Robot-assisted gait training versus equal intensity treadmill training in patients with mild to moderate Parkinson’s disease: A randomized controlled trial

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A B S T R A C T

Background: There is a lack of evidence about the most effective strategy for training gait in mild to moderate Parkinson’s disease. The aim of this study was to compare the effects of robotic gait training versus equal intensity treadmill training and conventional physiotherapy on walking ability in patients with mild to moderate Parkinson’s disease.

Methods: Sixty patients with mild to moderate Parkinson’s disease (Hoehn & Yahr stage 3) were randomly assigned into three groups. All patients received twelve, 45-min treatment sessions, three days a week, for four consecutive weeks. The Robotic Gait Training group (n = 20) underwent robot-assisted gait training. The Treadmill Training group (n = 20) performed equal intensity treadmill training without body-weight support. The Physical Therapy group (n = 20) underwent conventional gait therapy according to the proprioceptive neuromuscular facilitation concept. Patients were evaluated before, after and 3 months post-treatment. Primary outcomes were the following timed tasks: 10-m walking test, 6-min walking test.

Results: No statistically significant difference was found on the primary outcome measures between the Robotic Gait Training group and the Treadmill Training group at the after treatment evaluation. A statistically significant improvement was found after treatment on the primary outcomes in favor of the Robotic Gait Training group and Treadmill Training group compared to the Physical Therapy group.

Conclusions: Our findings support the hypothesis that robotic gait training is not superior to equal intensity treadmill training for improving walking ability in patients with mild to moderate Parkinson’s disease.

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1. Introduction

Gait impairment is one of the primary movement disorders in Parkinson’s disease (PD) [1–3]. It is characterized by a reduced gait speed, shortened stride length and longer double support phase [2]. Thus, one of the primary goals in PD rehabilitation is to improve walking ability [4]. The use of training programs focused on task-specific activities have been encouraged to improve walking ability, in line with the increased retention of motor skill learning observed in adults with mild PD after task practice [5]. On this basis, a wide range of conventional Physical Therapy (PT) approaches has been employed to treat PD, even though there is no consensus as to “best-practice” in the different phases of illness [4].

Forced use, task-specific, intensive, gait rehabilitation programs based on treadmill training (TT) have been reported to effectively improve gait speed, walking distance and stride length in mild to moderate PD [6]. In addition, robotic gait training (RGT) has been observed to improve gait speed, walking capacity, stride length and fatigue in patients with PD [7]. However, its effectiveness on walking impairment has been evaluated only in early stage PD [7,8], where it is not superior to TT [8]. Considering that gait hypokinesia...
Table 1
Protocol for treatment used in the Physical Therapy group.

<table>
<thead>
<tr>
<th>Techniques</th>
<th>Sequence activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhythmic initiation</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>The command “relax and let me move you” was used first to move the pelvis through the available range of motion of anterior elevation and then to return the pelvis through the posterior depression pattern.</td>
</tr>
<tr>
<td>B</td>
<td>When the therapist could not feel resistance during the movements, the command “now help me move you” was used to have the subject assist the movement for 3 to 4 repetitions.</td>
</tr>
<tr>
<td>C</td>
<td>Using the command “pull”, the subject was asked to superimpose resistance upon the movement, with the therapist gradually increasing the resistance with the increase in subject’s response. This was repeated for 3 to 4 repetitions.</td>
</tr>
<tr>
<td>D</td>
<td>The subject moved the pelvis actively through the anterior elevation pattern and returned to the starting position passively by relaxing.</td>
</tr>
<tr>
<td>E</td>
<td>Sequences (C) and (D) were repeated for the remaining time.</td>
</tr>
</tbody>
</table>

Slow reversal

| A                   | The subject was moved to the lengthened range of the pelvis anterior elevation.       |
| B                   | The therapist had the subject perform a contraction of the internal and external oblique abdominal muscles to anteriorly elevate the pelvis with maximal effort against resistance added by the physical therapist. |
| C                   | The therapist had the subject perform a contraction of the quadratus lumborum and iliocostalis lumborum muscles to posteriorly lower the pelvis against maximal resistance. |
| D                   | Sequences (B) and (C) were repeated for the remaining time.                           |

2. Methods

This study was performed in the Neurorehabilitation Unit of the Azienda Ospedaliera-Universitaria Integrata of Verona, Italy. Inclusion criteria: confirmed diagnosis of idiopathic PD according to the UK Brain Bank Criteria [9]; Hoehn and Yahr (H&Y) stage 3 determined in the “on” phase [10]; Mini Mental State Examination >24 [11]. Exclusion criteria: severe dyskinesias or “on-off” fluctuations; change of PD medication during the study; deficits of somatic sensation involving the lower limbs; vestibular disorders or paroxysmal vertigo; other neurological or orthopedic conditions involving the lower limbs (musculoskeletal diseases, severe osteoarthritis, peripheral neuropathy, joint replacement); cardiovascular morbidity (recent myocardial infarction, heart failure, uncontrolled hypertension, orthostatic hypotension).

All participants were outpatients and gave their informed written consent for participation in the study, which was carried out according to the Declaration of Helsinki and was approved by the local Ethics Committee.

Prior to testing, we randomly assigned participants in a one-to-one ratio to three arms: a group that performed RGT; a group that underwent TT and a group that received PT. We allocated patients to one of the three treatment arms according to a restricted randomization scheme [12]. One of the investigators (F.O.) checked correct patient allocation according to the randomization list. After unmasking at the end of the study, we checked that no errors had been made in allocation. During the study, participants were instructed to take their normal PD medications: they were tested and trained during the “on” phase, 1–2.5 h after taking their morning dose. Participants did not perform any type of rehabilitation in the three months before the study, nor undergo any form of rehabilitation other than that scheduled in the study protocol.

2.1. Treatment procedures

Each patient underwent a training program consisting of twelve, 45-min sessions (including rest periods); three days a week (Monday, Wednesday, Friday) for four consecutive weeks.

2.1.1. Robotic Gait Training (RGT) group

Patients allocated to this group were treated with the Gait Trainer GT1 (Rehastim, Berlin, Germany) [7,13]. The GT1 machine is a static suspension system consisting of two motor-driven footplates positioned on 2 bars that provide a robot-assisted propulsion with a planar screen system (ratio of 60%–40% between stance and swing) [13]. Individuals on the GT1 machine are secured in a harness while movements of the center of mass are controlled in a phase-dependent manner by ropes attached to the harness [13]. The GT1 machine allows patients to be treated with a gait speed ranging from 0 to 2 km/h and a step length set from 28 to 48 cm.

In this study, the step length of each patient was evaluated with the GAITRite system (CIR Systems, Haverton, PA) and individually defined. The maximum GT1 step length was chosen for patients with a step length >48 cm. Each training session consisted of three parts with a 5-min rest after each. First, we trained patients at 20% of body weight supported and 1 km/h of speed for 10 min; then, at 10% of body weight supported and 1.5 km/h of speed for 10 min; finally, at 0% of body weight supported and 2.0 km/h of speed for 10 min. Patients were instructed to “help” the GT1 gait-like movement during training. Patients unable to maintain the established pace were excluded.

2.1.2. Treadmill Training (TT) group

Patients allocated to this group performed TT without body-weight support with the Jog Now 500MD (Technogym, Cesena, Italy). Each training session consisted of three parts with a 5-min rest after each. First, we trained patients at 1 km/h of speed for 10 min; then, at 1.5 km/h of speed for 10 min; finally, at 2.0 km/h of speed for 10 min. Patients unable to maintain the established pace were excluded.

2.1.3. Physical Therapy (PT) group

Patients allocated to this group performed conventional gait training for 30 min according to the proprioceptive neuromuscular facilitation (PNF) concept, which defines the pelvis as a “key point of control” for maintaining a gait pattern [7,14,15]. Thus, we decided to facilitate pelvic motion and improve pelvic control during training [7,14,15]. Each training session consisted of 10 min each of rhythmic initiation, slow reversal and agonistic reversal exercises applied to the pelvic region (see Table 1 for treatment protocol) [7,14,15]. The same therapist treated all the patients in this group and standardized the duration and the intensity of each part of the treatment.

2.2. Testing procedures

Patients were evaluated before (T0), immediately after treatment (T1) (primary endpoint) and at three months of follow-up (T2). The same rater (C.M.), who was blinded to the group allocation, evaluated all patients. Asking the assessor to make an educated guess tested the success of blinding.
2.2.1. Primary outcomes

Primary outcomes were the timed 10-m walking test (10 MWT) [16,17], and the 6-min timed walking test (6 MWT) [18]. We chose these measures in order to facilitate the comparison of our results with those of previous studies about the role of RGT in PD [28]. The 10 MWT was selected as a measure of gait speed [16,17]. We required patients to walk on a flat hard floor at their fastest speed for 10 m without assistance (a 10-m walkway was marked by two lines on the floor, as well as a 2-m mark and an 8-m mark). In order to minimize acceleration and deceleration, we measured gait speed for the intermediate 6 m (timing started when the toes of the leading foot crossed the 2-m mark and stopped when the toes of the leading foot crossed the 8-m mark) [16,17]. A hand held stopwatch recorded time. Patients were not allowed to use walking aids.

Walking capacity was assessed using the 6 MWT [18]. Subjects were required to cover as much ground as possible over 6 min (patients were required to walk continuously at their fastest speed, if possible) along a marked distance (1 lap, 40 m). The distance covered was recorded [18]. Patients were not allowed to use walking aids.

2.2.2. Secondary outcomes

Spatiotemporal gait parameters were evaluated with the GAITRite system (CIR Systems Inc, Havertown, PA) [19,20]. To avoid acceleration and deceleration, patients were asked to ambulate along the 7.66 m GAITRite walkway at their fastest speed on a 12-m course. Patients were not allowed to use walking aids. Three trials were collected, with their average calculated. Stride length, cadence, coefficient of variation of stride time (SD stride time/mean stride time × 100) and ratio between single and double support duration were evaluated. The Berg Balance Scale is a 14-item (0–4 points/task; best score = 56) scale that evaluates balance abilities during sitting, standing and positional changes [22]. The Parkinson’s Fatigue Scale was used to assess fatigue [22]. This is a 16-item scale (item response options ranging from 1—strongly disagree to 5—strongly agree) with a total score ranging from 16 to 80 [22]. The Unified Parkinson’s Disease Rating Scale (UPDRS) has 4 subsections and was used to follow the longitudinal course of PD. The score ranges from 0 to 147 (high: worst performance) [23].

2.3. Statistical analysis

Pre-study power calculation estimated that 14 subjects per group would provide 90% power to detect a difference of 0.25 m/s in the 10 MWT between groups [24]. We used the one-way analysis of variance (ANOVA) to assess the homogeneity of the three groups before the study for age, length of illness and primary outcomes. For the interval variables, the three groups (RGT, TT and PT) were compared at three time points (T0, T1 and T2) in a 3 × 3 repeated measures ANOVA, in order to analyze between and within groups effects. Post hoc comparisons were performed between groups with the Tukey HSD test. For ordinal variables, the Kruskall–Wallis test was used to analyze changes in performance in the different evaluation sessions between the three groups (RGT, TT and PT). In the presence of significant main effects, the Mann Whitney U test was performed to determine the location of any significant differences between groups. The level for significance was P < 0.05. The Bonferroni correction was used when investigating multiple comparisons with non-parametric statistics (P < 0.016). Statistical analysis was performed with SPSS 20.0 (SPSS Inc, Chicago, IL).

3. Results

Sixty subjects (23 males, 37 females; mean age: 68.3 ± 8.3 years) presenting with idiopathic PD (mean disease duration: 6.8 ± 5.8 years; H&Y 3) were recruited from among 97 outpatients consecutively admitted to our Neurorehabilitation Unit from March 2011 to May 2012. Twenty patients were allocated to each of the treatment groups. No adverse events occurred during the study. The flow diagram of the study is shown in Fig. 1.
3.1. Baseline

One-way ANOVA analysis showed that there was no significant difference between groups as to age, length of illness and primary outcomes (10 MWT: P = 0.869; 6 MWT: P = 0.941) at T0 evaluation. Patients’ characteristics and outcome measures are detailed in Tables 2 and 3.

3.2. Primary outcomes

As to the 10 MWT, a significant main effect was found for treatment ($F_{1,85} = 6.216, P = 0.004$; effect size = 0.179; observed power = 87.7%); time ($F_{1,114} = 152.717, P < 0.001$; effect size = 0.728; observed power = 100%) and the interaction between treatment and time ($F_{3,414} = 32.104, P < 0.001$; effect size = 0.530; observed power = 100%). Post hoc comparisons showed a significant difference between RGT vs. PT ($P = 0.003$) and TT vs. PT ($P = 0.041$).

As to the 6 MWT, a significant main effect was found for treatment ($F_{2,157} = 4.543, P = 0.015$; effect size = 0.137; observed power = 75.1%); time ($F_{1,52} = 104.713, P < 0.001$; effect size = 0.648; observed power = 100%) and the interaction between treatment and time ($F_{3,854,109.845} = 25.570, P < 0.001$; effect size = 0.473; observed power = 100%). Post hoc comparisons showed a significant difference between RGT vs. TT ($P = 0.021$) and TT vs. PT ($P = 0.048$).

As to the stride length, a significant main effect was found for treatment ($F_{2,157} = 13.856, P < 0.001$; effect size = 0.327; observed power = 99.8%); time ($F_{1,114} = 138.783, P < 0.001$; effect size = 0.709; observed power = 100%) and the interaction between treatment and time ($F_{1,114} = 28.534, P < 0.001$; effect size = 0.500; observed power = 100%). Post hoc comparisons showed a significant difference between RGT vs. PT ($P < 0.001$) and TT vs. PT ($P = 0.008$).

As to the cadence, a significant main effect was found for time ($F_{1,406,83} = 29.563, P < 0.001$; effect size = 0.342; observed power = 100%) and the interaction between treatment and time ($F_{2,93} = 5.055, P = 0.003$; effect size = 0.151; observed power = 90.2%). No significant main effect was revealed for treatment.

As to the ratio between single and double support duration, a significant main effect was found for time ($F_{1,903,108.445} = 19.137, P < 0.001$; effect size = 0.251; observed power = 100%) and the interaction between treatment and time ($F_{3,806,108.445} = 25.570, P = 0.006$; effect size = 0.121; observed power = 88%). No significant main effect was revealed for treatment.

As to the coefficient of variation of stride time, no significant main effect was found for treatment, time and their interaction.

As to the Berg Balance Scale, overall significant improvements were found between groups at both T1 ($\chi^2: 18.010, P < 0.001$) and T2 ($\chi^2: 12.499, P = 0.002$) evaluations. In particular, a significant difference was found between RGT vs. PT at both T1 ($Z: 2.932, P = 0.003$) and T2 ($Z: 2.932, P = 0.003$) evaluations as well as between RGT vs. PT at T1 ($Z: 2.388, P = 0.001$) evaluations.

As to the Parkinson’s Fatigue Scale, overall significant improvements were found between groups at both T1 ($\chi^2: 13.055, P < 0.001$) and T2 ($\chi^2: 8.634, P = 0.013$) evaluations. In particular, a significant difference was found only between RGT vs. PT at both T1 ($Z: 3.563, P < 0.001$) and T2 ($Z: 3.197, P = 0.001$) evaluations.

As to the UPDRS, overall significant improvements were found between groups at both T1 ($\chi^2: 7.662, P = 0.022$) and T2 ($\chi^2: 7.816, P = 0.020$) evaluations. In particular, a significant difference was found only between RGT vs. PT at both T1 ($Z: 2.848, P = 0.004$) and T2 ($Z: 2.941, P = 0.003$) evaluations.

Table 3: Patients’ performance in all outcome measures.

<table>
<thead>
<tr>
<th>Group</th>
<th>Before treatment mean (SD)</th>
<th>After treatment mean (SD)</th>
<th>Follow-up mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 MWT (m/s)</td>
<td>RGT 1.06 (0.08)</td>
<td>1.34 (0.08)</td>
<td>1.33 (0.10)</td>
</tr>
<tr>
<td>TT 1.09 (0.17)</td>
<td>1.26 (0.15)</td>
<td>1.26 (0.16)</td>
<td></td>
</tr>
<tr>
<td>PT 1.09 (0.20)</td>
<td>1.09 (0.19)</td>
<td>1.09 (0.18)</td>
<td></td>
</tr>
</tbody>
</table>

| 6 MWT (m) | RGT 325.45 (60.62) | 410.20 (55.15) | 398.95 (54.54) |
| TT 320.10 (82.19) | 400.15 (61.65) | 395.65 (64.53) |
| PT 327.10 (52.21) | 329.95 (54.78) | 325.10 (59.09) |

| Stride length (cm) | RGT 82.10 (3.39) | 96.06 (2.55) | 94.95 (5.02) |
| TT 83.57 (3.43) | 90.84 (4.21) | 91.73 (5.17) |
| PT 84.22 (3.83) | 86.21 (4.81) | 85.48 (4.54) |

| Cadence (cyc/min) | RGT 6 MWT 325.45 (52.21) | 410.20 (55.15) | 398.95 (54.54) |
| TT 320.10 (82.19) | 400.15 (61.65) | 395.65 (64.53) |
| PT 327.10 (52.21) | 329.95 (54.78) | 325.10 (59.09) |

| Coefficient of variation of stride time (%) | RGT 5.75 (7.22) | 6.55 (6.95) | 4.89 (4.77) |
| TT 5.57 (2.31) | 6.09 (2.43) | 5.32 (2.31) |
| PT 5.61 (4.78) | 6.09 (7.15) | 5.78 (5.32) |

| Berg balance scale (0–56) | RGT 42.85 (3.88) | 53.40 (3.30) | 52.55 (3.59) |
| TT 47.10 (4.71) | 50.70 (3.85) | 50.80 (5.14) |
| PT 48.65 (4.93) | 47.35 (5.28) | 47.45 (4.91) |

| Parkinson’s fatigue scale (16–80) | RGT 48.00 (11.54) | 38.20 (10.62) | 38.15 (10.39) |
| TT 47.65 (6.61) | 41.85 (12.74) | 43.05 (14.75) |
| PT 49.55 (9.18) | 50.65 (8.66) | 49.20 (8.63) |

| UPDRS (0–147) | RGT 36.70 (6.17) | 30.95 (6.96) | 30.55 (7.21) |
| TT 35.90 (7.77) | 34.05 (8.96) | 33.85 (9.95) |
| PT 37.59 (8.59) | 38.05 (8.00) | 37.95 (8.16) |

Abbreviations: SD, Standard Deviation; RGT, Robotic Gait Training; TT, Treadmill Training; PT, Physical Therapy; m, meters; s, seconds; cm, centimeters; cyc/min, cycles/minute; UPDRS, Unified Parkinson’s Disease Rating Scale.

4. Discussion

As to the primary outcomes of this single blind, randomized, controlled trial, we failed to find statistically significant differences...
between RGT and equal intensity TT without body-weight support in patients with mild to moderate PD. Conversely, we observed that patients who underwent RGT and TT significantly improved gait speed and walking capacity compared to those who performed PT according to the PNF approach.

As to the RGT vs. TT comparison, our findings about individuals with mild to moderate PD seem to confirm those recently reported by Carda and colleagues regarding patients with early stage PD [8]. However, from a rehabilitative point of view, it is important to point out that only patients in the RGT group obtained clinically significant improvements in both primary outcomes (>0.25 m/s in the 10 MWT and ≥82 m in the 6 MWT) after treatment [24]. In order to explain these findings, the characteristics of our study population have to be considered. Indeed, patients with mild to moderate PD (H&Y 3) not only have gait hypokinesia but also suffer from an impairment of balance [9], which is a key element for the ability to walk [25]. As to the effect of RGT on balance, a recent study examined thirty-one patients with PD (H&Y 3–4) treated with the GT1 machine, reporting statistically and clinically relevant improvements in postural instability after treatment [26]. On the other hand, despite TT has been reported to improve balance skills in PD, its effectiveness has been mainly evaluated in patients with H&Y 3 [27–29]. Our results showed that balance significantly improved after RGT compared to TT. Thus, it is plausible that patients in the RGT group improved gait speed and walking capacity in a more clinically relevant way than patients who underwent equal intensity TT due to the greater effect of RGT on a fundamental element for walking ability such as balance. This would be in keeping with the GT1 machine characteristics, which is an end-effector system that allows a constant balance from one leg to the other during training, according to the slow walking speeds used [26]. Moreover, the role of body-weight support cannot be neglected, considering that impaired load receptor function has been found to contribute to gait impairment in PD [30]. In particular, body-weight support has been suggested to influence lower leg extensors activity as well as load receptor proprioceptive feedback mechanisms that are essential for the maintenance of balance during gait [30]. In this study, only the RGT group had a support of body-weight, in line with previous studies [7,8]. Conversely, we decided not to support body-weight in the TT group, because the combination of body-weight support with TT still remains unclear in PD and is not strictly recommended [6,8].

Consistent with previous findings, we observed that patients who underwent RGT and TT improved walking ability more than by conventional PT [6,7]. In this study we based PT on the PNF approach consisting of exercises performed lying in bed (see Table 1). Conversely, patients in the RGT and TT groups performed an intensive training based on a great number of step repetitions. Thus, even though the PNF approach has been previously proposed for training gait in patients with PD [7,15], it is plausible that the scant effects of conventional PT observed in this study may be due to its low intensity. On this basis, further studies with matched-scant effects of conventional PT observed in this study may be due to its low intensity. On this basis, further studies with matched-scant effects of conventional PT observed in this study may be due to its low intensity. On this basis, further studies with matched-scant effects of conventional PT observed in this study may be due to its low intensity. On this basis, further studies with matched-scant effects of conventional PT observed in this study may be due to its low intensity. On this basis, further studies with matched-scant effects of conventional PT observed in this study may be due to its low intensity. On this basis, further studies with matched-scant effects of conventional PT observed in this study may be due to its low intensity. On this basis, further studies with matched-scant effects of conventional PT observed in this study may be due to its low intensity. On this basis, further studies with matched-scant effects of conventional PT observed in this study may be due to its low intensity. On this basis, further studies with matched-scant effects of conventional PT observed in this study may be due to its low intensity. On this basis, further studies with matched-scant effects of conventional PT observed in this study may be due to its low intensity.

Regarding previous studies about the use of RGT for improving gait in PD, only one randomized controlled trial evaluated the effects of the GT1 machine in patients with H&Y 2.5–3, reporting statistically but not clinically significant improvements in the 10 MWT and the 6 MWT [7]. This was partially not confirmed by the present study that found also clinically significant improvements in gait speed and walking capacity after treatment with the GT1 machine in patients with H&Y 3. This probably occurred because RGT was more intense in this study due to the higher training speed. This study has several limitations. First, we did not compare RGT and equal intensity TT with the same amount of body-weight support. Second, considering the PT group as a placebo group, it would have been useful to compare the three groups on a scale of satisfaction or expectancy. Third, we did not compare RGT and TT with a PT program of the same intensity of energy expenditure. In conclusion, our findings support the hypothesis that RGT is not superior to equal intensity TT for improving walking ability in patients with mild to moderate PD. Considering that some parameters, such as balance, seem to improve better after RGT than after TT, further multicenter trials dealing with gait training in PD are needed to clarify the role of robotic and electromechanical devices in terms of effectiveness related to the phase of illness.

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References


