Comparison Between the Outcomes of Robot-Assisted Gait Training (RAGT) and Conventional Walking Training (CWT) in Patients with Multiple Sclerosis (MS): A Systematic Review and Meta-Analysis

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Abstract

Introduction: Robotic technology and physical therapy are of paramount significance for treating gait impairment in Multiple Sclerosis (MS) patients. However, there is still a lack of comparative studies between these two approaches. This systematic review and meta-analysis compares the effectiveness of Robot-assisted Gait Training (RAGT) with Conventional Walking Training (CWT) in MS patients.

Method: Following PRISMA guidelines, a comprehensive literature search was done through Pubmed/Medline, Google Scholar, Cochrane library, and ClinicalTrials.gov registry from 2001 to 2023. After careful screening, 14 articles of highly significant variables were involved in synthesising this meta-analysis. Data analysis was done through Review Manager (RevMan, Version 5.4.1; The Cochrane Collaboration, Copenhagen, Denmark).

Result: In our review, 14 studies comprising 457 subjects were shortlisted, of which 233 participants belonged to the Robot-Assisted Gait Training (RAGT) group, and 224 participants belonged to the Conventional Walking Training (CWT) group. The mean age of study participants in the RAGT and control groups is 51.67 ± 10.67 years and 52.36 ± 10.83 years, respectively. These studies' male and female populations were 35.66% and 57.33%, respectively. Our analysis showed that RAGT and CWT are equally effective in improving most outcomes. However, RAGT may be more effective than CWT in improving gait speed (MD, 23.65; 95% CI, 0.81, 46.50; P = 0.04; I2 = 74%), as measured by the six-minute walk test.

Conclusion: Our findings suggest that RAGT could be a viable alternative to CWT for MS patients with difficulty walking. Hence this study serves as a foundation for future investigations that minimize the study's limitations to provide a more robust conclusion. Future research should aim to replicate our findings and investigate RAGT and CWT's long-term effects on MS patients.

Keywords: Robot-assisted Gait Training (RAGT) • Multiple sclerosis • Conventional Walking Training • Antibody • Neuro immunology • Myelin basic protein microglia

Introduction

Multiple Sclerosis (MS) is characterized by a variable distribution of demyelinated neurons and axons, which can result in a range of neurological impairments [1]. Inadequate mobility, tiredness, stiffness, balance issues, loss of strength, sensory problems, sexual dysfunctions, depression, cognitive deficits, and a lower Quality of Life (QoL) are just a few of the symptoms caused by these neurological deficiencies in patients with MS [2].

Mobility issues are the most common symptom experienced by individuals with Multiple Sclerosis (MS). Studies have shown that as many as 80% of MS patients never fully regain their ability to walk or move around normally. These gait problems can significantly negatively impact the quality of life, social life, job opportunities, and overall level of independence for MS patients [3].

The predominance of motor abnormalities in MS patients indicates the necessity for long-term care in rehabilitation. Physical therapy is successful in treating gait and mobility issues in addition to improving balance [4]. A relatively new approach for a task-oriented practice known as Body Weight Supported Treadmill Training (BWSTT) has shown promising results in improving gait recovery and reducing the risk of long-term mobility impairments in individuals with MS. By using task-oriented repetition and a symmetrical gate design, BWSTT helps maintain balance while walking and allows the patient to begin weight-bearing activities earlier than otherwise expected [5]. Studies have shown that BWSTT can improve gait speed and endurance in individuals with Multiple Sclerosis (MS) while helping maintain a manageable level of fatigue. Intense, efficient, targeted training has been shown to positively impact patient outcomes, making BWSTT an effective approach for MS rehabilitation [6].

The use of robotic technology has revolutionised physical treatment, and Robot-Assisted Gait Training (RAGT) is one such example. RAGT utilises robotic devices to provide a range of inputs that activate the brain and stimulate the central pattern generator, resulting in improved motor capabilities. This is achieved through constant and symmetrical lower limb trajectories [7]. In addition, two other techniques have been developed that focus on controlling the pelvic and distal portions of the legs, respectively; these are the exoskeleton approach and the end effector approach. Both strategies have proven effective in improving functional abilities and gait metrics [8]. RAGT is effective in treating a range of neurological disorders, including stroke, Traumatic Brain Injury (TBI), Spinal and Brain Injury (SCI), Parkinson's disease, and cerebral palsy [9-12]. Its success has resulted in its implementation in physical therapy worldwide.

While previous research has extensively studied physical therapy and the use of robotic equipment in patients with Multiple Sclerosis (MS), there is still a lack of comparative studies between these two approaches. This systematic review and meta-analysis aim to bridge this gap by examining and comparing the effectiveness of ground-based traditional gait training with robot-driven gait orthosis in MS patients. In addition, this study aims to assess the impact of RAGT on various parameters such as fatigue levels, quality of life, balance, and mobility in MS patients. This comprehensive analysis will provide clinicians and patients with valuable insights into the most effective treatments for MS-related gait impairment.

Materials and Methods

Search strategy

"Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA)" guidelines were applied to carry out research regarding this meta-analysis [13]. The literature search was carried out systematically on the databases of Pubmed/Medline, Google Scholar, Cochrane library, and ClinicalTrials.gov registry from 2001 to 2023 with the MeSH terms "multiple sclerosis", "robot-assisted gait training", "robot-assisted rehabilitation", and "motor devices" in various combinations. Studies were filtered using titles, abstracts, and full texts in English on the human specimen. Additionally, references of included studies were manually screened for any qualifying data.

Inclusion and exclusion of articles

The criteria for inclusion and exclusion of studies were fixed after discussion with the authors. Only studies that involved gait-specific outcome parameters of Robot-Assisted Gait Training (RAGT) in known multiple sclerosis adult patients, compared to a control group, were included. After a thorough search and applying relevant filters, 103 studies were extracted, from which 4 duplicate articles were removed. Based on irrelevant titles and abstracts, and screening of full-text formats, 79 studies were excluded. Poor-quality trials, letters to editors, commentaries, case reports, cross-sectional studies, conference posters, proceedings, and personal communications were excluded. Further exclusion based on the overlapping study population, non-English texts, and non-availability of sufficient data resulted in 14 studies, which have been included in the meta-analysis. This has been illustrated in the Prisma chart, as shown in Figure 1.

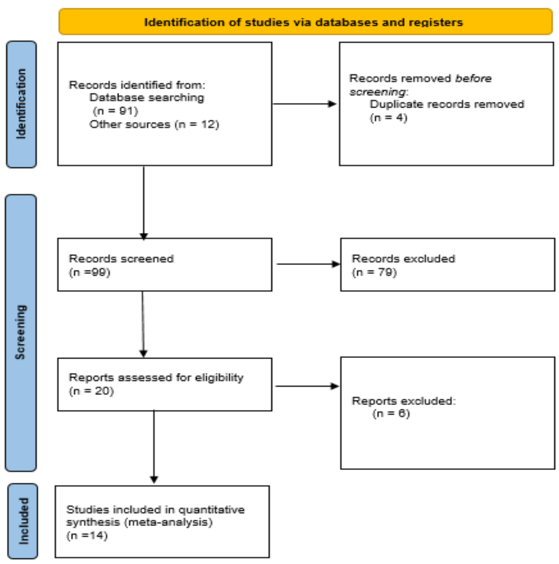

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram of included studies, n=14.

Data extraction

The authors performed the extraction of data on the characteristics of each study and its patient population, including the year of publication, country of study, the total number of participants, age and gender of the participants, number of years passed from the onset of the disease, the type of MS (relapsing-remitting, primary progressive, secondary progressive, or progressive relapsing) and the reported outcomes from each study that met the inclusion criteria.

Study outcomes

The primary endpoints studied in this analysis were the walking performance and speed assessed by conducting a walking test at 2 meters (2 MWT), 6 meters (6 MWT), 10 meters (10 MWT), and 25 feet (25 FWT). Other parameters, such as double support time, cadence, stride length, step length, and step time, were also analysed using the GAITRite system. The secondary endpoints included the Expanded Disability Status Scale (EDSS) and the Functional Independence Measure (FIM) to monitor the estimation of functional disability in MS patients, the Berg Balance Scale (BBS) for the assessment of functional balance, the Fatigue Severity Scale (FSS) to estimate the measure of self-perceived fatigue, the Timed Up and Go (TUG) test and the Functional Ambulatory Category (FAC) to assess positive development in mobility, the Visual Analog Scale (VAS) for the assessment of wellbeing and improvement in spasticity and pain, and the 54-item Multiple Sclerosis Quality of Life (MSQoL-54) questionnaires involving the assessment of Physical Health Composite (PHC) and Mental Health Composite (MHC). Moreover, the 9-item Patient Health Questionnaire (PHQ-9) and the 36-item Short Form Health Survey (SF-36) data were also studied.

Risk of bias assessment

The quality assessment of selected studies was done using the Cochrane collaboration risk of the bias assessment tool [14], as shown in Table 1. The performance bias, selection bias, reporting bias, detection bias, attrition bias, and other biases were estimated for each study. We graded the risk of bias in each study as low, high, or unclear. In many of the included studies, the overall risk of bias was low. Eleven studies were scored as fair-to-good quality, whereas two studies were of poor quality due to high-performance bias, as blinding investigators and participants were not feasible [15-28].

Results

Review Manager, version 5.4.1 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration) was used to perform all statistical analyses.

Search results

As a result of a detailed literature search carried out following the PRISMA guidelines resulted in 14 studies [14-27] being shortlisted. These studies comprise 457 subjects, of which 233 participants belong to the Robot-Assisted Gait Training (RAGT) group, and 224 belong to the Conventional Walking Training (CWT) group. The studies were conducted in the United States of America (n = 3), Italy (n = 6), Switzerland (n = 2), Turkey (n = 1), and Israel (n = 1). The mean age of study participants in the RAGT and control groups is 51.67 ± 10.67 years and 52.36 ± 10.83 years, respectively. These studies' male and female populations were 35.66% and 57.33%, respectively. The average duration from the onset of multiple sclerosis in the selected participants was 11.33 years.

Table 1. Quality assessment of Randomized Controlled Trials by Cochrane Risk of bias tool.

Study	Selection Bias		Performance Bias	Detection bias	Attrition bias	Reporting Bias	Other bias	Our evaluation
	Random Sequence Generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting	Anything else, ideally prespecified	

Lo AC (2008)	Low risk	Unclear risk	High risk	High risk	Low risk	Low risk	Low risk	Poor quality
Beer (2008)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Good quality
Vaney (2011)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Good quality
Schwartz (2011)	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Fair quality
Ruiz (2013)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Good quality
Straudi (2013)	Low risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk	Poor quality
Gandolfi (2014)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Good quality
Straudi (2015)	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Fair quality
Pompa (2016)	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Fair quality
Straudi (2019)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Good quality
Berriozabalgoitia (2020)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Good quality
Androwis (2021)	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Fair quality
Sconza (2021)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Good quality
Ozsoy-Unubol (2021)	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Fair quality

Change in double support time (Figure 2) was reported by 3 studies, with a total of 26 participants in RAGT and 25 participants in CWT participants Our analysis did not show a significant association Robot-assisted gait treadmill treadmill (RAGT) and the change in double support time (MD, -3.89; 95% CI, -8.75, 0.31; P = 0.12; I2 = 42%).

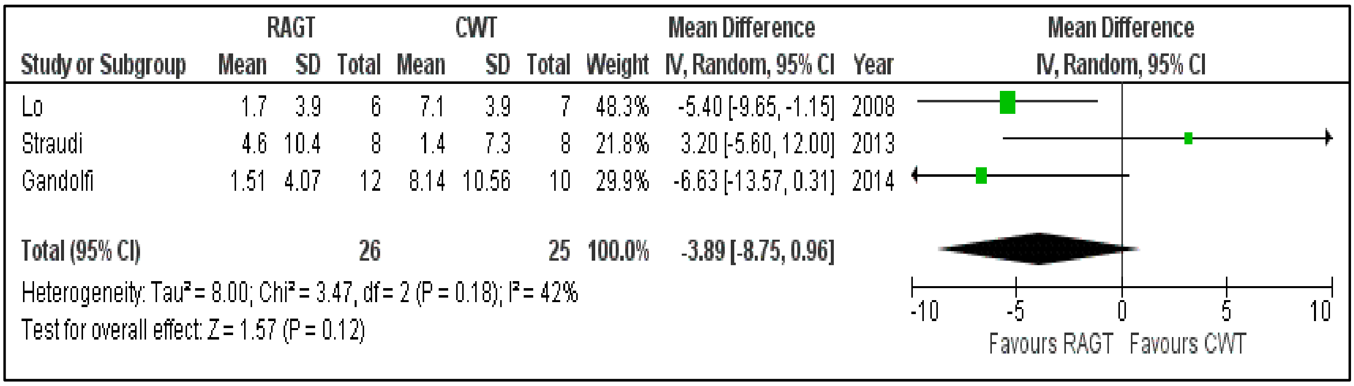

Figure 2. Comparative effectiveness of Robot-assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting the change in double support time.

Three studies reported changes in Cadence from baseline to post-treatment (Figure 3) was reported by 3 studies, with 23 participants in RAGT and 22 in CWT participants. Our analysis did not show a significant association between the Robot-assisted gait treadmill (RAGT) and change in cadence (MD, 5.73; 95% CI, -3.63, 15.09; P = 0.23; I2 = 0%).

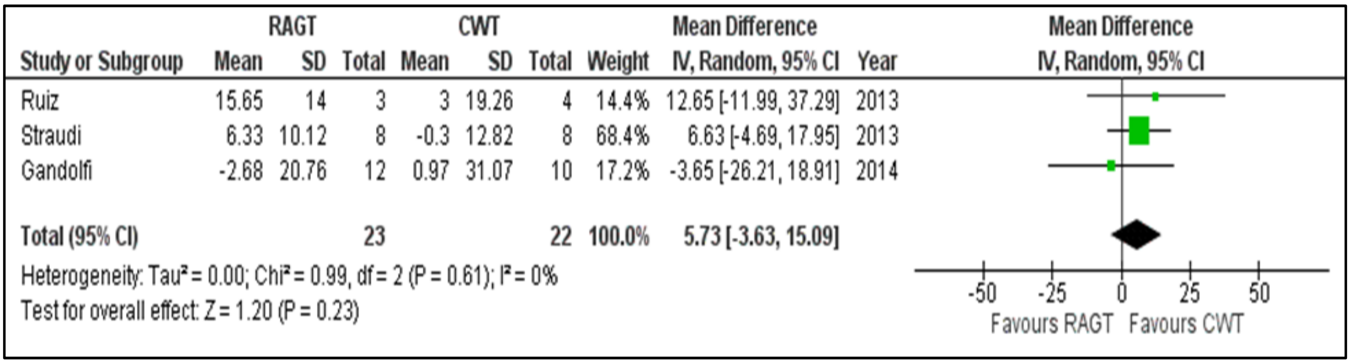

Figure 3. Comparative effectiveness of Robot-assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting change in Cadence.

Change in Gait Speed from baseline (6MWT) (Figure 4) was reported by 6 studies, with 68 participants in RAGT and 73 participants in CWT participants. Our analysis shows a significant association between Robot-Assisted Gait Treadmill (RAGT) and 6MWT (MD, 23.65; 95% CI, 0.81, 46.50; P = 0.04; I2 = 74%).

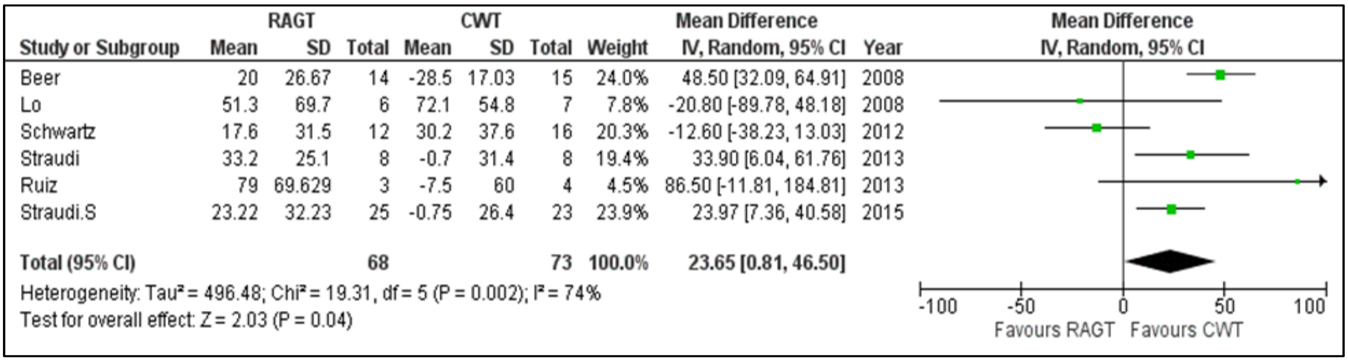

Figure 4. Comparative effectiveness of Robot-assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting the change in Gait Speed from baseline (6MWT).

Change in gait speed (10MWT) was reported by 3 studies, with 62 participants in RAGT and 62 participants in CWT participants. Our analysis did not show a significant association between the Robot-assisted gait treadmill (RAGT) and 10MWT (MD, -0.03; 95% CI, -0.13,0.07; P = 0.55; I2 = 76%) (Figure 5).

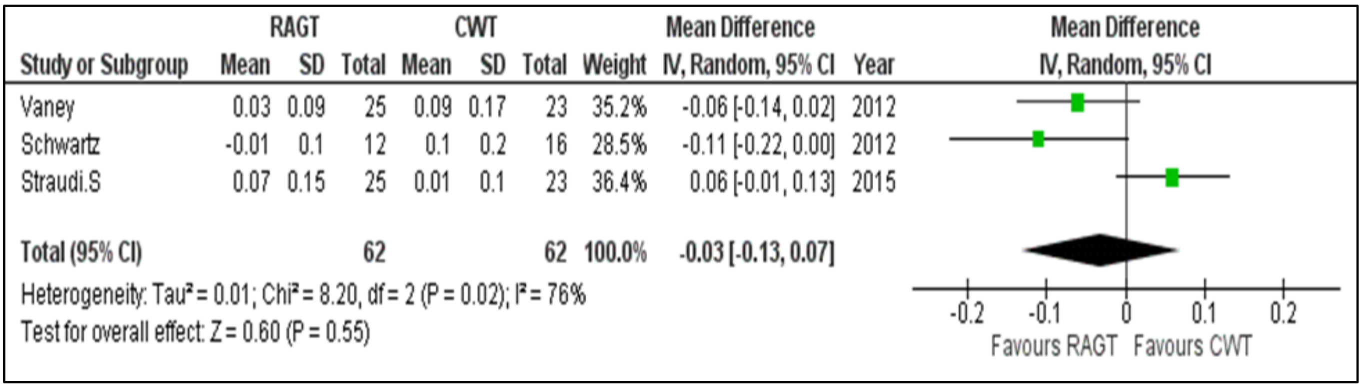

Figure 5. Comparative effectiveness of Robot-assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting the change in gait speed (10MWT).

Post

Post-treatment for change in gait speed (T25WT) was reported by 4 studies, with 55 participants in RAGT and 56 in CWT participants (Figure 6). Our analysis did not show a significant association between the Robot-assisted gait treadmill (RAGT) and T25WT (MD, 0.01; 95% CI, -0.17, 0.19; P = 0.92, I2 = 0%)

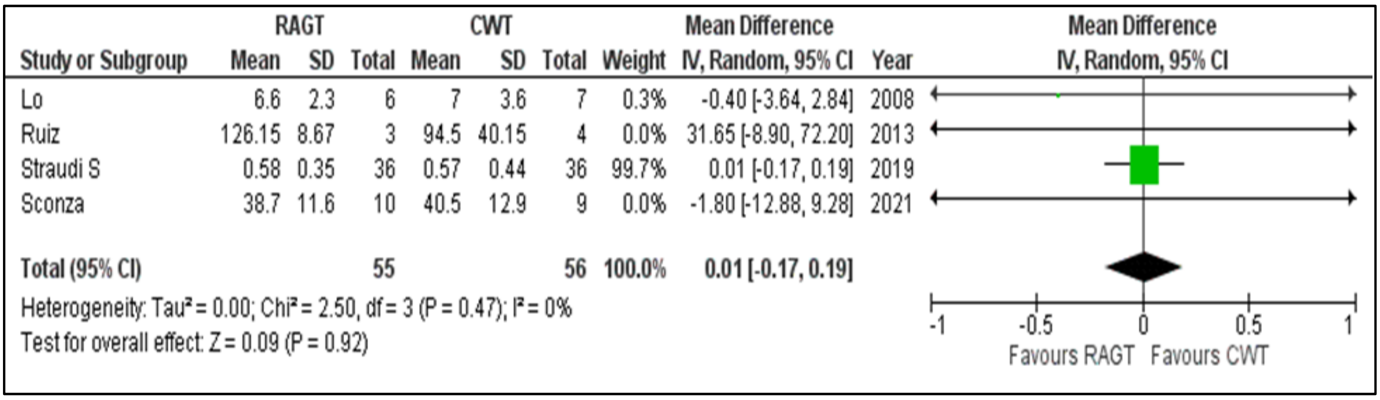

Figure 6. Comparative effectiveness of Robot-assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting Post-treatment for change in gait speed (T25WT).

Post-treatment for change in Expanded Disability Status Scale (EDSS) (Figure 7) was reported by 3 studies, with a total of 51 participants in RAGT and 57 participants in CWT participants. Our analysis did not show a Significant association between the Robot-Assisted Gait Treadmill (RAGT) and EDSS (MD, 0.07; 95% CI, -0.13, 0.27; P = 0.49, I2 = 0%)

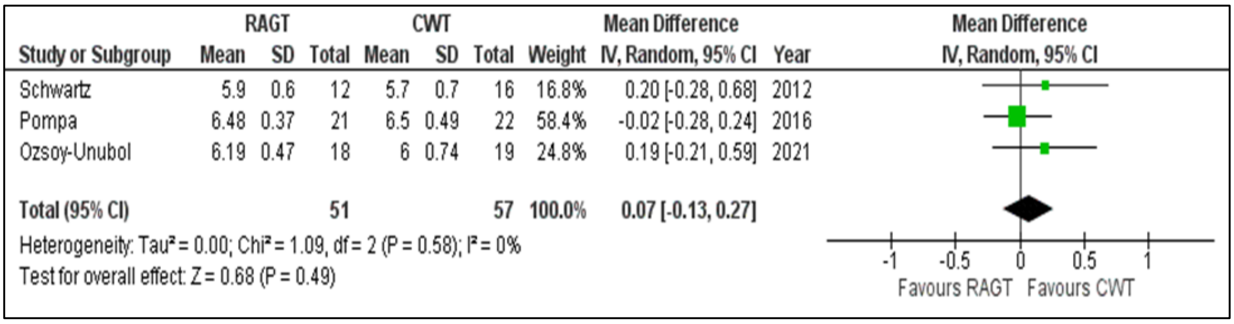

Figure 7. Comparative effectiveness of Robot-assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting Post-treatment for change in Expanded Disability Status Scale (EDSS).

Post-treatment for change in Mental QoL was reported by 4 studies, with a total of 91 participants in RAGT and 94 participants in CWT participants (Figure 8). Our analysis did not show a significant association between the Robot-assisted gait treadmill (RAGT) and Mental QoL (MD, 0-0.48; 95% CI, -4.71, 3.76; P = 0.49, I2 = 0%)

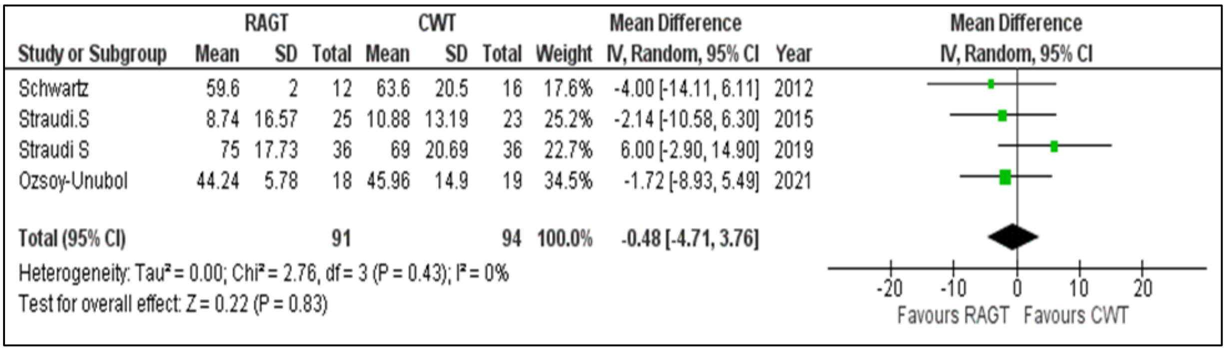

Figure 8. Comparative effectiveness of Robot-assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting Post-treatment for change in Mental QoL.

Post-treatment for change in Physical QoL was reported by 4 studies, with a total of 91 participants in RAGT and 94 participants in CWT participants (Figure 9). Our analysis did not show a significant association between the Robot-Assisted Gait Treadmill (RAGT) and physical QoL (MD, -1.42; 95% CI, -3.42, 0.59; P = 0.17, I2 = 0%)

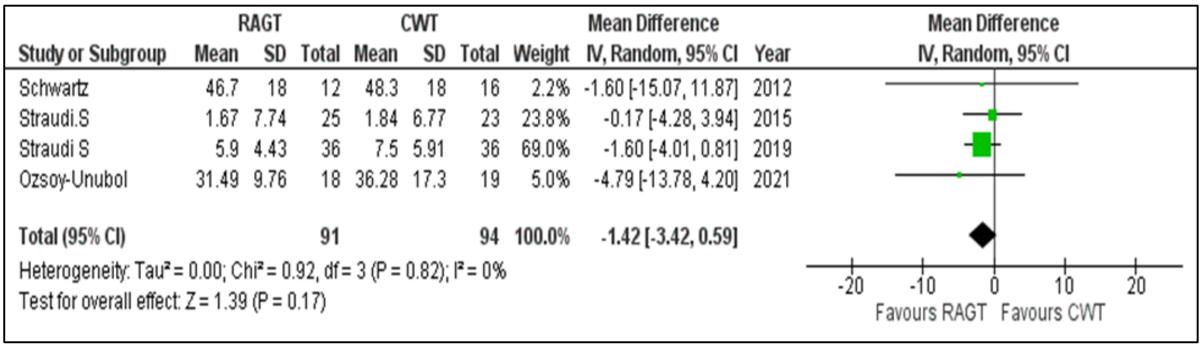

Figure 9. Comparative effectiveness of Robot-assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting Post-treatment for change in Physical QoL.

Post-treatment data on the Fatigue Severity Scale (FSS) was reported by 5 studies, with a total of 113 participants in RAGT and 110 participants in CWT participants (Figure 10). Our analysis did not show a significant association between the Robot-Assisted Gait Treadmill (RAGT) and FSS (MD, 0.14; 95% CI, -1.86, 2.14; P = 0.89; I2 = 0%).

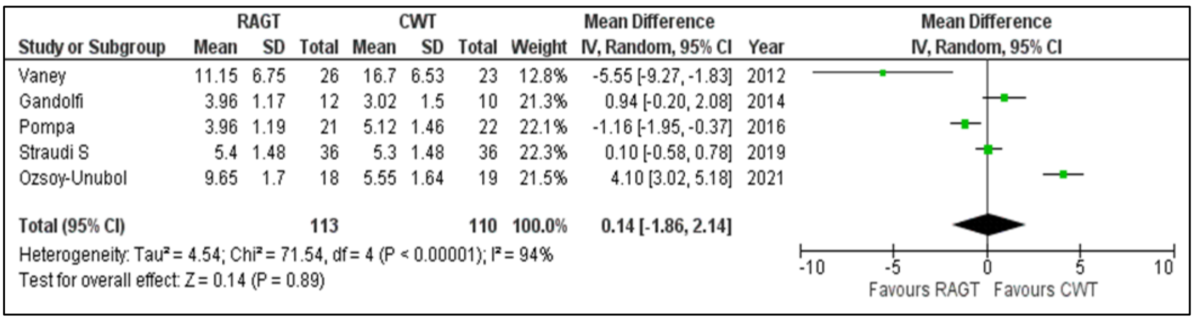

Figure 10. Comparative effectiveness of Robot-Assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting Post-treatment data on Fatigue Severity Scale (FSS).

Post-treatment data on the berg balance scale (BBS) was reported by 5 studies, with a total of 104 participants in RAGT and 104 participants in CWT participants (Figure 11). Our analysis did not show a significant Association between the Robot-Assisted Gait Treadmill (RAGT) and BBS (MD, 0.15; 95% CI, -2.37,2.67; P = 0.91; I2 = 0%).

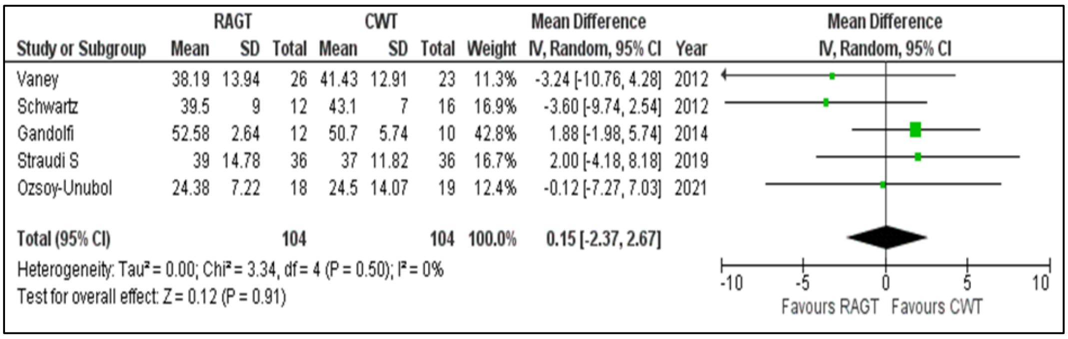

Figure 11. Comparative effectiveness of Robot-Assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting Post-treatment data on Berg Balance Scale (BBS).

Post-treatment data on the time up and go test (TUG) was reported by 5 studies, with a total of 80 participants in RAGT and 78 participants in CWT participants (Figure 12). Our analysis did not show a significant association between the Robot-Assisted Gait Treadmill (RAGT) and TUG (MD, -3.78; 95% CI, -8.05, 0.50; P = 0.08; I2 = 5%).

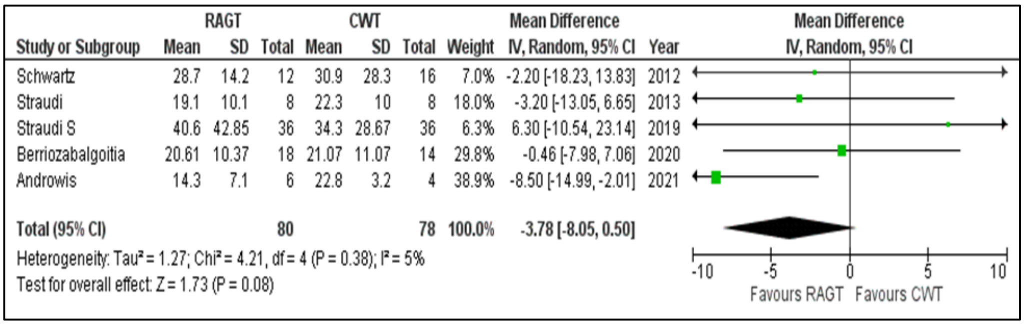

Figure 12. Comparative effectiveness of Robot-Assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT) in reporting Post-treatment data on time up and go test (TUG).

Discussion

The present study aimed to investigate the effect of Robot-assisted Gait Training (RAGT) on individuals with Multiple Sclerosis (MS) compared to Conventional Walking Training (CWT). A comprehensive literature search was conducted according to PRISMA guidelines, which included 14 studies with a total of 457 participants, of which 233 belonged to the RAGT group and 224 to the CWT group.

Various outcomes were measured, including post-treatment data on fatigue severity scale (FSS), Berg balance scale (BBS), time up and go test (TUG), change in double support time, change in cadence, change in gait speed from baseline (6MWT), change in gait speed (10MWT and T25WT), change in Expanded Disability Status Scale (EDSS), mental QoL, and physical QoL.

The findings of our analysis did not show any significant differences between RAGT and CWT in terms of FSS, BBS, TUG, change in double support time, change in cadence, change in gait speed (10MWT and T25WT), EDSS, mental QoL, and physical QoL. However, a significant association was found between RAGT and change in gait speed from baseline, as measured by the 6MWT. The MD between the RAGT and control groups was 23.65, with a 95% CI between 0.81 and 46.50. The P-value for this association was 0.04, indicating statistical significance. However, the study had a high degree of heterogeneity (I2=74%), meaning that the results varied widely between the different studies included in the analysis.

The clinical significance of the finding that RAGT is associated with an improvement in gait speed is that it suggests RAGT may be more effective than CWT in improving gait speed in patients with MS. Gait speed is an important predictor of overall health and functional ability in older adults and those with neurological or musculoskeletal conditions. Improvements in gait speed are associated with increased mobility, independence, and quality of life. Therefore, the findings of this study suggest that RAGT may be a valuable treatment option for individuals with gait impairments.

Our study has several strengths. We used a comprehensive search strategy to identify all relevant studies and only included randomized controlled trials, which are considered the gold standard for evaluating the effectiveness of interventions. Furthermore, we conducted a rigorous statistical analysis.

However, some limitations to our study should be acknowledged. First, the number of studies included in our analysis varied across outcomes, which may have affected the statistical power of our analysis. Second, the sample sizes of the individual studies were relatively small, which may have limited our ability to detect significant differences between RAGT and CWT. Finally, our analysis was limited to short-term outcomes, and the long-term effects of RAGT and CWT on patients with MS remain unclear.

Conclusion

In conclusion, our analysis showed that RAGT and CWT are equally effective in improving most of the outcomes we analyzed in patients with MS. However, RAGT may be more effective than CWT in improving gait speed, as measured by the six-minute walk test. Our findings suggest that RAGT could be a viable alternative to CWT for MS patients with difficulty walking. Future research should aim to replicate our findings and investigate RAGT and CWT's long-term effects on MS patients.

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