REVIEW ARTICLE

Rheumatol. Forum
2024, vol. 10, No. 2, 61–71
Copyright © 2024 Via Medica
ISSN: 2720-3921, e-ISSN: 2720-3913
DOI: 10.5603/rf.98609

VIA MEDICA
www.journals.viamedica.pl

Anna Krzyżańska [1], Magdalena Dziurda [1], Mateusz Maćkowiak [1], Michał Michalak [2], Marek Jóźwiak [1]

[1]Department of Pediatric Orthopedics and Traumatology, Poznan University of Medical Sciences, Poznan, Poland
[2]Department of Computer Science and Statistics, Poznan University of Medical Sciences in Poznan, Poland

Effect of robot-assisted gait training on functional capabilities in individuals with cerebral palsy: a systematic review and meta-analysis

ABSTRACT

The present study evaluates the effectiveness of robot-assisted gait training (RAGT). Lower limb function treatment in patients with cerebral palsy (CP) includes functional testing: UP&GO, 6-Minute Walking Test (6MWT), and the Gross Motor Function Measure (GMFM).

PubMed, Web of Science, Cochrane Library, Embase, Scopus, and EBSCO databases were searched to collect RAGT studies on lower limb dysfunction in CP patients. The GMFM, GMFM D, and GMFM E scales assessed motor function, and the UP & GO test assessed balance function and walking speed. 6MWT assessed endurance and walking speed. Due to the occurrence of only one publication with the UP&GO test, it was impossible to analyze this element.

The review included a total of 17 studies. The meta-analysis showed that RAGT significantly improved GMFM, GMFM D and E and 6MWT scores in patients with CP. Results are a compilation of all publications combined, as well as by group for randomized and non-randomized trials, and for RAGT alone or combined with conventional physiotherapy. The results regarding the assessment of functional status using the GMFM scale present the lowest heterogeneity.

RAGT positively affects gait and balance functions in CP patients. Future high-quality, long-term follow-up studies are needed to investigate the clinical efficacy of RAGT thoroughly.

Rheumatol. Forum 2024, vol. 10, No. 2: 61–71

KEY WORDS: neurological disorders of gait; rehabilitation; nervous system disorders

INTRODUCTION

Cerebral palsy (CP) is a neurodevelopmental disorder caused by brain damage during early development, clinically manifested by postural and motor dysfunction [1]. Sensory, perceptual, cognitive and communication deficits, as well as behavioral problems, epilepsy and secondary musculoskeletal problems, often accompany this CP-related motor dysfunction. CP exhibits clinical features that fall into four categories: spastic, irregular, atactic, or mixed [1]. The prevalence of CP ranges from 0.20 to 0.35% among living infants. In 2023, the number of people with CP reached 17 million worldwide [1]. About 40% of these patients cannot walk independently, significantly affecting their daily functioning [2]. Clinical rehabilitation interventions for CP patients mainly include neurodevelopmental therapy, physiotherapy and hydrotherapy, which succeeded but they are less effective in treating gait and balance functions [2].

Robot-assisted gait training (RAGT) is a new rehabilitation intervention that facilitates repetitive and effective gait training with

Address for correspondence:
Anna Krzyżańska, ul. Mediolańska 3/12, 62–080 Tarnowo Podgórne;
e-mail: s52032@student.ump.edu.pl

external mechanical support [3]. In patients with crouch gait, the robotic exoskeleton has improved knee range of motion in patients with spastic cerebral palsy [4]. Training on a robot-assisted treadmill significantly improved in standing and walking function [5].

The studies are still few, outcome measures and treatment effects vary, clinical effectiveness remains controversial, and more high-quality evidence-based medicine is needed to support this [6]. Meta-analysis is a statistical method that quantifies several interventions and prioritizes the effects of interventions based on different outcome measures. In this study, we used the meta-analysis method to search for RAGT studies for patients with CP, extract relevant outcome measures to assess their effectiveness, and provide evidence-based references for the clinical application of RAGT training.

MATERIAL AND METHODS

This study was registered on the PROSPERO platform CRD4202346954. The search time window lasted from 6.10.2023 to 4.11.2023. Three reviewers conducted the main search independently (A.K., M.D., M.M.).

SEARCH STRATEGY

The authors conducted a meta-analysis after a systematic search of all relevant articles in Med of Science, Cochrane, PubMed, Science, EBSCO, and Embase databases (Supplementary File) with a limitation of the search by language-only English-language publications, a range of 10 years and only publications published as articles or book chapters based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The search was conducted from 2013 to 2023. Three independent reviewers conducted the leading search, and keywords included:

— 1# “Cerebral palsy” OR “cerebral paralysis” OR “spastic cerebral paralysis” OR “monoplegic cerebral palsy” OR “diplegic cerebral palsy” OR “hemiplegic cerebral palsy” OR “tetraplegic cerebral palsy”.
— 2# “Robot-assisted gait therapy” OR “Robotic gait rehabilitation” OR “exoskeleton” OR “HAL” OR “trexo” OR “Lokomat” OR “ekso” OR “RoboGait” OR “wearable robot”.
— 1# AND 2#.

The condition was limited to studies measuring GMFM, UP& GO and 6MWT. After completing the search, the results were checked, and, in case of discrepancies, the decision was discussed with a third researcher (Fig. 1).

Three reviewers screened and independently checked the titles and abstracts (AK, MD, MM). After combining studies from six databases and removing duplicates, we obtained texts of potentially relevant articles. Three independent reviewers evaluated each article for eligibility based on the purpose of the study. Articles were included based on the following:

— population (people with CP);
— Gross Motor Function Classification System (GMFCS) I–IV;
— type of intervention (robot-assisted gait training with or without other rehabilitation);
— outcomes (GMFM, 6MWT, UP&GO).

Any discrepancies were assessed and resolved by discussion among three reviewers. We collected relevant data from each study included in the analysis using a standard data recording form. The form included details such as publication title, authors and year. Further information collected included the number and age of participants, the intervention protocol (including intervention duration, comparators, number of sessions and any additional interventions), and outcome measures and results (mean and standard deviation). After extraction, studies were excluded if they included non-CP populations, did not include a mean score and standard deviation for 6MWT, UP& GO and GMFM, and had fewer than five patients.

ASSESSING THE RISK OF BIAS

Three review authors (A.K., M.D., M.M.) independently assessed the risk of bias using the Risk Of Bias In Non-Randomized Studies 1 (ROBINS 1). The discussion between the three reviewers resolved any disagreements. The following areas were evaluated: bias due to confounding, bias in selecting participants for the study, bias in intervention classification, bias due to deviations from the intended intervention, bias due to missing data, bias in reported results selection, and overall risk of bias. Each area was addressed and labeled: low, moderate and serious. For randomized trials, RoB 2 was used. The following areas were assessed: bias arising from the randomization process, bias due to deviations from the intended intervention, bias due to missing outcome

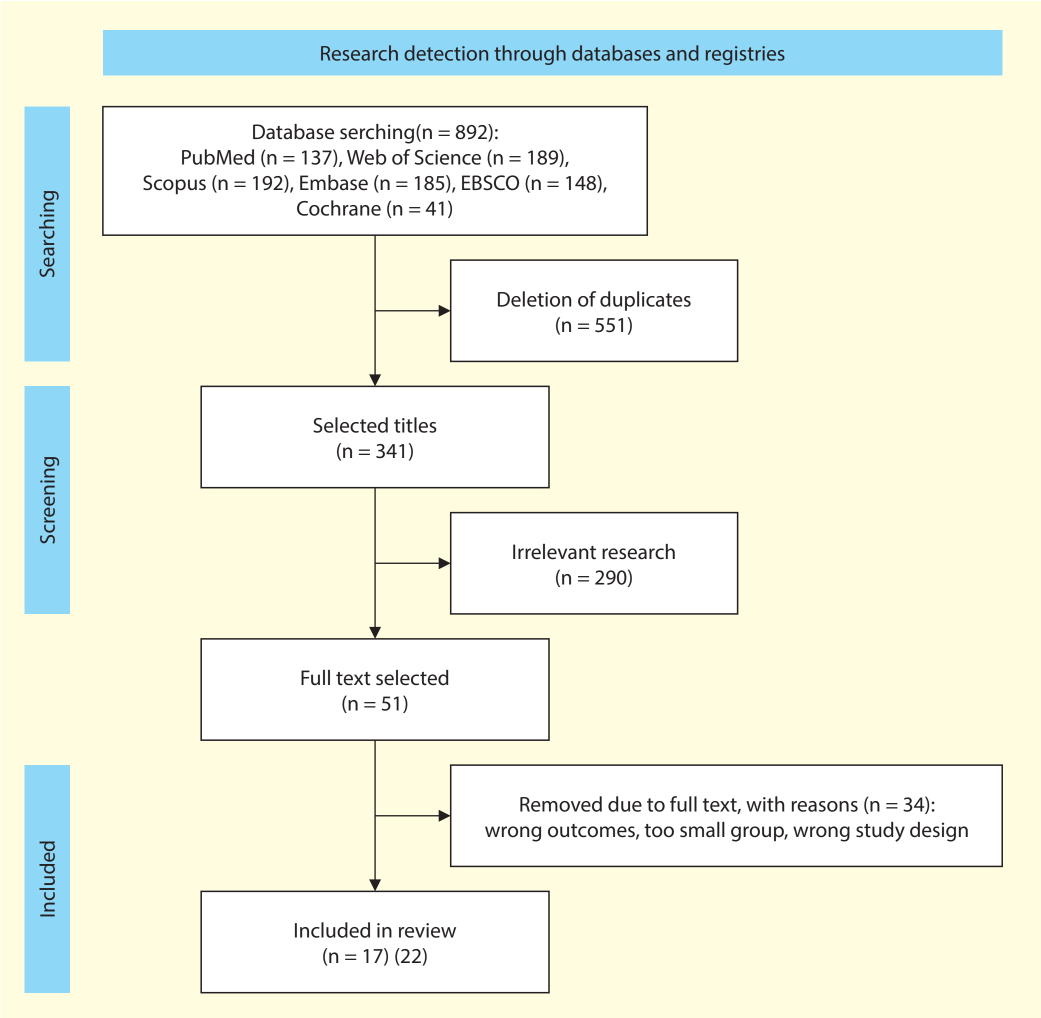

Figure 1. Flow chart of the study

data, bias in the measurement of the outcome, and bias in the selection of the reported result. The answers are the same as in ROBINS 1; each domain was answered: low, moderate and severe (Fig. 2) [7, 8].

DATA ANALYSIS

Several comparisons of the collected results were made: comparison 1 - the effects of robot-assisted gait training alone compared to the conditions of robot-assisted training and conventional rehabilitation; comparison 2 - the maintenance of the effects of robot-assisted gait training in randomized trials compared to the effects in non-randomized trials. The comparisons included results such as gait distance in the 6MWT, gait speed in the UP & GO test, and GMFM functional test score in domains D (standing) and E (walking, running and jumping).

The mean difference (MD) was chosen as the effect size metric for this meta-analysis. The results were presented as MD, with a 95% confidence interval (95% CI). To account for potential heterogeneity, a random effects model was employed. A random effects model was employed to account for potential heterogeneity. The I2 index, also known as the inconsistency index, was used to quantify the proportion of total variation across studies due to heterogeneity rather than chance. The publication bias was assessed with funnel plots and the Egger's test. Additionally, sub-analyses were conducted based on whether the study was observational or randomized, as well as whether physiotherapy was administered solely by a robot or with the support of a physiotherapist.

The statistical analysis was performed using Rstudio version 2023.06.0 (2009–2023 posit software) using R-4.2.2 software incorporating packages readxl, ggplot2, meta, and robvis. All tests were significant at $p < 0.05$ except Cochran's Q statistic. Given its low power, heterogeneity was deemed significant if $p < 0.10$.

RESULTS

STUDIES SELECTION

We identified 892 articles using an electronic search strategy during this systematic review. A cross-analysis of 17 full texts using a standardized data entry form that included outcome measures followed the identification process. The cross-analysis verified exclusion criteria and facilitated data extraction.

Figure 1 shows a detailed study of our qualitative analysis after extracting eligible studies. Seventeen articles in this systematic review and meta-analysis covered 464 people with cerebral palsy. These studies examined the effects of RAGT through assessments such as the 6MWT, the UP&GO test and the measurement of GMFM.

QUALITATIVE ANALYSIS

Study quality was assessed based on risk of bias using the ROBINS 1 tool for non-randomized trials and Risk of Bias 2 (RoB 2) for randomized trials. Figure 2 shows the results.

Study quality assessment classifies randomized trials of four [9–12] as low risk and three [16–15] as medium risk. Among the non-randomized studies, eight studies [16–23] were rated as low risk and two papers [24, 25] as medium risk.

QUANTITATIVE ANALYSIS

The meta-analyses included 17 studies. Ten studies analyzed gait speed using the 6MWT (10,11,13,15,16,19–21,26,27) a controlled force was applied to the pelvis and legs during treadmill walking. For participants who were assigned to the treadmill only group, manual assistance was provided as needed. Each participant trained 3 times/wk for 6 wks. Outcome measures included walking speed, 6-min walking distance, and clinical assessment of motor function, which were evaluated before, after training, and 8 wks after the end of training, and were compared between two groups. Results Significant increases in walking speed and 6-min walking distance were observed after robotic training (P = 0.03. Ten articles analyzed the GMFM total [9, 12, 15, 17, 18, 21, 23, 25], and the D and E dimensions of the GMFM were presented in eight papers [9, 10, 12, 13, 15, 17, 19, 23]. The meta-analysis results for all variables are shown in Figures 3–6, respectively. For 6MTW, the publications discussed the results; the vast majority achieved improvements; the vast majority achieved improvements, but the meta-analysis shows a high degree of heterogeneity. When considering randomized and non-randomized trials separately, a decrease in heterogeneity is in the non-randomized group. According to the publication groups with RAGT alone and RAGT with conventional rehabilitation, heterogeneity shows only low levels in the RAGT alone group. Observers reported significant improvements in functional status when using the GMFM scale for functional assessment. There was minimal variation in the results of each analysis, regardless of whether randomized or non-randomized trials were considered. The same was true for publications describing RAGT alone or RAGT with conventional therapy. We observe average heterogeneity in the total works analyzed in the D and E dimensions of the GMFM scale.

DISCUSSION

This systematic review aimed to provide a comprehensive overview of RAGT therapy's effectiveness in increasing total gait distance and functional status among people with CP at different levels of the GMFCS. The results showed that RAGT led to an increase in total gait distance as measured by 6MWT and improved functional abilities as assessed by the measurement of GMFM. The systematic review found a positive clinical effect for gait speed and GMFM total in the D and E dimensions. These findings align with results from other studies that specifically assessed the short-term effects of RAGT [27–29]. The observed lack of statistically significant differences may be due to the sample size. The literature shows that meter increments of 20, 50 meters in 6MTW are rated as small to medium effects in the adult population [30]. Therefore, when the meta-analysis showed a mean improvement of 29.65m, the results of 6MWT should be considered clinically non-significant. Improvements in GMFM may indicate that RAGT has the potential to generate greater independence and functionality for these individuals. A study by van Hedel et al. found that the more significantly reduced a child's walking ability (GMFCS IV), the greater the benefit gained from RAGT, including improvements in physical and cardiorespiratory fitness [19].

Currently, no objective data are available regarding the optimal RAGT protocol.

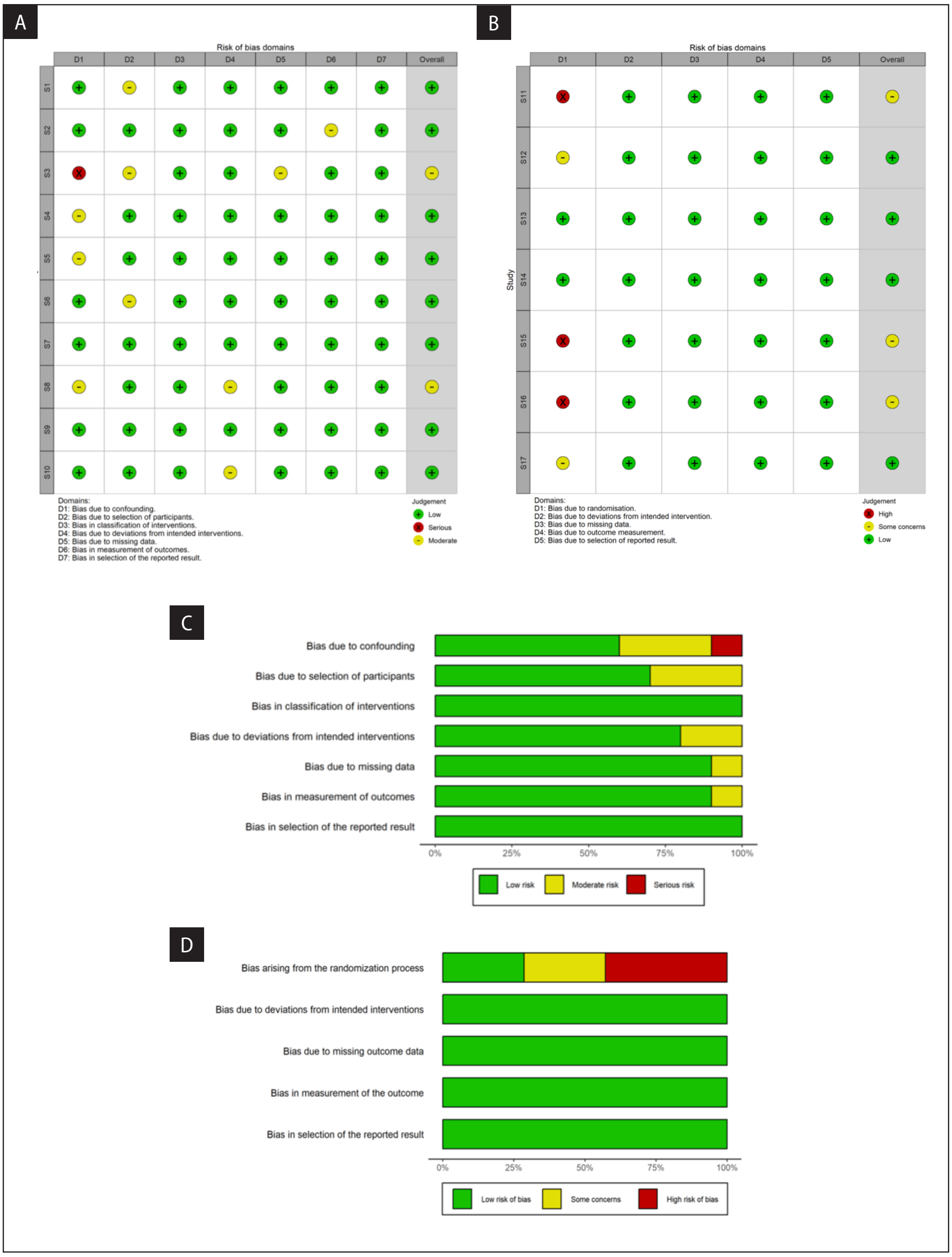

Figure 2. Risk of bias. **A.** Traffic lights for non — randomized trial; **B.** Traffic lights for randomized trial V; **C.** Risk of bias graph for non — randomized trial; **D.** Risk of bias graph for randomized trial

Larger controlled studies are required to determine the optimal timing and protocol design that will maximize efficacy and long-term outcomes in cerebral palsy patients. Another important issue is the availability and cost of these devices. At present, their usage is limited to highly specialized centers with the required space and resources. Therefore, more compact and affordable devices for home use are needed.

CONCLUSIONS

Evidence from this systematic review with meta-analysis showed that RAGT can clinically improve balance, gait distance, and function in people with CP. The results show that both 6MWT and GMFM improve after the therapies. Therefore, RAGT is a valid intervention to benefit balance, gait distance, walking distance and functional

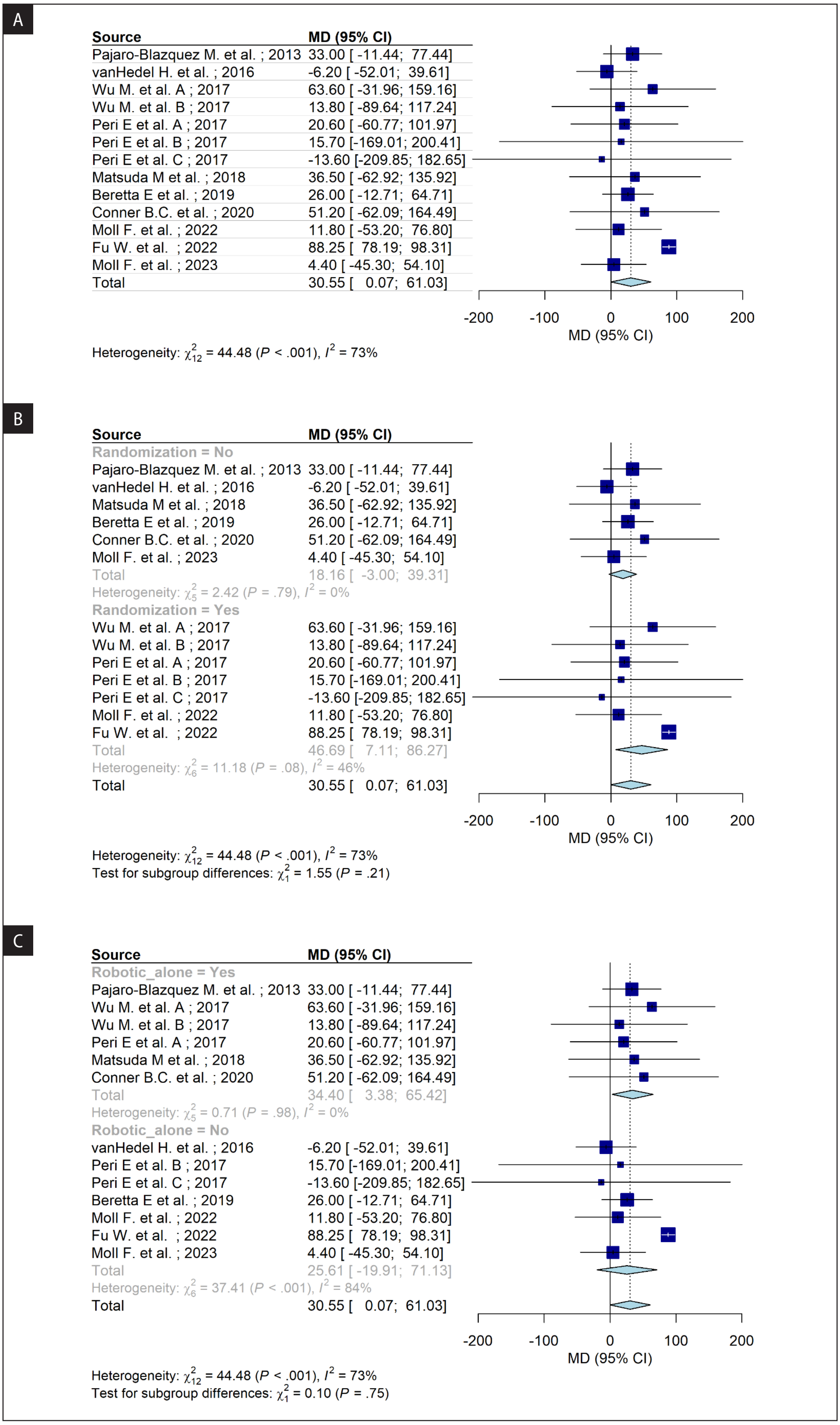

Figure 3. Forest plot. **A.** 6-Minute Walking Test (6MWT) all; **B.** 6MWT non- randomized trials and randomized trials; **C.** 6MWT robotic alone and robotic with conventional physiotherapy. MD — mean difference; CI — confidence interval

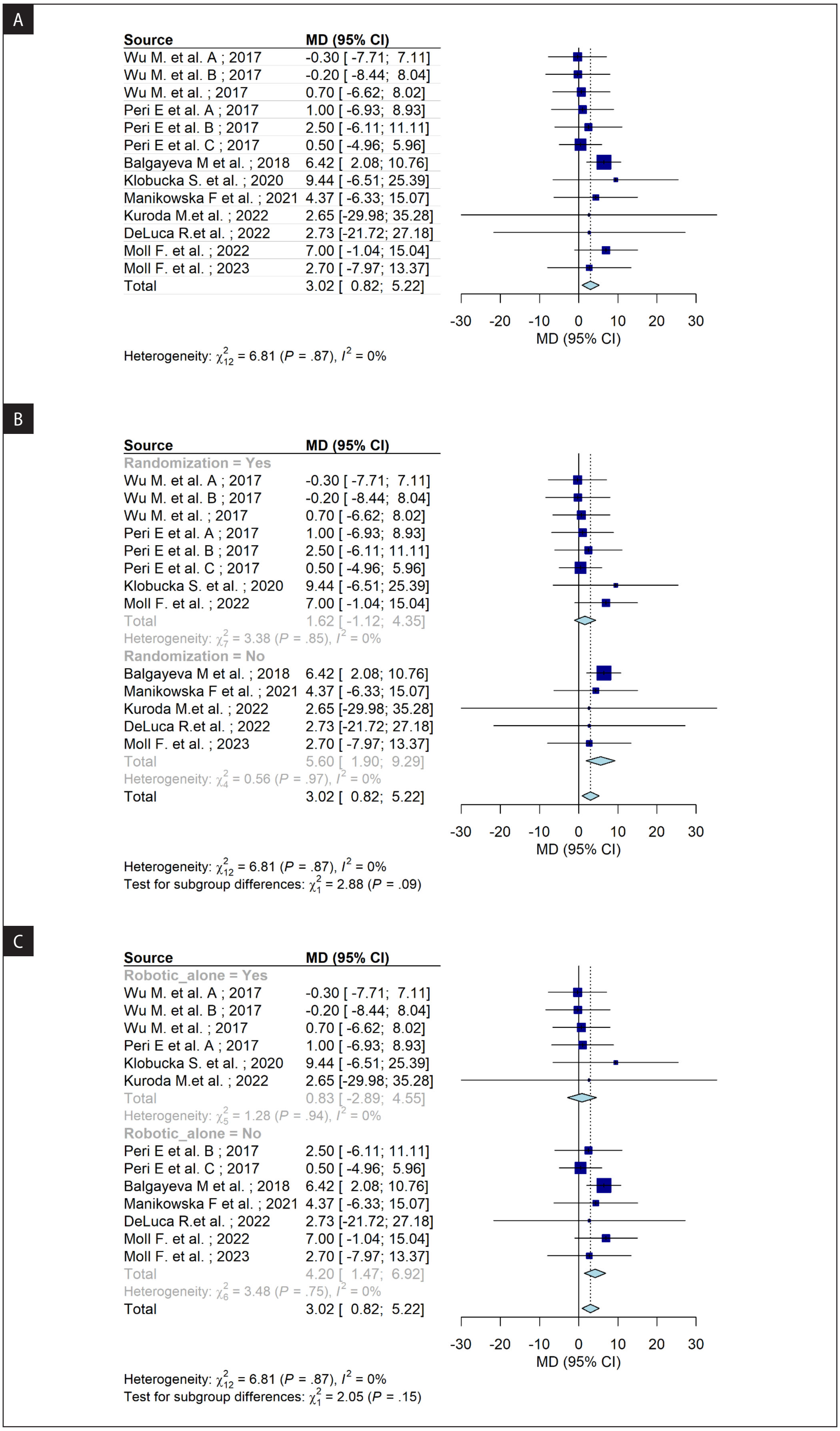

Figure 4. Forest plot. **A.** Gross Motor Function Measure (GMFM) all; **B.** GMFM non-randomized trials and randomized trials; **C.** GMFM robotic alone and robotic with conventional physiotherapy. MD — mean difference; CI — confidence interval

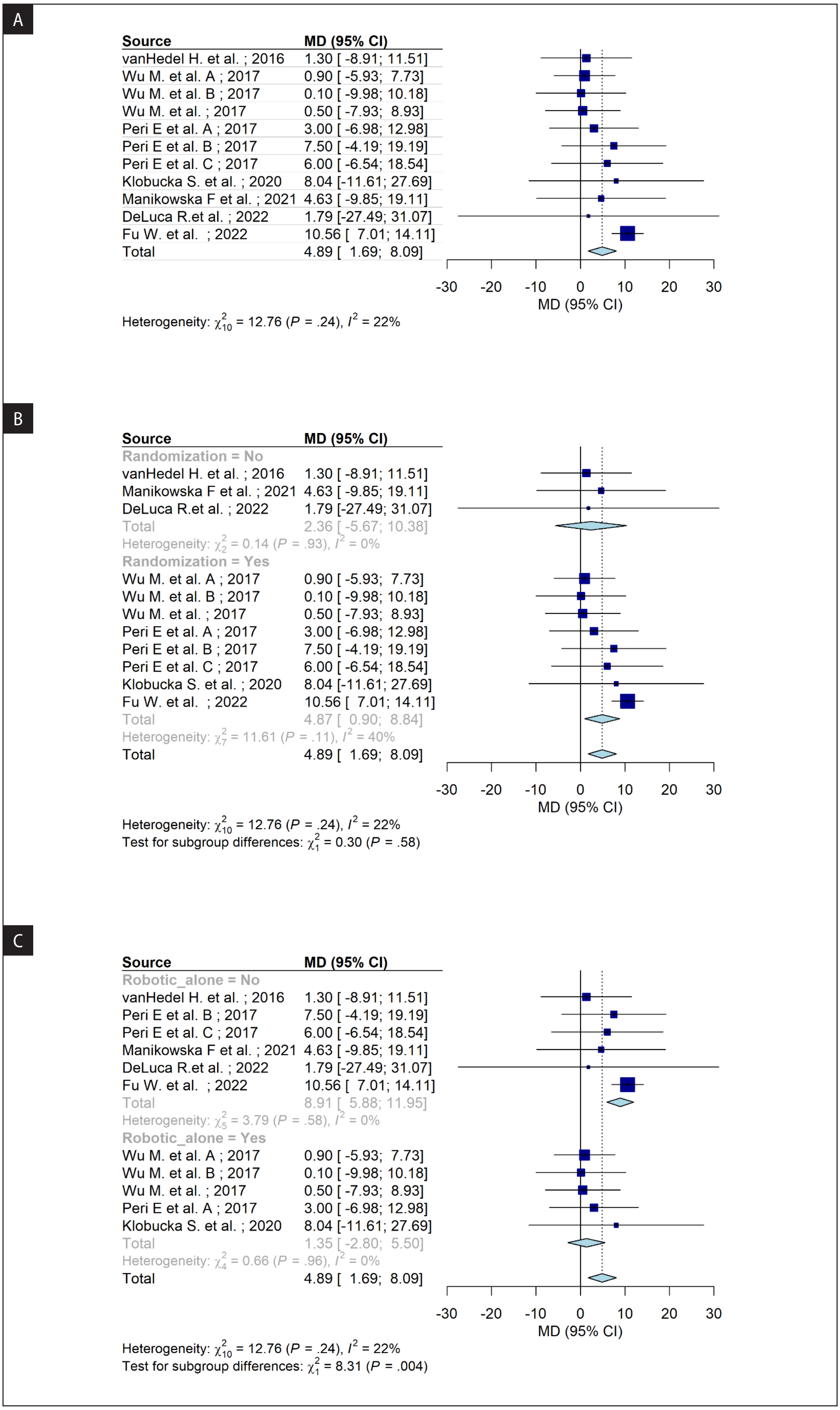

Figure 5. Forest plot. **A.** Gross Motor Function Measure D dimension (GMFM_D) all; **B.** GMFM_D non- randomized trials and randomized trials; **C.** GMFM_D robotic alone and robotic with conventional physiotherapy. MD — mean difference; CI — confidence interval

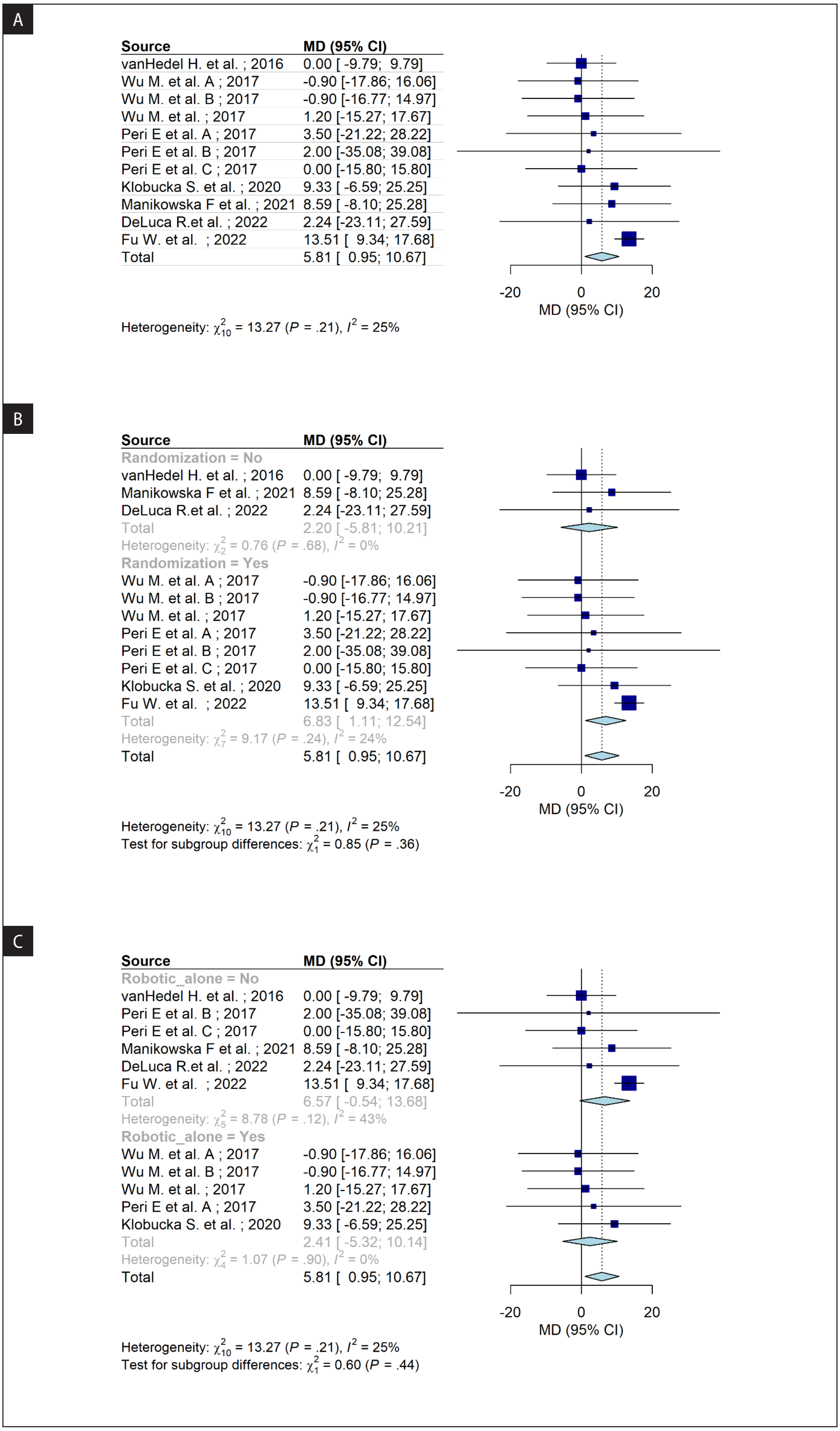

Figure 6. Forest plot. **A.** Gross Motor Function Measure E dimension (GMFM_E) all; **B.** GMFM_E non-randomized trials and randomized trials; **C.** GMFM_E robotic alone and robotic with conventional physiotherapy. MD — mean difference; CI — confidence interval

ability in people with CP. Our findings reinforce the importance and need for more randomized clinical trials that examine outcome maintenance.

ACKNOWLEDGEMENTS

Most appreciation goes to the team that searched databases and analyzed articles that qualified for systematic review.

AUTHOR CONTRIBUTIONS

A.KK.: designed the study, conducted database searches, then analysis, prepared data for processing by a statistician and wrote the manuscript with support from M.D., M.M., M.M., M.J. M.D.: conducted database searches, then analyzed and prepared data for processing by a statistician. M.M.: conducted database searches, then analyzed and prepared data for processing by a statistician. M.M.: made statistical calculations and performed advisory functions. M.J.: supervised the findings of this work.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

FUNDING

The work was done as part of scientific development without financial support.

References

1. Rosenbaum P, Paneth N, Leviton A, et al. A report: the definition and classification of cerebral palsy April 2006. Dev Med Child Neurol Suppl. 2007; 109: 8–14, indexed in Pubmed: 17370477.
2. Rodda J, Graham HK. Classification of gait patterns in spastic hemiplegia and spastic diplegia: a basis for a management algorithm. Eur J Neurol. 2001; 8 Suppl 5: 98–108, doi: 10.1046/j.1468-1331.2001.00042.x, indexed in Pubmed: 11851738.
3. Oudenhoven LM, van Vulpen LF, Dallmeijer AJ, et al. Improved Walking Capacity and Muscle Strength After Functional Power-Training in Young Children With Cerebral Palsy. Neurorehabil Neural Repair. 2017; 31(9): 827–841, doi: 10.1177/1545968317723750, indexed in Pubmed: 28786309.
4. Lerner ZF, Damiano DL, Bulea TC. Relationship between assistive torque and knee biomechanics during exoskeleton walking in individuals with crouch gait. IEEE Int Conf Rehabil Robot. 2017; 2017: 491–497, doi: 10.1109/ICORR.2017.8009296, indexed in Pubmed: 28813868.
5. Aurich-Schuler T, Grob F, van Hedel HJA, et al. Can Lokomat therapy with children and adolescents be improved? An adaptive clinical pilot trial comparing Guidance force, Path control, and FreeD. J Neuroeng Rehabil. 2017; 14(1): 76, doi: 10.1186/s12984-017-0287-1, indexed in Pubmed: 28705170.
6. Volpini M, Aquino M, Holanda AC, et al. Clinical effects of assisted robotic gait training in walking distance, speed, and functionality are maintained over the long term in individuals with cerebral palsy: a systematic review and meta-analysis. Disabil Rehabil. 2022; 44(19): 5418–5428, doi: 10.1080/09638288.2021.1942242, indexed in Pubmed: 34232847.
7. Sterne JAc, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016; 355: i4919, doi: 10.1136/bmj.i4919, indexed in Pubmed: 27733354.
8. Flemyng E, Moore TH, Boutron I, et al. Using Risk of Bias 2 to assess results from randomised controlled trials: guidance from Cochrane. BMJ Evid Based Med. 2023; 28(4): 260–266, doi: 10.1136/bmjebm-2022-112102, indexed in Pubmed: 36693715.
9. Klobucká S, Klobucký R, Kollár B. Effect of robot-assisted gait training on motor functions in adolescent and young adult patients with bilateral spastic cerebral palsy: A randomized controlled trial. NeuroRehabilitation. 2020; 47(4): 495–508, doi: 10.3233/NRE-203102, indexed in Pubmed: 33136072.
10. Wu M, Kim J, Arora P, et al. Effects of the Integration of Dynamic Weight Shifting Training Into Treadmill Training on Walking Function of Children with Cerebral Palsy: A Randomized Controlled Study. Am J Phys Med Rehabil. 2017; 96(11): 765–772, doi: 10.1097/PHM.0000000000000776, indexed in Pubmed: 28644244.
11. Moll F, Kessel A, Bonetto A, et al. Use of Robot-Assisted Gait Training in Pediatric Patients with Cerebral Palsy in an Inpatient Setting-A Randomized Controlled Trial. Sensors (Basel). 2022; 22(24), doi: 10.3390/s22249946, indexed in Pubmed: 36560316.
12. Wu M, Kim J, Gaebler-Spira DJ, et al. Robotic Resistance Treadmill Training Improves Locomotor Function in Children With Cerebral Palsy: A Randomized Controlled Pilot Study. Arch Phys Med Rehabil. 2017; 98(11): 2126–2133, doi: 10.1016/j.apmr.2017.04.022, indexed in Pubmed: 28576629.
13. Fu WS, Song YC, Wu BA, et al. Virtual reality combined with robot-assisted gait training to improve walking ability of children with cerebral palsy: A randomized controlled trial. Technol Health Care. 2022; 30(6): 1525–1533, doi: 10.3233/THC-212821, indexed in Pubmed: 35661029.
14. Yaşar B, Atıcı E, Razaei D, et al. Effectiveness of Robot-Assisted Gait Training on Functional Skills in Children with Cerebral Palsy. J Pediatr Neurol. 2021; 20(03): 164–170, doi: 10.1055/s-0041-1725128.
15. Peri E, Turconi AC, Biffi E, et al. Effects of dose and duration of Robot-Assisted Gait Training on walking ability of children affected by cerebral palsy. Technol Health Care. 2017; 25(4): 671–681, doi: 10.3233/THC-160668, indexed in Pubmed: 28436398.
16. Conner BC, Remec NM, Orum EK, et al. Wearable Adaptive Resistance Training Improves Ankle Strength, Walking Efficiency and Mobility in Cerebral Palsy: A Pilot Clinical Trial. IEEE Open J Eng Med Biol. 2020; 1: 282–289, doi: 10.1109/ojemb.2020.3035316, indexed in Pubmed: 33251524.

17. Manikowska F, Krzyżańska A, Chmara P, et al. Baseline Gross Motor Function Affects the Outcome of Robot-Assisted Therapy in Ambulatory Individuals with Spastic Cerebral Palsy. Brain Sci. 2021; 11(12), doi: 10.3390/brainsci11121563, indexed in Pubmed: 34942865.
18. Maira B, Sholpan B. Effectiveness of the combined use of robotic kinesiotherapy and botulinum therapy in the complex rehabilitation of children with cerebral palsy. Asian J Pharmaceut Clin Res. 2018; 11(9): 360, doi: 10.22159/ajpcr.2018.v11i9.26541.
19. van Hedel HJA, Meyer-Heim A, Rüsch-Bohtz C. Robot-assisted gait training might be beneficial for more severely affected children with cerebral palsy. Dev Neurorehabil. 2016; 19(6): 410–415, doi: 10.3109/17518423.2015.1017661, indexed in Pubmed: 25837449.
20. Pajaro-Blazquez M, Shetye R, Gallegos-Salazar J, et al. Robotic-Assisted Gait Training in Children with Cerebral Palsy in Clinical Practice. Biosystems Biorobot. 2013: 29–33, doi: 10.1007/978-3-642-34546-3_5.
21. Moll F, Kessel A, Bonetto A, et al. Safety and Feasibility of Robot-assisted Gait Training in Adults with Cerebral Palsy in an Inpatient Setting - an Observational Study. J Dev Phys Disabil. 2023 [Epub ahead of print]: 1–16, doi: 10.1007/s10882-023-09895-8, indexed in Pubmed: 36817800.
22. Beretta E, Storm FA, Strazzer S, et al. Effect of Robot--Assisted Gait Training in a Large Population of Children With Motor Impairment Due to Cerebral Palsy or Acquired Brain Injury. Arch Phys Med Rehabil. 2020; 101(1): 106–112, doi: 10.1016/j.apmr.2019.08.479, indexed in Pubmed: 31562873.
23. De Luca R, Bonanno M, Settimo C, et al. Improvement of Gait after Robotic-Assisted Training in Children with Cerebral Palsy: Are We Heading in the Right Direction? Med Sci (Basel). 2022; 10(4), doi: 10.3390/medsci10040059, indexed in Pubmed: 36278529.
24. Bonato P. Unraveling Mechanisms Underlying the Effectiveness of Robot-Assisted Gait Training in Children with Cerebral Palsy. Biosystems Biorobot. 2013: 1139–1142, doi: 10.1007/978-3-642-34546-3_187.
25. Kuroda MM, Mutsuzaki H, Nakagawa S, et al. Short-Term Outcome of Rehabilitation Program with Hybrid Assistive Limb after Tendon Lengthening in Patients with Cerebral Palsy. Pediatr Rep. 2022; 14(4): 505–518, doi: 10.3390/pediatric14040059, indexed in Pubmed: 36412666.
26. Matsuda M, Iwasaki N, Mataki Y, et al. Immediate effects of a single session of robot-assisted gait training using Hybrid Assistive Limb (HAL) for cerebral palsy. J Phys Ther Sci. 2018; 30(2): 207–212, doi: 10.1589/jpts.30.207, indexed in Pubmed: 29545679.
27. Beretta E, Storm FA, Strazzer S, et al. Effect of Robot--Assisted Gait Training in a Large Population of Children With Motor Impairment Due to Cerebral Palsy or Acquired Brain Injury. Arch Phys Med Rehabil. 2020; 101(1): 106–112, doi: 10.1016/j.apmr.2019.08.479, indexed in Pubmed: 31562873.
28. Wallard L, Dietrich G, Kerlirzin Y, et al. Robotic-assisted gait training improves walking abilities in diplegic children with cerebral palsy. Eur J Paediatr Neurol. 2017; 21(3): 557–564, doi: 10.1016/j.ejpn.2017.01.012, indexed in Pubmed: 28188024.
29. Wallard L, Dietrich G, Kerlirzin Y, et al. Robotic-assisted gait training improves walking abilities in diplegic children with cerebral palsy. Eur J Paediatr Neurol. 2017; 21(3): 557–564, doi: 10.1016/j.ejpn.2017.01.012, indexed in Pubmed: 28188024.
30. Gardner AW, Montgomery PS, Wang M. Minimal clinically important differences in treadmill, 6-minute walk, and patient-based outcomes following supervised and home-based exercise in peripheral artery disease. Vasc Med. 2018; 23(4): 349–357, doi: 10.1177/1358863X18762599, indexed in Pubmed: 29671381.