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The Effect of Physical Exercise on Gross Motor Function in Children with Cerebral Palsy: A Meta-Analysis

Gao Yang[1], Haibing Su[1], Ming Yang[1,2], Jindong Chang[1,2,*]

[1]School of Physical Education, Southwest University, Chongqing, 400715, China
[2]Institute of Motor Quotient, Southwest University, Chongqing, 400715, China

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Abstract This study aimed to evaluate the effect of physical exercise intervention on gross motor function in children with cerebral palsy (CP). Computer searches of Web of Science, PubMed, Embase (Ovid), Cochrane Library, and Medline databases were conducted on October 6, 2021. Randomized controlled trials (RCTs) or quasi-experimental studies were included. Ten methodological quality trials were identified, and the literature's quality was assessed using the PEDro scale. Data from the Gross Motor Function Assessment Scale GMFM-66, GMFM-88 and A (lying and turning), B (sitting), C (climbing and kneeling), D (standing), and E (walking, running, and jumping) dimension scores were extracted, and Meta-analysis was performed using Revman 5.4. Data were pooled and expressed as mean difference (MD) or standardized difference (SMD) with 95% CI. The results showed that GMFM-66 [SMD=1.90,95%CI (0.55~3.25), Z=2.76, P=0.006], GMFM-88 [SMD=1.49,95%CI (0.83 ~ 2.15), Z=4.42, P<0.00001] and D dimension [SMD=3.13, 95%CI (1.23 ~ 5.02), Z=3.23, P=0.001] and E dimension [SMD=3.34, 95% CI (2.00 ~ 4.69), Z=4.88, P<0.00001]. The study results showed that the differences between the results of the experimental and control groups were statistically significant. Physical exercise could significantly improve gross motor function in children with CP and could be used as a reference for physical therapy in children with CP. These findings should be used with caution based on the limitations of this study.

Keywords Physical Exercise, Cerebral Palsy, Gross Motor Function, Meta-Analysis

1. Introduction

Cerebral palsy (CP) is a neurodevelopmental disorder that begins in the fetus or infant and has lifelong consequences, resulting in impaired motor and postural development and limited physical exercise in children [1]. Children with cerebral palsy are primarily affected by non-progressive disorders of the brain, manifested by low sensory, perceptual, cognitive, and communication deficits and gross and fine motor and control deficits [2]. The prevalence of children with cerebral palsy reached a rate of 2.11/1000 in countries with high levels of economic development in North America and Europe, and the probability of prevalence in low and middle income is uncertain but appears to be higher and more severe [3]. A review of studies by Ostojic et al. found that the incidence of pain in children with cerebral palsy was as high as 74% [4]. Children with cerebral palsy are severely affected by motor dysfunction with epilepsy [5], balance dysfunction [6], muscle fatigue [7], poor selective motor control [8], poor neuromuscular coordination [9], and a substantial economic and psychological burden on the families of children with CP [10].

Physical exercises to treat children with CP are becoming increasingly popular as an intervention option. The American College of Sports Medicine defines physical exercises as planned, structured, repetitive physical activity to promote and maintain physical fitness [11,12]. It is characterized by the ability to improve health by promoting human growth and development and improving the cardiovascular system's capacity while practicing motor skills [13]. Physical exercise is usually divided into three types: aerobic exercises, anaerobic exercises, flexibility exercises, stretch and lengthen muscles exercises [14]. Cardiorespiratory endurance or strength has been shown to improve physical function and structure in children with CP [15]. In addition, participation in aerobic exercises also improves gait endurance, gait speed and limb support time in children with CP [16]. Therefore, it is necessary to explore the effect of physical exercises on the improvement of children with CP.

Currently, the main goal of interventions for children with cerebral palsy is to improve their motor function and enhance the performance of gross motor functions [17]. Traditional treatments for children with cerebral palsy include whole-body vibration therapy, neurodevelopmental therapy, physical therapy, and acupuncture. These traditional physical therapies improve an overall joint range of motion, muscular endurance, and muscle strength [18]. However, a systematic review of 34 trials noted that seven different sports-type interventions positively enhanced gross motor function in children with cerebral palsy [19]. Similarly, another meta-analysis, including 847 patients with cerebral palsy, reported positive effects on gross motor function, balance, gait speed, and muscle strength in children with cerebral palsy after receiving strength training in physical exercise [20]. In both studies, it was noted that improvements after interventions using different types or a particular type of physical exercise in children with cerebral palsy were more significant than in traditional physical therapy [19,20]. However, a meta-analysis involving children with CP showed no improvement in gross motor function from physical exercise interventions, but a positive effect on gait speed and muscle strength [21]. Therefore, whether the benefits of physical exercise improve gross motor function in children with CP requires further study, and a Meta-analysis will investigate the role of physical exercise on the recovery of gross motor function in children with CP and explain the mechanism of its effects.

2. Methods

2.1 Study Area and Duration

The preferred reporting items of the guidelines for systematic reviews and meta-analyses were used in this study. Computerized keyword searches were performed in Web of Science, PubMed, Embase (Ovid), Cochrane Library, and Medline databases. A literature search was conducted from the beginning of the database to October 6, 2021. The keywords used in the search were "sports," "exercise," and "cerebral palsy," and the language of the search was limited to English. The titles and abstracts of the articles were combined as much as possible to retrieve all relevant articles, and literature screening and data extraction were performed independently by two evaluators (GY and HS). In addition, other relevant studies were included manually if their references met the inclusion criteria for this study.

2.2. Study Design

For inclusion in the exercise intervention trials designed in this study, the following inclusion and exclusion criteria were required: (1) study design: randomized controlled trial (RCT) and or quasi-experimental study; (2) study population: children with a precise diagnosis of cerebral palsy and aged 7-15 years; (3) intervention: the experimental group underwent different types of sports interventions (such as movement observation training, multimodal home sports training, cycling training, golf training, hippotherapy, water sports training) for at least three weeks and exercise at least once a week. (4) Control group criteria: No specific exercise intervention was performed in the control group, i.e., the control group only performed daily physical exercise or conventional rehabilitation. (5) Outcome indicators: The instruments in the Gross Motor Function Assessment Scale (GMFM-66; GMFM-88) were used to measure subjects' overall GMFM or specific indicators in the GMFM, such as A (prone and rolling), B (sitting), C (crawling and kneeling), D (standing), and E (walking, running, and jumping); (5) Unavailability of full-text, review-type, conference abstract-type, and book review-type literature was excluded. (6) Excluded children over the age of 18 years; (7) Excluded studies without the total score, mean, and standard deviation in the results.

2.3. Instrument

To ensure the accuracy of the source of evidence, the risk of bias was assessed in 10 articles using the PEDro scale [22], which has 11 items, each with a score of 1, and is judged on a "yes" or "no" basis. A PEDro score of 6-8 was obtained as good, 9-10 as excellent, 4-5 as acceptable, and <4 as poor evidence level [23]. This process was completed independently by two assessors (GY and HS) to assess the risk of bias for the included studies, and disagreements that arose were resolved through discussion with the two corresponding authors (MY and JC).

2.4. Statistical Analysis

In this study, a meta-analysis was conducted using Revman 5.4 software. The mean and standard deviation of the standard scores before and after the intervention of the GMFM-66 and GMFM-88 scales and the mean and standard deviation of the scores of different dimensions (A, B, C, D, E), were extracted. The measures were expressed as mean difference (MD) or standardized difference (SMD) with their 95% CI. The heterogeneity of the studies was assessed using the I^2 index; if the data analysis showed $I^2 \leq 50\%$, $p > 0.05$, its heterogeneity was low, and the analysis model should be a fixed-effects model; if $I^2 > 50\%$, $p < 0.05$, heterogeneity was high and the analysis model should be a random-effects model; when $I^2 > 75\%$, the level of heterogeneity was high, and the statistical inclusion in the studies using the χ^2 test and I^2 values heterogeneity was assessed[24].

3. Results

3.1 Study Identification

In this study, 2856 papers were retrieved using a computerized search of PubMed, Embase (Ovid), Cochrane Library, Web of Science, and Medline electronic databases through a predetermined search strategy. In addition, six journal articles were retrieved from other sources. A total of 1335 irrelevant studies were excluded by reviewing abstracts and titles, of which 1020 articles were excluded that were not journal articles (news, product descriptions, advertisements, or conference abstracts) or were not available in full text. 48 studies were further evaluated in full text, and 28 articles were excluded after reading the full text. Finally, ten studies were included in the systematic review and meta-analysis (see Figure 1).

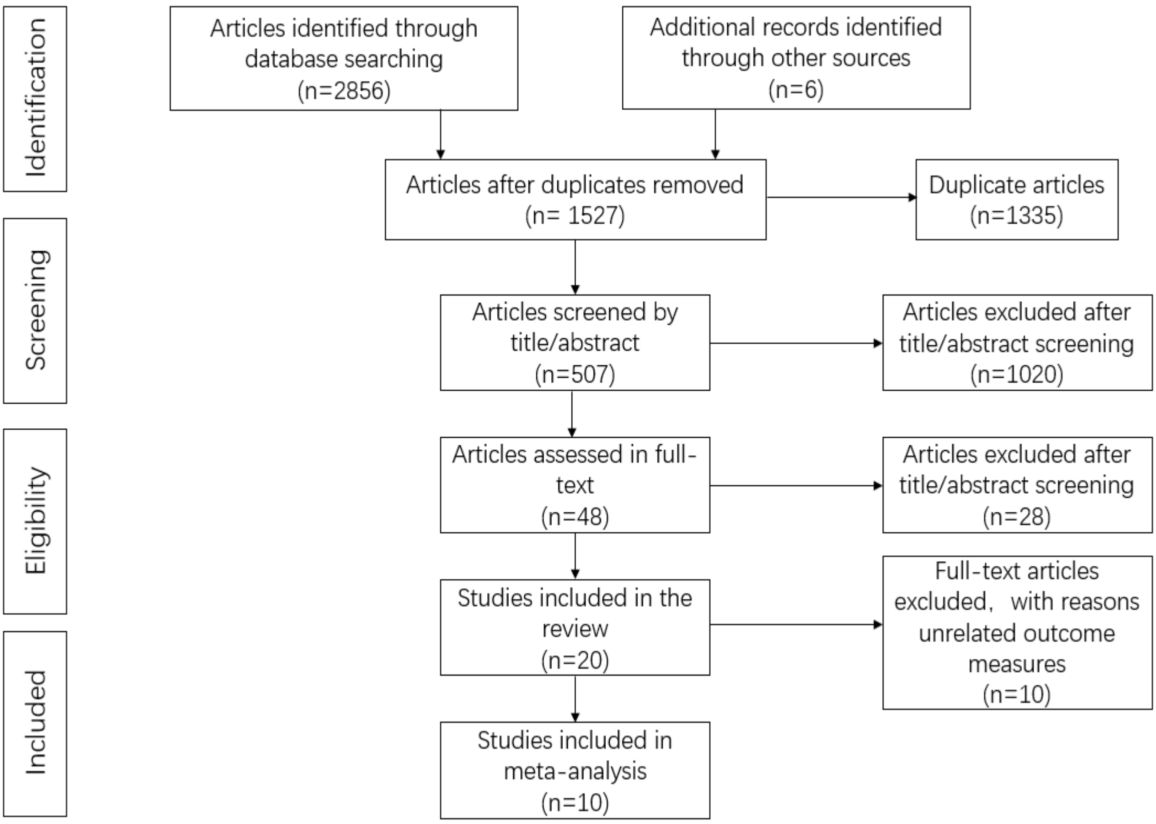

Figure 1. Flowchart of the selected literature

Table 1. Characteristics of included trials in this review

Author, year (Ref.)	N(m/f)	Age	Blind method	Experimental design	Functionality level	Measurement indicators	Intervention method	Frequency of exercise
Jeong 2020[18]	N=18 M=8 F=10	EG:7.44±1.88 CG:6.90 ± 1.79	Unknown	RCT	GMFCS I-III	GMFM-B、C、D、E	EG: Action Observation Training CG: General Physical Therapy	EG:6wk,3d/wk,30min/d CG:6wk,3d/wk,30min/d
Lee 2021[19]	N=14 M=7 F=7	EG:9.42 ± 2.07 CG:9.42 ± 2.29	Single-blind	RCT	GMFCS I-III	GMFM-88 GMFM-D、E	EG: Dual-task training program CG: Neurodevelopmental treatment	EG:8wk,2times/wk,30min/each time CG:8wk,2times/wk,30min/each time
Park 2014[20]	N=55 M=35 F=20	EG:6.68±2.64 CG:7.76±3.67	Unknown	pre-post experimental design	GMFCS I-IV	GMFM-88 GMFM-66 GMFM-A、B、C、D、E	EG: Outpatient Physical and Occupational Therapy +Hippotherapy CG：Outpatient Physical and Occupational Therapy	EG:1times/wk,30min+8wk,2times/wk,45min CG： 1times/wk,30min
Herrero 2012[21]	N=38 M=24 F=14	EG:9.95 CG:9.05	single-blind	RCT	GMFCS I–V	GMFM-66 GMFM-B	EG: Hippotherapy (simulator ON) CG: Hippotherapy (simulator OFF)	EG:10wk,1times/wk,15min CG:10wk,1times/wk,15min
Polat 2020[22]	N=44 M=33 F=11	EG:7±2.10 CG:7±2.80	Unknown	RCT	GMFCS I-III	GMFM-88	EG: 40min physical therapy program+ multi-model sport activity CG: 40min physical therapy program	EG:8wk,5day/wk,50min CG:8wk,2day/wk,40min
Armstrong 2020[23]	N=21 M=8 F=13	EG:6-18y CG:6-18y	Unknown	RCT	GMFCS II-IV	GMFM-66 GMFM-88	EG: (FES) cycling, goal-directed training, and adapted cycling, CG: conventional physiotherapy	EG:8wk,3times/wk,30min+30min CG:8wk
Kwon 2015[24]	N=91 M=49 F=42	EG: 5.7±1.9 CG:5.9±1.8	Unknown	RCT	GMFCS I-IV	GMFM-88 GMFM-66 GMFM-A、B、C、D、E	EG: conventional physiotherapy +Hippotherapy CG: conventional physiotherapy	EG:8wk,3times/wk,30min CG: 8wk
Kwon 2011[25]	N=32 M=21 F=11	EG:6.4±1.7 CG:6.1±1.7	non-blind	Nonrandomized prospective controlled trial	GMFCS I-II	GMFM-88 GMFM-66 GMFM-D、E	EG: conventional physiotherapy +Hippotherapy CG: conventional physiotherapy	EG:8wk,2times/wk,30min CG: 8wk
Lee 2008[26]	N=17 M=10 F=7	EG:6.3±2.1 CG:6.3±2.9	non-blind	RCT	GMFCS II- III	GMFM-88 GMFM-D、E	EG: muscle groups of lower limbs strengthening exercise CG: conventional physiotherapy	EG:5wk,3times/wk,60min CG: 5wk
Seniorou 2007[27]	N=20 M=10 F=10	EG:13 CG:13	non-blind	RCT	GMFCS I–III	GMFM 88 GMFM-E	EG: Weight for progressive resistance exercises CG: conventional physiotherapy	EG:6wk,3times/wk CG: 6wk,3times/wk

3.2. Characteristics of the Included Studies

Table 1 lists the different characteristics of the ten studies, eight randomized controlled studies and two non-randomized controlled studies. The ten studies involved 350 CP participants (205 males and 145 females) and used sport as an intervention. Four of them used Hippotherapy interventions compared with conventional physical therapy or simulator training [26,28,31,32], one study conducted a strength training intervention compared with traditional treatment [33], and one study conducted a Dual-task training program compared with Neurodevelopmental treatment [26]. The remaining four studies were Action Observation Training, multi-model sports activity (FES) cycling, goal-directed training, weight for progressive resistance exercises versus conventional physiotherapy treatments [25,29,30,34], where conventional physiotherapy included stretching, strengthening, walking balance, or active movement of the lower extremities, weight-bearing, bridging, kneeling/half-kneeling, and perturbation in all positions [35,36,37]. In terms of intervention duration and frequency, the majority of physical exercise interventions in the ten studies were 5-12 weeks and 15-90 minutes, with the frequency of interventions between 3-5 times per week, except for Park et al. [27] and Herrero [28], who were one time per week. In terms of participants, most of the studies had small sample sizes (14-55 participants), except for Kwon et al. [31], who had a sample size of 91 participants, and most of the studies were conducted with children aged 6-15 years. In this study, Jeong et al. [25], Lee et al. [26], Polat et al. [29], and Seniorou et al. [34] mainly selected children with GMFCS I-III as subjects; Park and Kwon et al.'s [26,30] studies selected children with GMFCS I-IV as subjects; the remaining Herrero et al. [28], Armstrong et al. [30], Kwon et al. [32], Lee et al. [33] studies used children with GMFCS I-V, GMFCS II-IV, GMFCS I-II, and GMFCS II- III as subjects, respectively. Different physical exercise modalities were compared in these studies with conventional or other treatments with moderate intensity, the number of activities, and in some studies, altered GMFCS levels in children with CP.

3.3. Bias Risk of the Included Studies

The articles included in this study were assessed for risk of bias using the PEDro scale to obtain PEDro scores for the corresponding studies, where item 1 was not included in the total score. Eight of the ten articles had high or good methodological quality, two articles had poor evidence ratings, and the overall methodological quality of this study was acceptable. Details of the PEDro scale scores of the included literature are shown in Table 2.

3.4. Meta-Analysis of the Study Groups

Testing the gross motor function ability of children with cerebral palsy is commonly measured by the GMFM instrument, and the analysis of this study can be divided into seven groups, with the GMFM-88 and GMFM-66, both of which have been validated for assessing changes in gross motor function in children with CP, with the GMFM-66 being an updated version of the GMFM-88, which has improved the reliability and validity of the instrument after the removal of 22 items [37]. And the GMFM-88 includes five dimensions, in order A (lying and turning), B (sitting), C (climbing and kneeling), D (standing), and E (walking, running, and jumping).

Table 2. Analysis of the methodological quality of the studies (PEDro scores)

Study	1	2	3	4	5	6	7	8	9	10	11	Total
Jeong et al.2020	-	Y	Y	Y	N	N	N	Y	N	Y	Y	6
Lee et al.2021	-	Y	Y	Y	Y	N	N	Y	N	Y	Y	7
Park et al.2014	-	Y	N	Y	N	N	N	Y	N	Y	Y	5
Herrero et al.2012	-	Y	Y	Y	Y	N	Y	Y	N	Y	Y	8
Polat et al.2020	-	Y	N	Y	N	N	N	Y	N	Y	Y	5
Armstrong et al.2020	-	Y	N	Y	N	N	Y	Y	Y	Y	Y	7
Kwon et al.2015	-	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Kwon et al.2011	-	N	N	Y	N	Y	Y	N	Y	Y	Y	6
Lee et al.2008	-	Y	Y	N	N	N	N	Y	N	N	Y	4
Seniorou et al.2007	-	Y	N	Y	N	N	N	Y	N	N	Y	4

Note: 1= Clear description of subject inclusion criteria (not included in the total score); 2=Random al-location; 3=Assign hidden; 4=Baseline similarity of key indicators; 5=Subjects blinding; 6=Therapist blind; 7=Assessor blinding; 8=>85% follow up; 9=Intention-to-treat analysis; 10=Intergroup statistics for at least one primary outcome are reported; 11= Estimates and confidence intervals for at least one primary outcome.

Five articles in this study analyzed changes in gross motor function in children with CP using the GMFM-66 assessment tool, and the results of the GMFM-66 analysis showed an SMD=1.90, 95% CI (0.55~3.25), Z=2.76, p=0.006. It is known that after receiving the physical exercise intervention, the experimental group showed statistically significant differences in GMFM-66 scores of children with cerebral palsy when compared with the control group. Details are shown in Figure 2.

There were eight studies that used the GMFM-88 to measure changes in gross motor function before and after the GMFM-88, and the results of the GMFM-88 showed that SMD=1.49,95% CI (0.83~2.15), Z=4.42, p<0.00001. i.e., after the physical exercise intervention, the differences between the experimental and control groups were statistically significant. Details are shown in Figure 3.

Among the 5 different latitudes in the GMFM-88 scale, dimension A showed SMD=0.33,95%CI (-0.31~0.98), Z=1.02, *p*=0.31 after Meta-analysis of 2 included papers; dimension B had 4 papers included for analysis and showed SMD=1.07,95%CI (-0.4~ 2.53), Z=1.42, *p*=0.15; dimension C had 3 papers included in the analysis, showing SMD=1.44, 95% CI (-0.49 ~ 2.91), Z=1.46, P=0.14; dimension D had 6 papers included in the analysis, showing SMD=3.13, 95% CI (1.23 ~ 5.02), Z=3.23, *p*= 0.001; E dimension had 7 literature included in the analysis and showed SMD=3.34, 95% CI (2.00 ~ 4.69), Z=4.88, p<0.00001.

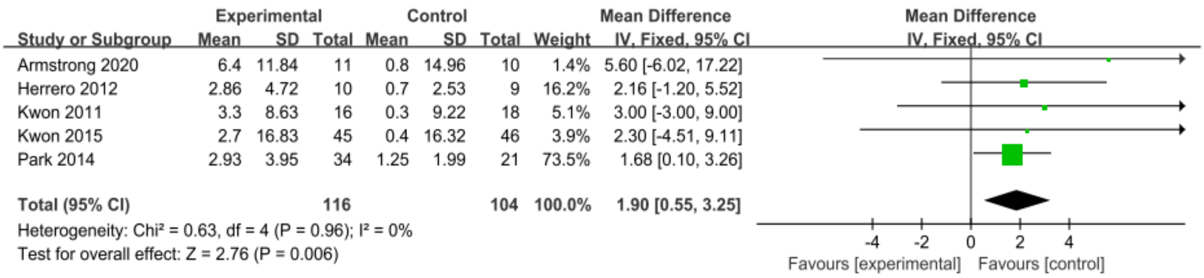

Figure 2. GMFM-66 total score forest map

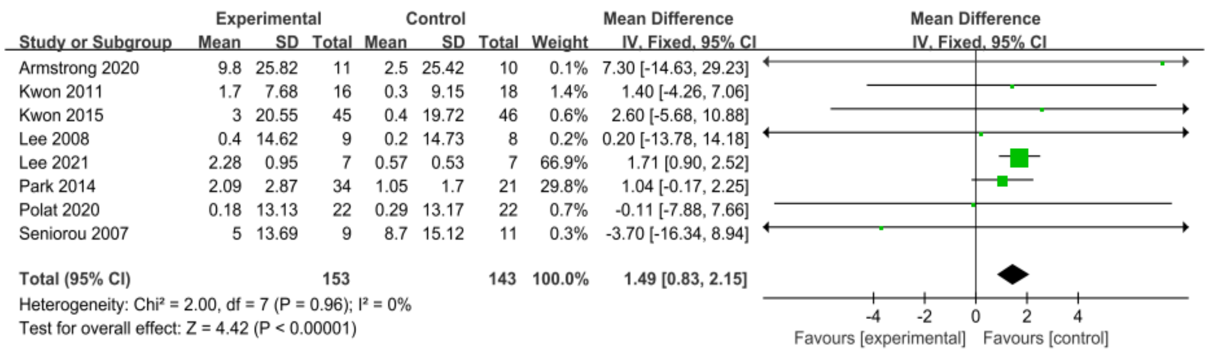

Figure 3. GMFM-88 total score forest map

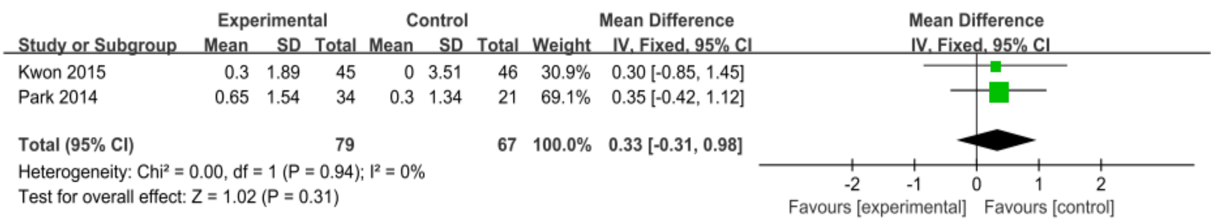

Figure 4. A dimensional score forest diagram

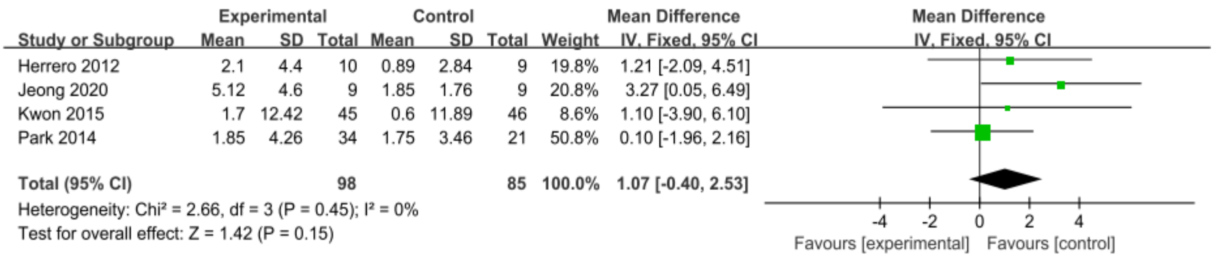

Figure 5. B dimensional score forest diagram

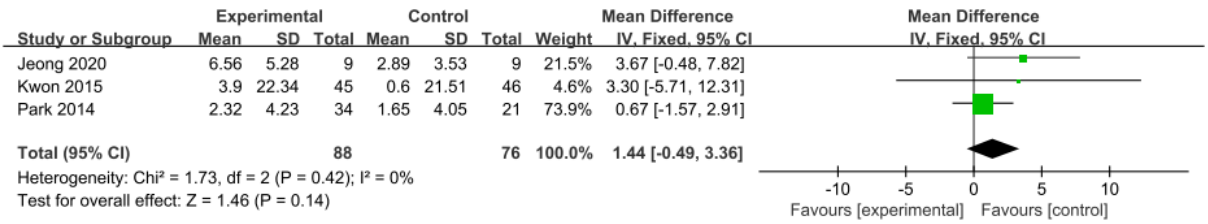

Figure 6. C dimensional score forest diagram

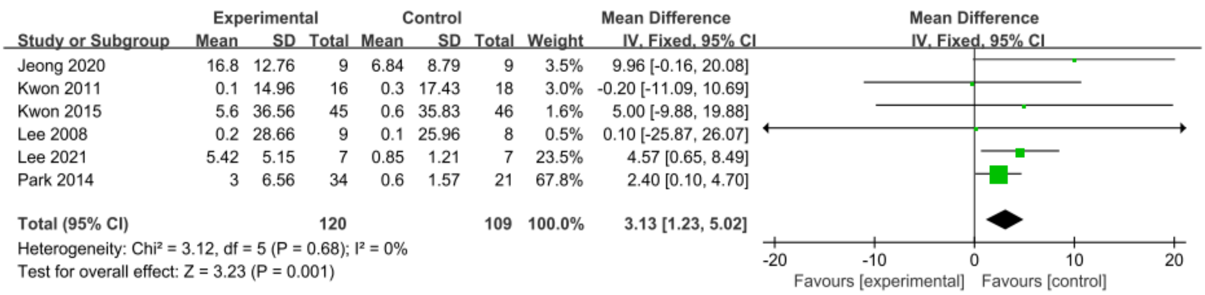

Figure 7. D dimensional score forest diagram

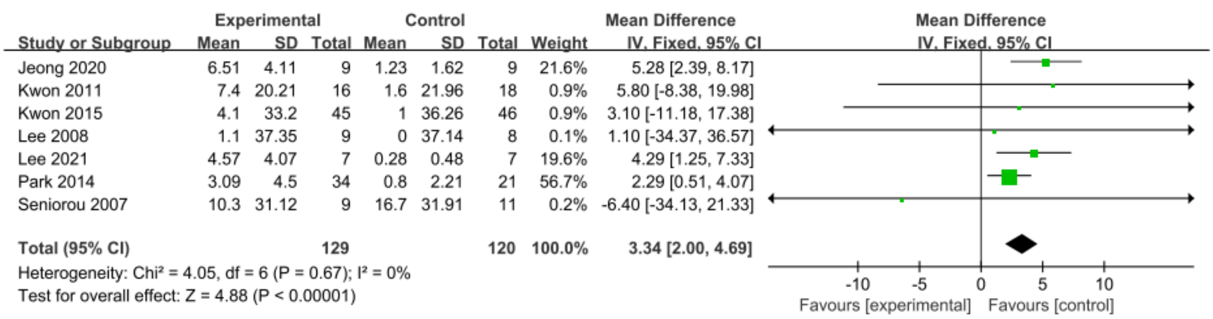

Figure 8. E dimensional score forest diagram

The results of the five dimensions in GMFM-88 after Meta-analysis showed that the before-and-after differences between the experimental and control groups in dimension D and dimension E were statistically significant, while the P values obtained for dimensions A and dimension B, and dimension C were more significant than 0.01. Therefore, it can be concluded that the before-and-after differences between the experimental and control groups were not statistically significant, and the results are shown in Figures 5-8.

4. Discussion

This study conducted a systematic review and Meta-analysis, which focused on analyzing the effect of physical exercise interventions on the improvement of gross motor function in pediatric patients with CP. In the analysis of ten studies, a total of 350 children with CP were involved. The results of the analysis of the GMFM-66 and GMFM-88 scales and the D and E dimensions in this study demonstrate that physical exercise interventions are effective in improving gross motor function in children with CP, specifically in terms of positive improvements in overall gross motor function and the ability to stand, walk, run and jump.

Of the five studies that used the GMFM-66 assessment scale, the control group established in four of the studies was the traditional means treatment group, whereas the study by Herrero et al. [28] used a simulated horse treatment and established a control group that was trained for 15 minutes with the simulator off, whose control group did not receive traditional means treatment, and the credibility of their results needs to be further confirmed. Also, the results of one study in the Meta-analysis of GMFM-88 were inconsistent with the results of this study, and the use of different physical education interventions may not improve gross motor function in children with CP [29]. For example, the use of a multimodal physical exercise intervention for eight weeks in the study by Polat et al. [29] did not have a positive effect on GMFCS levels in children with CP, and total GMFM-88 scores on pre-and post-tests in the experimental and control groups were not statistically significant, whereas the physical exercise interventions used in the other seven studies all showed improvements in total GMFM-88 scores that were statistically significant.

Three of these studies used the Hippotherapy intervention [27,31,32], and the remaining four used each Dual-task training program, (FES) cycling, goal-directed training, muscle groups of lower limbs strengthening exercise, weight for progressive resistance exercises Improvements in the hip, muscle tone, and gait were observed in children with CP [26,33,34]. The most common problem in children with CP is hip subluxation/dislocation, followed by dystonia, musculoskeletal deformities, muscle contractures, and gait abnormalities. Polat et al. were selected from basic gymnastic exercises to develop an 8-week multimodal home physical exercise intervention [29], and their findings showed no significant improvement in gross motor function in children with CP. In addition, of the six articles included in the analysis of the D dimension, one paper reported a negative result in the intergroup comparison of D dimension scores, which may also be related to the content of the intervention. The study by Lee et al. [26] used the Dual-task training program, a physical education intervention that focuses on the transition from sitting to standing posture exercises, and reported no significant differences in D-dimension results. Therefore, these negative results above may be related to the content of the physical education intervention. In terms of intervention characteristics, most studies used a total intervention duration of 5-10 weeks and an intervention frequency of 1-3 times per week, with the highest frequency intervention in the study having a treatment duration of about 30 minutes and two studies exceeding 45 minutes of treatment. It has been noted in some studies that a long duration of interventions can instead cause fatigue in children with CP and is not conducive to achieving positive improvements in gross motor function. Therefore, it is recommended that interventions for children with CP can be used for 5-10 weeks by means of physical exercise for 30-45 minutes 1-3 times per week, which is positive for the improvement of gross motor function in children with CP.

5. Strengths and Limitations

The strength point of this research review lies in our systematic methodological design. The strength of our research design lies in the following three aspects; firstly, the focus of the study is mainly on physical exercise. By defining the concept of physical exercise, moderate-intensity physical exercise means of intervention for children with CP were identified as inclusion criteria. In addition, the physical exercise programs selected for children with CP were mainly Action Observation Training, Dual-task training program, Hippotherapy, multi-model sports activity, (FES) cycling, goal-directed training, muscle groups of lower limbs strengthening exercise, Weight for progressive resistance exercises; Second, we focused on introducing the use of the gross motor function assessment scales GMFM-66, GMFM-88, and the A-E dimensions, and only experiments using the GMFM measurement tool were included in this study. Excluding the effect of other measurement tools on outcome indicators while enabling us to validate the consistency of the findings across experiments. Third, we not only analyzed the effect of physical exercise on the overall gross motor function of children with CP but also discussed the effect on different dimensions of A-E function in the GMFM-88. Finally, the average age of the CP children in the study was between 7 and 15 years, which allowed for an analysis of improvements in gross motor function in CP children at a specific age, thus excluding other age groups from influencing the results of this study.

The results of the systematic review and meta-analysis showed statistically significant for GMFM-66, GMFM-88, and dimensions D and E before and after the experimental versus control groups, but we have the following limitations for this study. First, there was variability in the quality level of the literature included in the Meta-analysis, with eight RCT studies and two non-RCT studies, which may have biased the results of the analysis; second, there was variability in the physical exercise interventions included in the studies, such as Polat et al. who used a multimodal family physical exercise intervention that did not positively improve outcomes for children with CP and reported no significant differences in the GMFM-88 results [29]. Third, the only databases searched for this study were Web of Science, PubMed, Embase (Ovid), Cochrane Library, and Medline databases. There was potentially available literature in other databases that were not included. Fourth, only a small number of studies in this study were followed up; fifth, the size of the sample may have limited the interpretability of the results, with the largest sample size of 91 in 10 studies, including 2 with a sample size of less than 20. In conclusion, based on the results of the Meta-analysis, it was confirmed that there was a significant improvement in gross motor function by physical exercise in children with CP, which can be used as a reference method for physical therapy in children with CP, but the above-mentioned shortcomings remind us that the effect values provided by the Meta-analysis should be interpreted with caution.

6. Conclusions

Preliminary evidence from this study suggests that physical exercise interventions positively affect gross motor function in children with CP. An improvement was produced in terms of the GMFM-66 and GMFM-88 and dimensions D and E. In addition, the type, frequency, and duration of the interventions used in the study varied, and the mechanism by which physical exercise affects overall gross motor function in CP patients is unclear. This study has contributed to physical exercise to intervene in gross motor function in children with CP, providing factors that can be analyzed to explore specific areas of influence and mechanisms of action. However, there is still a need for additional, rigorous randomized controlled trials to identify appropriate intervention programs.

Data Availability Statement

The original data supporting the conclusions of this paper will be provided by the authors without reservation.

Author Contributions

GY and HS: Data collection, Data analysis, conceptualization and design. GY, HS and MY: Study design, manuscript writing. GY and JC revision. All authors contributed to the article and approved the submitted version.

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