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ORIGINAL ARTICLE

Effect of Robotic Training on the Mobility of Children With Cerebral Palsy: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

In this study, we conducted a systematic review and meta-analysis to investigate the effect of robotic training on the mobility of children with cerebral palsy. The PubMed, Cochrane Library, PEDro, and Embase databases were searched for relevant studies from their inception to June 17, 2023. We selected studies that (1) were randomized controlled trials (RCTs), (2) included patients with cerebral palsy aged <18 years, (3) compared robotic training with conventional rehabilitation alone, and (4) reported mobility outcomes. Continuous variables are expressed as standardized mean differences (SMDs) with 95% confidence intervals (CIs). The analysis was performed using RevMan 5.4 software. We included 10 RCTs with a total of 298 patients. The intervention groups significantly outperformed the control groups in terms of cadence (SMD = 0.77, 95% CI: 0.18, 1.36; P = 0.01). No adverse events were noted in the included studies. In addition, no improvement was observed in walking speed, walking endurance, Gross Motor Function Measure, WeeFIM score, or any other spatiotemporal gait parameter. Additional high-quality, large-scale RCTs are required to confirm the benefits and long-term effects of this intervention.

Keywords: Cerebral palsy, Gait, RAGT, Systematic review, Meta-analysis

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1. Introduction

Cerebral palsy comprises a group of chronic and nonprogressive conditions affecting movement and coordination that are caused by damage to one or more areas in the developing fetal or infant brain.[1] In cerebral palsy, motor impairments are often accompanied by sensory, cognitive, communicative, perceptive, and behavioral disturbances.[2] The prevalence of cerebral palsy is estimated to be 2 per 1000 live births.[3,4] One of the most disabling mobility conditions in cerebral palsy is gait impairment, which is characterized by low walking speed, poor endurance, and small stride length.[5] Improving the gait of patients with cerebral palsy is a primary goal for both the patients and their families, as well as rehabilitation teams.[6,7] Recently proposed gait rehabilitation methods for patients with neurological impairment rely on devices that improve a patient's gait while supporting their body weight and emphasize the benefits of repetitive practice.[7,8] Locomotor training is task-specific and highly repetitive and requires active participation by the child.[9] This training often takes the form of partial body weight–supported treadmill training with step retraining for safety.[10,11] With technological advancements, robotic training has become more accessible.[12] A study reported that robotic training improved mobility outcomes, particularly in patients with severe physical limitations.[13] However, the evidence regarding robotic training remains inconsistent, and further investigation of its efficacy is warranted.[13] In this study, we conducted a systematic review and meta-analysis to investigate the effect of robotic training on the mobility of children with cerebral palsy. The research question for this article is as follows:

Does robotic training improve mobility in children with cerebral palsy?

2. Methods

This review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines[14] and prospectively registered in PROSPERO under registration number CRD42021258717 on July 2, 2021.

2.1. Search strategy

We reviewed the literature, extracted data, and performed cross-checks based on the PRISMA guidelines.[14] We searched the PubMed (started in 1948), Cochrane Library, EMBASE (started in 1947), and PEDro databases for relevant articles. In our search, we employed terms related to both cerebral palsy and robot-assisted gait training (RAGT) as well as synonyms for these terms (the search terms are listed in Table S1 [https://rps.researchcommons.org/cgi/editor.cgi]). RCTs were identified using the filter function of the databases. Additional articles were identified through a manual search of the reference lists of relevant articles. We searched for articles published since the inception of each database until June 17, 2023. Two reviewers independently evaluated the eligibility of all titles and abstracts, and disagreements were resolved through discussion. When necessary, a third reviewer was involved. The full texts of the remaining articles were screened to determine their eligibility. The selected relevant studies were exported into EndNote 20, which was used to identify and remove duplicates.[15]

We included studies that met the following criteria:

(P) Participants: Studies had to involve participants with a diagnosis of cerebral palsy. We considered all types of cerebral palsy, namely spastic, ataxic, athetoid, hypotonic, and mixed. We focused on children aged <18 years.

(I) Intervention: Studies had to employ robotic training as the therapeutic intervention as follows. During robotic training, the patient is placed in a partial body weight–supported harness, and a robotic exoskeleton is attached to their lower extremities. The exoskeleton enables the application of guidance force provided by the robotic orthosis during ambulation, thus enabling the patient to engage in repeated practice of complex gait patterns at near-normal speed over a long period.

(C) Comparator: Studies had to provide conventional rehabilitation to the control group. The rehabilitation

program had to focus on improving motor control, sitting and standing stability, gait, and activities of daily living.

(O) Outcome: Intervention studies had to perform preassessments and post assessments using outcome measurements of mobility, including standing, walking, running, jumping, and spatiotemporal gait parameters.

(T) Type of study: RCT.

We excluded studies that were not RCTs, lacked peer reviewing, were published conference abstracts without full texts, were study protocols, did not compare the effects of robot-assisted training with those of traditional physiotherapy alone, and did not include only patients with cerebral palsy.

2.2. Data items

Two authors extracted information from the selected articles independently. The following data were obtained from each RCT: the type of cerebral palsy; study design; inclusion and exclusion criteria; number, mean age, and GMFCS level of the participants; protocols used to train participants in the intervention and control groups; and outcome measurements of mobility. We contacted the authors of articles through email to clarify unclear data or obtain missing data.

2.3. Outcome measurements

The outcome measurements considered were Gross Motor Function Measure (GMFM) scores, walk test results, WeeFIM scores, and spatiotemporal gait parameters. The GMFM is an assessment tool designed to measure changes in gross motor function over time in children with cerebral palsy.[16] The GMFM has five dimensions: (1) GMFM-A, lying and rolling; (2) GMFM-B, sitting; (3) GMFM-C, crawling and kneeling; (4) GMFM-D, standing; and (5) GMFM-E, walking, running, and jumping. Two versions of the GMFM are available, namely the GMFM-88 and GMFM-66. The GMFM-88 is the original measure containing 88 items, whereas the GMFM-66 is a 66-item subset of the original 88 items that best describes the gross motor function of patients with cerebral palsy.[17] We focused on the GMFM-D and GMFM-E in this study because they are crucial for assessing improvements in the mobility of patients with cerebral palsy. The included studies used the 10-m and 6-min walk tests.[18,19] The WeeFIM for children is a simple-to-administer scale used for assessing independence in three domains, namely self-care, mobility, and cognition.[20] The spatiotemporal gait parameters considered were cadence, gait speed, step length, and double support time.

2.4. Risk-of-bias assessment

The quality of the included studies was evaluated with the Physiotherapy Evidence Database (PEDro) scale.[21] The PEDro scale scores obtained by the two assessors were compared, and differences were resolved by discussing with a third researcher. The ratings of PEDro scale items 2–11 were summed to obtain a combined total PEDro scale score that ranged from 0 to 10. Scores of <4, 4–5, 6–8, and 9–10 are considered poor, fair, good, and excellent, respectively.[21] All articles were included in this review irrespective of their PEDro scale score.

2.5. Statistical analysis

Data on the outcome measures of mobility were extracted from the articles. Only outcomes documented in two or more RCTs were included in the meta-analysis. For the intervention studies that included a control group, between-group differences were examined. The standardized mean difference (SMD) was calculated to determine changes from baseline.

Statistical analyses were performed with RevMan 5.4 software which is obtained from the Cochrane Collaboration website (https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman/revman-5-download). Continuous data were analyzed in terms of the change from the baseline measurement. For the studies not reporting standard deviations (SDs), the articles' authors were contacted or, if possible, the data were estimated through calculation of correlation coefficients in accordance with the instructions provided in the Cochrane Handbook for Systematic Reviews of Interventions.[22] Results with P values of <0.05

were considered statistically significant. We used the I^2 test to objectively measure statistical heterogeneity, with $I^2 \geq 50\%$ indicating considerable heterogeneity.[23] A random-effects model was used in this meta-analysis because of the various clinical tests performed in the included studies. The results for continuous variables are expressed as SMDs with 95% confidence intervals (CIs). We measured the strength of the relationship between two variables in a population by calculating SMDs, with SMD values of <0.2, 0.2–0.5, 0.5–0.8, and >8 indicating a trivial effect with no clinical meaningfulness, a small effect, a moderate effect, and a large effect, respectively.[24]

A funnel plot was not used to examine publication bias because few studies (<10) were included in each analysis.

2.6. Quality of evidence

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used to measure the quality of evidence as confidence in effect estimates.[25] In this method, the quality of a publication is examined on the basis of the study design (randomized vs. non-randomized design), risk of bias, inconsistency, imprecision, indirectness, and publication bias; the size and trend in the effect are also considered.[25]

3. Results

3.1. Search results

A total of 187 RCTs were initially retrieved using the aforementioned search terms. Of these, 92 duplicates were identified using EndNote 20 and excluded.[15] A further 43 studies that did not meet the inclusion criteria were excluded after their titles and abstracts had been screened. The full texts of the remaining 52 studies were screened. The results indicated that 3 studies had the same study group, 13 studies had not yet been published, 10 studies did not compare the effects of robot-assisted training and conventional physical therapy, 5 studies were conference papers, 2 studies were a study protocol, 3 studies did not report mobility outcomes, 2 studies did not exclusively include patients with cerebral palsy, 1 study was not an RCT, and 3 studies did not report SDs. Finally, we included 10 articles in this study (Fig. 1).[12,26–34] We did not include the study of Klobucka et al.[27] in our meta-analysis because they included participants aged >18 years.

3.2. Study characteristics

The selected studies included 155 patients in the intervention group and 143 patients in the control group. Among these studies, nine were parallel studies[12,26,27,29–34] and one was a crossover study.[28] According to the Cochrane Handbook for Systematic Reviews of Interventions, inclusion of crossover studies in a meta-analysis is acceptable.[22] In addition, inclusion of the final outcome data is more appropriate than inclusion of outcome data only from the first period (before the crossover). We followed this suggestion while conducting the meta-analysis. Seven studies focused on spastic cerebral palsy,[27–30,32–34] whereas the remaining three studies did not specify the type of cerebral palsy that they focused on.[12,26,31] Nine studies involved participants aged <18 years,[12,26,28–34] whereas one study involved participants aged >18 years.[27] Two studies included participants with GMFCS level I[27,31]; the other studies enrolled patients with a higher GMFCS level.[12,26,28–30,32–34] The training duration was ≤4 weeks in four studies,[29–31,34] 5 weeks in one study,[28] 4–6 weeks in one study,[27] 6 weeks in two studies,[12,33] 8 weeks in one study,[26] and 10 weeks in one study.[32] The training frequency was two times a week in two studies[26,34]; two to three times a week in two studies,[27,28] three times a week in two studies,[12,33] four times a week in one study,[32] and five times a week in three studies.[29–31] Seven studies reported GMFM results,[12,27–29,32–34] five studies reported walk tests results,[12,28,31,32,34] three studies reported WeeFIM results,[12,26,31] and four studies reported spatiotemporal gait parameters.[29–31,33] Table 1 presents the main characteristics of the 10 RCTs.

The robot-assisted gait training involved a treadmill, a suspension system, and electronically controlled lower-limb orthoses.[27,29] An electromechanical unit monitors and adjusts the level of body weight support in real time at the requested level.[27]

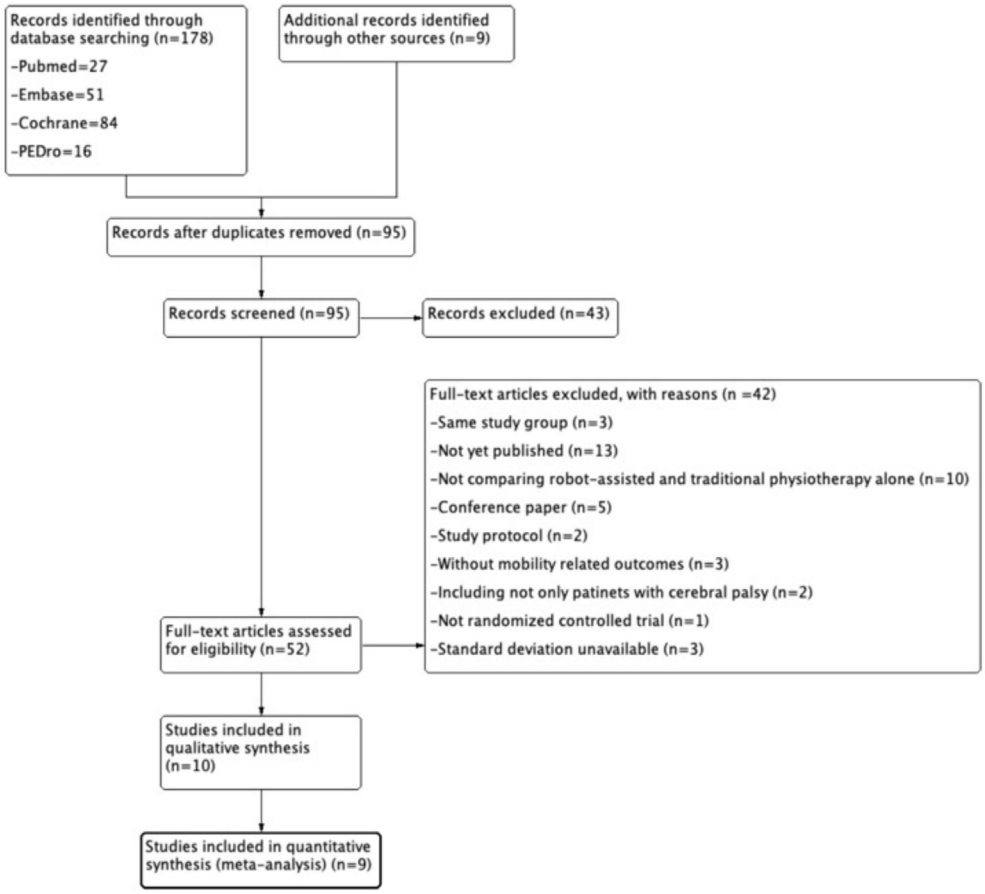

Fig. 1. Flowchart for study selection.

Computer-controlled controls at each joint are synchronized with the speed of the treadmill.[27,28] The parameters of each training type (e.g., the distance, speed, number of steps, rate of body weight support, and guidance force) are clearly defined and constantly monitored.[27] The characteristics of the interventions are shown in Table 1.

3.3. Risk-of-bias assessment

The quality of the included RCTs was independently examined by two reviewers using the PEDro scale. The PEDro scale scores for the included studies ranged from 5 to 8. On the basis of these scores, two studies were considered to be "fair"[29, 30], and eight studies were considered to be "good".[12,26–28,31–34] Table 2 presents the detailed results of the bias risk assessment.

3.4. GMFM-88

The GMFM-88 was used in three studies,[12,32,34] which collectively included 45 and 42 patients in the intervention and control groups, respectively. The level of heterogeneity among the included studies was low (I^2 = 0%; P = 0.83). No significant intergroup differences in GMFM-88 score were noted between the two groups (SMD = 0.15; 95% CI: −0.27, 0.57; P = 0.48; Fig. 2A).

3.5. GMFM-D

The GMFM-D was employed in four studies,[28,29,32,33] which together included 53 and 54 patients in the intervention and control groups, respectively. The heterogeneity of the studies was low (I^2 = 27%, P = 0.25). No significant intergroup differences in GMFM-D scores were noted

Table 1. Characteristics of selected randomized controlled trials.

Study (Author, year)	Study design	Inclusion criteria	Exclusion criteria	Group	Participants	Protocol	Outcome
Yasar et al., 2021[26]	Parallel	1) 7–14 years; 2) GMFCS levels II–V; 3) diplegic cerebral palsy	1) disorder involving the peripheral nervous system or another neurological disorder	Intervention group	n = 13 Age (years) = *10.46 (2.76)	RoboGait-assisted gait system was used in this study. Robot-assisted training for 25 min and conventional therapy twice a week were administered to patients for 8 weeks. The gait speed was 1.5 km/h in all sessions. Gait training was performed with the support of 45%–75% of patients' weight.	WeeFIM
				Control group	n = 13 Age (years) = *9.69 (2.32)	Conventional physical therapy twice a week for 8 weeks, with each session lasting at least 40 min.	
Klobucka et al., 2020[27]	Parallel	1) bilateral spastic cerebral palsy; 2) age >15 years; 3) GMFCS levels I–IV; 4) able to reliably signal pain, fear, or discomfort and follow simple instructions; 5) no previous experience with robot-assisted gait training	1) severe lower extremity muscle contractures; 2) botulinum toxin-A injections in the lower limbs within the last 3 months; 3) a neurosurgical or orthopaedic surgical intervention in the lower limbs within the last 9 months before the initiation of therapy; 4) seizure disorder that is not controlled by medication; 5) open skin lesions or vascular disorder of the lower limbs; 6) inability to cooperate	Intervention group	n = 21 Age (years) = *18.3 (3.84)	Lokomat (Hocoma AG, Switzerland) was used in this study. Twenty therapeutic units of the Lokomat were used for 4–6 weeks. The gait speed was 1.1–1.7 km/h. Gait training was performed with the support of 100% of patients's body weight, which was subsequently reduced.	GMFM-88 score, GMFM-D and GMFM-E scores
				Control group	n = 26 Age (years) = *23.4 (5.33)	Twenty therapeutic sessions of conventional physical therapy two to three times a week for 4–6 weeks.	

Peri et al., 2017[32]	Parallel	1) with bilateral spastic cerebral palsy; 2) with GMFCS I–III; 3) able to walk independently with or without the use of assistive devices; 4) aged 4–17 years	1) underwent multi-level surgery within 6 months before the onset of the study; 2) received botulinum toxinA injections within past 3 months	Intervention group	n = 12 Age (years) = *8.0 (3.0)	Lokomat pro paediatric V6 device (Hocoma, Switzerland) was used. The exoskeleton was connected to a body weight support system that provided vertical stability. The patients received 4 weekly sessions over 10 weeks of robot-assisted gait training.	GMFM-88 scores, GMFM-D, GMFM-E and 6-min walk test,
				Control group	n = 10 Age (years) = *9.3 (3.9)	Intensive task-orientated physiotherapy was administered to patients with 4 sessions a week for 10 weeks.	
Pool et al., 2020[12]	Parallel	1) GMFCS levels III–V; 2) age between 5 and 12 years; 3) requirement of a gait trainer or well-fitting ankle foot orthoses; 4) ability to follow simple instructions; 5) having a reliable form of communication; 6) already visiting a community therapy provider	1) uncontrolled seizure disorder; 2) orthopaedic surgery in the past 12 months; 3) presence of orthopaedic metalware in the lower limbs; 4) receipt of botulinum neurotoxin A injections in the lower limbs less than 3 months before; 5) engagement in activity-based rehabilitation locomotor training in the past 6 months	Intervention group	n = 20 Age (years) = **8:4 (1:11)	RT600 was used. 1-Hour sessions three times a week over 6 weeks of robot-assisted training and locomotor training were assigned to the patients.	GMFM-88 scores, 10-m walk test results, and WeeFIM scores
				Control group	n = 20 Age (years) = **8:1 (2:1)	Locomotor training only, three times weekly 1-h sessions for 6 weeks.	

(*continued on next page*)

Table 1. (continued)

Study (Author, year)	Study design	Inclusion criteria	Exclusion criteria	Group	Participants	Protocol	Outcome
Wallard et al., 2018[29]	Parallel	1) bilateral spastic cerebral palsy; 2) ability to independently walk without or with assistance for at least 60 m; 3) GMFCS level II	1) severe contracture; 2) receipt of surgical treatment or injections of botulinum toxin in the recent 1 year before the intervention period	Intervention group	n = 14 Age (years) = *8.3 (1.2)	Lokomat Pediatric system was used. The patients received 20 sessions of robot-assisted training for 4 weeks. The initial body weight support for all patients was 70%, which was subsequently decreased to 40% during sessions.	GMFM-D and GMFM-E scores and spatiotemporal gait parameters
				Control group	n = 16 Age (years) = *9.6 (1.7)	Daily physical or occupational therapy with a physical therapist for 4 weeks.	
Wu et al., 2017[33]	Parallel	1) with bilateral spastic cerebral palsy; 2) aged 4–16 years; 3) with GMFCS level I–IV	1) with severe contracture; 2) received botulinum toxin treatment within past 3 months; 3) received operations within past 6 months	Intervention group	n = 11 Age (years) = *11.3 (3.8)	Patients received robotic training and locomotor training with three weekly sessions for 6 weeks. A controlled assistance load was applied to the pelvis (i.e., in the mediolateral direction started from heel strike to mid-stance of the ipsilateral leg to facilitate weight shifting) and legs (i.e., started from toe-off to mid-swing to facilitate leg swing).	GMFM-D and GMFM-E and spatiotemporal gait parameters
				Control group	n = 12 Age (years) = *10.5 (2.6)	Locomotor training was assigned to the patients with three weekly sessions for 6 weeks.	

Druzbicki et al., 2013[30]	Parallel	1) spastic diplegia cerebral palsy; 2) ability to independently stand and walk or walk with assistance; 3) GMFCS level II–III; 4) no disorders of higher mental functions	1) treatment with botulinum toxin during the last 6 months; 2) surgery within a 1-year period before the date of the examination; 3) active drug-resistant epilepsy; 4) anatomical leg length discrepancy larger than 2 cm (due to lokomat system limitations); 5) fixed contractures; 6) bone and joint deformities; 7) having bone-articular instability (joint dislocation); 8) receipt of baclofen therapy using an implanted infusion pump; 9) inhibiting casts during the last 6 months; 10) presence of significant amblyopia and hearing loss; 11) inflammation of the skin and open skin lesions around the trunk or limb; 12) contraindications for training on a treadmill; 13) lack of patient cooperation	Intervention group	n = 26 Age (years) = ***10.1 (10.5)	Lokomat system was used. Robot-assisted training and individual exercises were assigned to the patients with 20 sessions lasting 45 min for 4 weeks. The body weight support was determined according to the patients' abilities.	Spatiotemporal gait parameters
				Control group	n = 9 Age (years) = ***11.0 (11.0)	Conventional physical therapy, with 20 therapeutic sessions lasting for 45 min over 4 weeks.	

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Table 1. (continued)

Study (Author, year)	Study design	Inclusion criteria	Exclusion criteria	Group	Participants	Protocol	Outcome
Smania et al., 2011[31]	Parallel	1) bilateral lower limb (diplegic or tetraplegic) cerebral palsy; 2) age between 10 and 18 years; 3) GMFCS levels II–IV; 4) ability to walk by themselves or with the use of an assistance device for at least 10 m; 5) ability to maintain a sitting position without assistance; 6) ability to follow instructions and participate in the rehabilitative programme	1) severe lower limb spasticity; 2) severe lower limb contractures; 3) cardiovascular diseases; 4) receipt of orthopaedic surgery or neurosurgery in the past 12 months; 5) botulinum toxin injections within 6 months before the beginning of the study	Intervention group	n = 9 Age (years) = *13 (2.83)	Gait Trainer GT I was used. The patients received 30 min of robot-assisted training and 10 min of passive joint exercises with the help of a physical therapist, with a total of 10 sessions for 40 min for 2 weeks. Partial body-weight support was decreased from 30% to 0% during sessions.	10-m walk test, 6-min walk test, WeeFIM scores, and spatiotemporal gait parameters
				Control group	n = 9 Age (years) = *12 (3.08)	40 min of conventional physical therapy; ten 40-min daily sessions for 2 weeks.	
Moll et al., 2022[34]	Parallel	1) Age between 8 and 18 years with spastic cerebral palsy; 2) GMFCS level II–IV; 3) ability to follow instructions	1) Lower-limb surgery in the previous 6 months; 2) botulinum toxin therapy in the previous 3 months; 3) use of alternative RAGT in the previous 6 months; 4) inability to follow instructions	Intervention group	n = 13 Age (years) = *12 (3.61)	A hybrid assistive limb system was used for six sessions during 11-day-long hospital stay. Each session lasted 90 min and included the actual walking time in the hybrid assistive limb system (20 min), time for putting on and taking off the HAL, time for rest, and time for evaluating the patient's skin and well-being before and after the session.	GMFM-88 score, 10-m walk test, and 6-min walk test
				Control group	n = 12 Age (years) = *13 (2.79)	Conventional physical therapy was performed for six sessions during 11-day-long hospital stay. Each session lasted 90 min.	

Reiffer et al., 2020[28]	Crossover	1) age between 6 and 18 years with bilateral spastic cerebral palsy; 2) GMFCS levels II–IV; 3) ability to follow instructions and communicate pain or discomfort	1) receipt of neurological or ortho paedic surgery on the lower extremity or trunk within the last 6 months; 2) having participated in another Lokomat training regimen within the previous 6 months as well as a change in concomitant drug therapy within the last 4 weeks before or during the study period; 3) children showing contraindications as outlined in the Lokomat manufacturer's manual	Intervention group	n = 16 Age (years) = ****11.4 (6.0–15.1)	Lokomat system was used. Body-weight support, gait speed, training duration, and guidance force of the system were individually adjusted according to the patients' abilities. Robotic training three times per week over 5 weeks with a maximum of 45 min per session, followed by crossover to one to two sessions (30–45 min) of physical therapy per week for 5 weeks.	GMFM-D and GMFM-E scores, 10-m walk test results, and 6-min walk test results
				Control group	n = 16 Age (years) = ****11.2 (6.1–15.3)	One or two sessions (30–45 min) of physical therapy per week for 5 weeks, followed by cross over to robotic training thrice per week over 5 weeks, with a maximum of 45 min per session.	

GMFCS, Gross Motor Function Classification System; GMFM, Gross Motor Function Measure; SD, standard deviation; WeeFIM, Functional Independence Measure.
*Age (years), mean (SD); **Year: month, mean (SD); ***Median (SD); ****Mean (range).

Table 2. PEDro scale.

	1*	2	3	4	5	6	7	8	9	10	11	Total	Rating
Yasar et al., 2021[26]	√	√		√			√	√	√	√	√	7	Good
Klobucka et al., 2020[27]		√		√				√	√	√	√	6	Good
Peri et al., 2017[32]	V	V		V				V	V	V	V	7	Good
Pool et al., 2020[12]	√	√	√	√			√	√	√	√	√	8	Good
Wallard et al., 2018[29]	√	√		√			√			√	√	5	Fair
Wu et al., 2017[33]	V	V		V				V	V	V	V	7	Good
Druzbickiet al, 2013[30]		√		√			√			√	√	5	Fair
Smania et al., 2011[31]	√	√	√	√			√	√		√	√	7	Good
Reiffer et al., 2020[28]	√	√		√				√	√	√	√	6	Good
Moll et al., 2022[34]	V	V		V				V	V	V	V	7	Good

PEDro scale criteria: 1, eligibility criteria and source of participants; 2, random allocation; 3, concealed allocation; 4, baseline comparability; 5, blinded participants; 6, blinded therapists; 7, blind assessors; 8, adequate follow-up; 9, intention-to-treat analysis; 10, between-group comparisons; 11, point estimates and variability. *Not included in the calculation of the total score.

(SMD = −0.02, 95% CI: −0.47, 0.43; P = 0.92; Fig. 2 A).

3.6. GMFM-E

The GMFM-E was employed in four studies,[28,29,32,33] which together included 53 and 54 patients in the intervention and control groups, respectively. The heterogeneity of the studies was low (I^2 = 0%, P = 0.43). No significant differences in GMFM-E scores among the groups were noted (SMD = 0.35, 95% CI: −0.04, 0.74; P = 0.08; Fig. 2 A).

3.7. 10-M walk test

The 10-m walk test was used in four studies,[12,28,31,34] which collectively included 58 and 57 patients in the intervention and control groups, respectively. The heterogeneity of the studies was moderate (I^2 = 38%; P = 0.18). No significant intergroup differences in 10-m walk test results were discovered (SMD = 0.08; 95% CI: −0.40, 0.56; P = 0.74; Fig. 2B).

3.8. 6-Min walk test

The 6-min walk test was used in five studies,[28,31–34] which collectively included 61 and 57 patients in the intervention and control groups, respectively. The heterogeneity of the studies was low (I^2 = 14%; P = 0.32). No significant intergroup differences in 6-min walk test results were found (SMD = 0.36; 95% CI: −0.04, 0.76; P = 0.08; Fig. 2B).

3.9. WeeFIM

The WeeFIM was used in three studies,[12,26,31] which together included 42 patients each in the intervention and control groups. The heterogeneity of the studies was low (I^2 = 0%, P = 0.68). No significant intergroup differences in WeeFIM scores were noted (SMD = 0.17, 95% CI: −0.26, 0.59; P = 0.45; Fig. 2 B).

3.10. Cadence

Cadence was reported in two studies,[29,31] which together included 23 and 25 patients in the intervention and control groups, respectively. The heterogeneity of the studies was low (I^2 = 0%, P = 0.74). Cadence was significantly better in the intervention group than in the control group (SMD = 0.77, 95% CI: 0.18, 1.36; P = 0.01; Fig. 2 C).

3.11. Gait speed

Gait speed was reported in four studies,[29–31,33] which together included 60 and 46 patients in the intervention and control groups, respectively. The heterogeneity of the studies was high (I^2 = 83%, P = 0.0005). No significant intergroup differences in gait speed were discovered (SMD = 0.70, 95% CI: −0.37, 1.78; P = 0.20; Fig. 2 C).

3.12. Step length

Step length was reported in four studies,[29–31,33] which together included 60 and

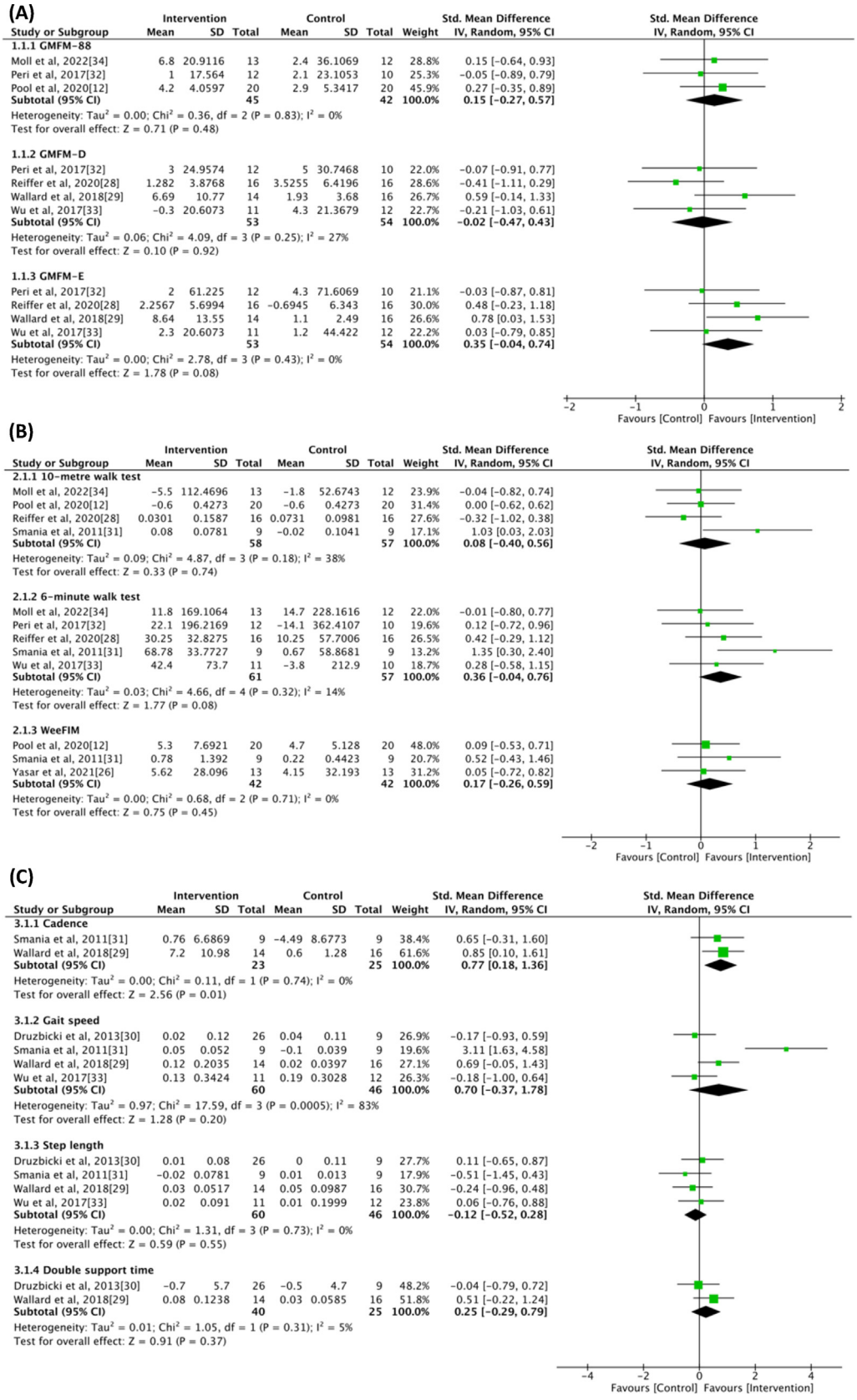

Fig. 2. ***Forest plots for outcome analyses.*** *(A) Forest plot for the Gross Motor Function Measure (GMFM)-88, GMFM-D, and GMFM-E. (B) Forest plot for walk test (10-m and 6-min) results and Functional Independence Measure (WeeFIM) scores. (C) Forest plot for spatiotemporal gait parameters (cadence, gait speed, step length, and double support time). SD, standard deviation; CI, confidence interval.*

46 patients in the intervention and control groups, respectively. The heterogeneity of the studies was low ($I^2 = 0\%$, P = 0.59). No significant intergroup differences in step length were noted (SMD = −0.18, 95% CI; −0.63, 0.28; P = 0.45; Fig. 2 C).

3.13. Double support time

Double support time was reported in two studies,[29,30] which together included 40 and 25 patients in the intervention and control groups, respectively. The heterogeneity of the studies was low ($I^2 = 5\%$, P = 0.31). No significant intergroup differences in double support time were found (SMD = 0.25, 95% CI: −0.29, 0.79; P = 0.37; Fig. 2 C).

3.14. Adverse effects

Of the included studies, four examined the adverse effects of robot-assisted training.[12,27,31,34] No adverse effects were observed in these studies, indicating that the interventions were well tolerated by the participants.

3.15. Quality of evidence

Quality of evidence was determined using the GRADE approach, and we determined that the quality of evidence was low for all outcomes. The reasons for this are that some studies did not blind participants or therapists and included participants of various ages. Table 3 presents details regarding the quality of evidence.

4. Discussion

We conducted this systematic review and meta-analysis to investigate the effect of training with robot-assisted devices on the mobility of patients with cerebral palsy. We discovered significant intergroup differences favoring robot-assisted training in terms of cadence. The effect size for cadence was moderate, with the corresponding SMDs being 0.77. No significant intergroup differences were found in GMFM-88 score, GMFM-D score, GMFM-E score, walk test (10-m and 6-minnute) results, WeeFIM score, or other spatiotemporal gait parameters (i.e., gait speed, step length, and double support time). We also assessed the quality of evidence by using the GRADE system and revealed low quality of evidence. In some studies, the participants or therapists were not blinded because of the nature of the intervention. Therefore, certain bias might have emerged from the study design.

Neural plasticity, which is the tendency of synapses and neural circuits to change in response to activity, may be improvable by using robot-assisted devices to provide intensive locomotor gait training.[27,35] According to the findings of previous studies and the RCTs included in this meta-analysis, robotic training may improve gait in patients with cerebral palsy through several mechanisms, which are described in the following.

Repetitive robotic training may help patients regain their head and gaze orientation, which can lead to improvement of postural and locomotor function.[27,36,37] Wallard et al. reported that such reorganization enhances vestibular−ocular balance.[36] Moreover, Pozzo et al. suggested that head stability is crucial to proper coordination of the vestibular and visual information required for balance.[38] Reorientation of the head can affect the posture and swing process of the arms during walking.[36] According to Ledebt et al. this influence is strongly correlated to mobility outcomes because the positions of the arms are expected to become lower with improvement in balance during walking.[39] With the aforementioned improvement in organization, mobility kinematics can be improved to reach a relatively normal condition, particularly by improving the angle of the initial contact and in-stance phase for the knee and ankle, as reported by Wallard et al.[36] Increasing single support time and decreasing double support can result in enhanced postural stability and dynamic balance during imbalance phases.[40,41] Furthermore, Borggraefe et al. observed task-specific improvements in gait parameters after robotic training, with these parameters measured using the GMFM-E.[42]

Wallard et al.[29] indicated that the normalization of propulsive forces, which can be interpreted as the minimal effort required to move forward with balance,[43] was necessary for moving forward and resulted in dynamic gait stability in their study. Moreover, they found that the time

Table 3. Grading of recommendations, assessment, development, and evaluation approach.

Certainty assessment							Number of patients		Effect	Certainty	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention group	Control group	Absolute (95% CI)		
GMFM - GMFM-88											
3	RCT	serious[a]	serious[b]	not serious	not serious	none	45	42	SMD 0.15 higher (−0.27 lower to 0.57 higher)	⨁⨁◯◯ Low	IMPORTANT
GMFM - GMFM-D											
4	RCT	serious[a]	serious[b]	not serious	not serious	none	53	54	SMD -0.02 higher (−0.47 lower to 0.43 higher)	⨁⨁◯◯ Low	IMPORTANT
GMFM - GMFM-E											
4	RCT	serious[a]	serious[b]	not serious	not serious	none	53	54	SMD 0.35 higher (−0.04 higher to 0.74 higher)	⨁⨁◯◯ Low	IMPORTANT
Walk test - 10-m walk test											
4	RCT	serious[a]	serious[b]	not serious	not serious	none	58	57	SMD 0.08 higher (−0.40 lower to 0.56 higher)	⨁⨁◯◯ Low	IMPORTANT
Walk test - 6-min walk test											
5	RCT	serious[a]	serious[b]	not serious	not serious	none	61	57	SMD 0.36 higher (−0.04 lower to 0.76 higher)	⨁⨁◯◯ Low	IMPORTANT
Walk test - WeeFIM											
3	RCT	serious[a]	serious[b]	not serious	not serious	none	42	42	SMD 0.17 higher (−0.26 lower to 0.59 higher)	⨁⨁◯◯ Low	IMPORTANT
Spatio-temporal gait parameters - Cadence											
2	RCT	serious[a]	serious[b]	not serious	not serious	none	23	25	SMD 0.77 higher (0.18 higher to 1.36 higher)	⨁⨁◯◯ Low	IMPORTANT
Spatio-temporal gait parameters - Gait speed											
4	RCT	serious[a]	serious[b]	not serious	not serious	none	60	46	SMD 0.70 higher (−0.37 lower to 1.78 higher)	⨁⨁◯◯ Low	IMPORTANT

(*continued on next page*)

Table 3. (continued)

Certainty assessment							Number of patients		Effect	Certainty	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention group	Control group	Absolute (95% CI)		
Spatio-temporal gait parameters - Step length											
4	RCT	serious[a]	serious[b]	not serious	not serious	none	60	46	SMD -0.12 lower (−0.52 lower to 0.28 higher)	⨁⨁◯◯ Low	IMPORTANT
Spatio-temporal gait parameters - Double support time											
2	RCT	serious[a]	serious[b]	not serious	not serious	none	40	25	SMD 0.25 higher (−0.29 lower to 0.79 higher)	⨁⨁◯◯ Low	IMPORTANT

RCT, randomized controlled trial; CI, confidence interval; SMD, standardized mean difference.

[a] Some studies did not blind participants or therapists.

[b] Included participants with different age.

lag between imbalance and forward propulsive force generation was shorter in the intervention group than the control group.[29]

In summary, robotic training may improve the mobility of patients with cerebral palsy. An increasing number of studies, most of which were published after 2000, strongly suggest that activity-based strategies, which are within the purview of physical therapy, are key to unlocking greater potential in terms of function recovery in patients with cerebral palsy.[44]

Two studies investigated the maintenance effect of robotic training.[27,31] Klobucka et al. evaluated the effect of robotic training on patients with cerebral palsy,[27] and after the intervention, their patients (n = 16) continued with conventional physical therapy one to three times a week. They received their regular home-based therapy program (physical therapy or neurodevelopmental therapy once or twice per week) as established for each patient individually before the study period. At 3–4 months after the robotic training, the significant improvements that had been made by the experimental group (robotic training, n = 16) had been retained. The mean (SD; P value) improvements were 8.33 (8.02; P = 0.003) and 9.33 (10.01; P = 0.001) points on the GMFM-D and GMFM-E, respectively. Moreover, gait kinematics and gait velocity were further improved at the 1-month follow-up in the study conducted by Smania et al.[31]

Robotic training is a novel approach that offers several advantages. First, extensive exposure to task-specific repetitive training improves the clinical outcomes of patients with neurological conditions by enhancing their training-induced neuroplasticity.[45] Second, robotic training facilitates the repetition of specific and stereotypical movements to yield a correct and reproducible gait pattern.[27,30] Third, robotic training guides lower-limb movements, thus enabling prolonged walking training with a normal gait pattern.[29] Given these advantages, robotic training yields improved clinical outcomes, such as in cadence, which demonstrated a significant improvement in our analyses. Robotic training also provides an attractive rehabilitation program for children and can be combined with other technologies to enhance its effects.[46] In our

analyses, although the results of GMFM-88, GMFM-E, 10-m walk test, 6-min walk test, WeeFIM, and several spatiotemporal gait parameters revealed potentially positive trends, between-group differences did not reach statistical significance ($P > 0.05$), presumably because of the limited number of studies and participants included in each analysis. Future studies should investigate interventions involving robotic training alone or accompanied with other technological devices to improve the clinical outcomes of children with cerebral palsy.

The risk of bias of the studies included in this meta-analysis was examined using the PEDro scale. On the basis of the PEDro scale scores, two studies were considered to be "fair,"[29,30] and eight studies were considered to be "good."[12,26–28,31–34] Most of the studies did not blind the patients or therapist, possibly because of the nature of robotic training, in which blinding the assessor is possible but blinding the patient and therapist is difficult. Thus, this risk of bias may have affected the strength of the evidence.

Many studies have investigated the effects of robotic training on patients with cerebral palsy. For instance, Chiu et al.[47] reported that mechanically assisted gait training may improve walking speed. However, only three studies in their review reported the effects of robotic training. Carvalho et al.[48] argued that robotic training benefits individuals with cerebral palsy, particularly by increasing their walking speed and endurance and improving their gross motor function. However, the authors analyzed only two RCTs. Conner et al.[49] asserted that robotic devices that provide assistive gait training for individuals with cerebral palsy do not provide a greater benefit in terms of mobility than does the standard of care. However, the authors included participants aged >18 years. Overall, our results differ from those of other studies in multiple aspects. First, we included only RCTs focusing on robotic training. Second, we focused on children aged <18 years. Third, although we observed no improvement in most of the results, we identified an improvement in cadence. According to our search of electronic databases, numerous studies on this topic are currently in progress.[50–52] Such research will serve as a basis for future studies.

Our study has several limitations. First, the heterogeneity was moderate to high for some outcomes. This may have been due to differences in the number of intervention sessions, treatment durations, and GMFCS levels. Second, despite the varied ages and severities within the study populations, conducting further analysis is challenging due to the limited number of included studies and the mixed characteristics of participants in each independent study. Third, because of the nature of the treatment, blinding participants and physicians is challenging. Therefore, the studies could not conduct blinding, leading to some concerns regarding bias. Fourth, no universal or standard treatment guidelines are available regarding the most effective protocol; this may affect the potential of such an intervention to achieve improvements. Finally, because we included a small number of studies in our analysis, the outcomes of this study should be interpreted with caution. Additional reviews of high-quality, large-scale RCTs are required to overcome these limitations.

5. Conclusion

In this systematic review and meta-analysis of RCTs, we investigated the effects of robotic training on children with cerebral palsy. Our results indicated significant intergroup differences in cadence but no improvement in walking speed, walking endurance, GMFM, WeeFIM, or any other spatiotemporal gait parameter. No adverse events were noted in the included studies. Because of the few studies included in each analysis, additional high-quality, large-scale RCTs should be conducted to confirm the benefits and long-term effects of this intervention.

Author contributions

Fu-An Yang conceptualized and designed the study and drafted the manuscript. Hung-Chou Chen critically revised the manuscript for intellectual content. Ya-Chu Shih and Li-Fong Lin conducted a comprehensive search for articles that met the eligibility criteria. Fu-An Yang and Chih-Wei Peng extracted the relevant data and assessed the quality of the selected trials.

Chien-Hung Lai, Tsan-Hon Liou and Reuben Escorpizo provided statistical expertise, analyzed and interpreted the data, and submitted the manuscript.

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Availability of data and materials

Given the systematic review and meta-analysis nature of this study, all extracted data are readily available in the published manuscripts. All generated data are included in the present article.

Conflicts of interest

The authors declare that there is no conflict of interest.

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