 2008.
21. Murray, S.A.; Ha, K.H.; Goldfarb, M. An assistive controller for a lower-limb exoskeleton for rehabilitation after stroke, and preliminary assessment thereof. In Proceedings of the 2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Chicago, IL, USA, 23–30 August 2014; pp. 4083–4086.
22. Geroin, C.; Mazzoleni, S.; Smania, N.; Gandolfi, M.; Bonaiuti, D.; Gasperini, G.; Sale, P.; Munari, D.; Waldner, A.; Spidalieri, R.; et al. Systematic review of outcome measures of walking training using electromechanical and robotic devices in patients with stroke. *J. Rehabil. Med.* **2013**, *45*, 987–996. [CrossRef]
23. Esquenazi, A.; Lee, S.; Wikoff, A.; Packel, A.; Toczylowski, T.; Feeley, J. A Comparison of Locomotor Therapy Interventions: Partial-Body Weight−Supported Treadmill, Lokomat, and G-EO Training in People With Traumatic Brain Injury. *PMR* **2017**, *9*, 839–846. [CrossRef]
24. Gandolla, M.; Guanziroli, E.; D'Angelo, A.; Cannaviello, G.; Molteni, F.; Pedrocchi, A. Automatic Setting Procedure for Exoskeleton-Assisted Overground Gait: Proof of Concept on Stroke Population. *Front. Neurorobotics* **2018**, *12*, 10. [CrossRef] [PubMed]
25. Fayazi, M.; Dehkordi, S.N.; Dadgoo, M.; Salehi, M. Test-retest reliability of Motricity Index strength assessments for lower extremity in post stroke hemiparesis. *Med. J. Islam. Repub. Iran* **2012**, *26*, 27–30. [PubMed]
26. Bohannon, R.W.; Smith, M.B. Interrater Reliability of a Modified Ashworth Scale of Muscle Spasticity. *Phys. Ther.* **1987**, *67*, 206–207. [CrossRef] [PubMed]
27. Hsueh, I.-P.; Lin, J.-H.; Jeng, J.-S.; Hsieh, C.-L. Comparison of the psychometric characteristics of the functional independence measure, 5 item Barthel index, and 10 item Barthel index in patients with stroke. *J. Neurol. Neurosurg. Psychiatry* **2002**, *73*, 188–190. [CrossRef] [PubMed]
28. Franchignoni, F.P.; Tesio, L.; Ricupero, C.; Martino, M.T. Trunk Control Test as an Early Predictor of Stroke Rehabilitation Outcome. *Stroke* **1997**, *28*, 1382–1385. [CrossRef] [PubMed]
29. Holden, M.K.; Gill, K.M.; Magliozzi, M.R.; Nathan, J.; Piehl-Baker, L. Clinical Gait Assessment in the Neurologically ImpairedReliability and Meaningfulness. *Phys. Ther.* **1984**, *64*, 35–40. [CrossRef] [PubMed]
30. Chan, P.P.; Tou, J.I.S.; Tse, M.M.; Ng, S.S. Reliability and Validity of the Timed Up and Go Test With a Motor Task in People With Chronic Stroke. *Arch. Phys. Med. Rehabil.* **2017**, *98*, 2213–2220. [CrossRef]
31. Tyson, S.; Connell, L. The psychometric properties and clinical utility of measures of walking and mobility in neurological conditions: A systematic review. *Clin. Rehabil.* **2009**, *23*, 1018–1033. [CrossRef]
32. Pohl, P.S.; Duncan, P.W.; Perera, S.; Liu, W.; Lai, S.M.; Studenski, S.; Long, J. Influence of stroke-related impairments on performance in 6-minute walk test. *J. Rehabil. Res. Dev.* **2002**, *39*, 439–444.
33. Pournajaf, S.; Goffredo, M.; Agosti, M.; Massucci, M.; Ferro, S.; Franceschini, M. Community ambulation of stroke survivors at 6 months follow-up: An observational study on sociodemographic and sub-acute clinical indicators. *Eur. J. Phys. Rehabil. Med.* **2018**. [CrossRef]

34. Davis, R.B.; Õunpuu, S.; Tyburski, D.; Gage, J.R.; Iii, R.B.D. A gait analysis data collection and reduction technique. *Hum. Mov. Sci.* **1991**, *10*, 575–587. [CrossRef]
35. Hidler, J.; Nichols, D.; Pelliccio, M.; Brady, K.; Campbell, D.D.; Kahn, J.H.; Hornby, T.G. Multicenter randomized clinical trial evaluating the effectiveness of the Lokomat in subacute stroke. *Neurorehabilit. Neural Repair* **2009**, *23*, 5–13. [CrossRef] [PubMed]