Science and Technology and Social Development Proceedings Series

Review
2024 International Conference on Business Economics, Education, Arts and Social Sciences (EASS 2024)

The Impact of Strength Training on Lower Limb Muscles in Children and Adolescents with Cerebral Palsy: a Systematic Review

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Abstract: This study systematically reviewed the literature on the effects of strength training on lower limb muscles in children and adolescents with cerebral palsy from three online databases. These studies consistently showed that strength training has a positive effect on lower limb muscle volume and strength in children and adolescents with cerebral palsy, although the magnitude of the effect varies by intervention and load. Despite the positive indications, caution is needed in interpreting and comparing the results of these studies due to methodological quality, differences in interventions, and diversity of measures.

Keywords: cerebral palsy; strength training; lower limb muscles; children; adolescents

Published: 09 November 2024

1. Introduction

Cerebral palsy (CP), is a collection of syndromes resultant of non-progressive brain damage that occurs during early brain development, usually in the pre-natal period. Subtypes of CP include spastic, dyskinetic, ataxic, Worster-Drought syndrome and other specifically defined cerebral palsy, each with potentially different aetiologies [1]. According to the study of Martin et al., the majority of infants born before 34 weeks suffered white matter damage, leading to placental damage throughout pregnancy, increasing the risk of hypoxic ischaemia and ultimately leading to children being born with cortical/subcortical or basal ganglia damage [2]. Motor performance is usually coordinated through communication between the cerebral cortex, thalamus, basal ganglia, brainstem, cerebellum, spinal cord and communicative sensory-motor homunculi. However, because of damage to the neuromotor component of the central nervous system [3], the children who are patients with cerebral palsy usually have postural abnormalities and central motor deficits, which may also be accompanied by epilepsy, perceptual deficits and secondary musculoskeletal problems. CP is one of the most common causes of motor disability in children. These symptoms can have a serious impact on both the child's daily life and motor function. Musculoskeletal deformities, including contractures, were found to be the lowest cause of all health-related quality of life scores [4]. The persistent existence of pain and increasing age led to the negative influence on the health-related quality of life of those children with CP [5]. This highlights the importance of optimising musculoskeletal health as children age and in clinical practice.

Spastic CP accounts for approximately 75% of the clinical subtypes of CP [6], and prolonged muscle spasticity in children often leads to the development of abnormal postures and impaired motor function. In one study, children aged 2-5 years with spastic CP had a approximately 22% lower cross-sectional area of the medial gastrocnemius muscle when compared to typically developing children [7]. Clinically, spasticity is associated with increased muscle tone, stiffness, hyperreflexia and ultimately joint contraction [8]. Although the primary lesions of spasticity are located within the central nervous system, significant changes in the muscles of spastic patients also occur [9]. The skeletal muscle structure determines the function of the entire muscle [10]. In children with CP, skeletal muscle stiffens during activity because of spasticity, and this can reduce the child's activity level considerably because of fragility and imbalance [11]. The shorter length of the rectus femoris bundle in children with CP may result in a reduction in muscle strength, the product of force production and contraction velocity, and the range of motion in which the muscle can function during functional activity [12]. In children's life and motor activities, various postures such as crawling, sitting, walking and running require the support of skeletal muscles. Children with cerebral palsy have difficulty in maintaining movements or experiencing movement deformation due to abnormal muscle strength and weak muscle endurance, therefore, there should be detailed rehabilitation strategies for the dysfunction of children with CP to promote their overall development.

Resistance training is one of the most effective non-pharmacological interventions for improving muscle mass and function in health and disease. The positive effects of resistance exercise on muscle strength are well known. Resistance training increases muscle thickness and fascicle length, which limit the loss of fiber force and produce higher contraction velocities [13]. In children and adolescents, resistance training performed more frequently over time has a positive effect on muscle strength, but also on muscle morphology and structure, which determines muscle function [14]. Park & Kim found a large effect of strengthening intervention on strength and physical performance on individual with cerebral palsy. However, there is a lack of understanding in the literature of how strength training influences skeletal muscle structure. In patients with cerebral palsy, traditional resistance exercises focus on strengthening muscle strength and functional performance.[15] In a number of recent experiments, researchers have focused on the effects of resistance training on functional, performance and gross motor outcome measures in patients with CP [15]. Our main aim was therefore to investigate the effects of strength training on muscle volume, strength and function in the lower limbs of children and adolescents with CP.

2. Methods

2.1. Strategy Design

A comprehensive search of the following online databases was carried out in October 2021: Ovid Medline, Embase and The Cochrane Library. The search strategy is not time limited and contains the following keywords: (1) child and adolescent; (2) and cerebral palsy or spastic diplegia; (3) and exercise or physical activity or strength training or resistance training or sport or exercise therapy or rehabilitation; (4) and muscle or muscle mass or muscle function or muscle morphology or bone or skeleton or architecture; (5) and clinical trial or intervention or randomized controlled trial or prospective studies or case-control studies or pilot studies or cohort studies or random * control * trial or RCT or quasi-experimental. The titles and abstracts were filtered after removing duplicates, and finally the relevant articles were obtained.

2.2. Inclusion Criteria

Inclusion in the review was based on the following criteria: (1) RCT, Non-RCT or prospective cohort studies; (2) participants were aged 4-18 years, had a clinical diagnosis of CP, had not undergone surgery within the last 12 months, had a gross motor function classification system (GMFCS) level I-III, could walk independently without assistance, and ability to follow simple instructions; (3) study intervention consisted of strength training, progressive resistance training, physiotherapy management (including isolated muscle strengthening, functional muscle conditioning, muscle stretching, gait re-education, balance and stability training, and functional and play skills) for a minimum of 6 weeks; (4) the results are evaluated using one or more morphological or architectural parameters (volume, thickness, cross-sectional area(CSA), etc.).

2.3. Quality Assessment

After removing duplicates and screening title and abstract, the quality of the included literature was assessed. The included literature was assessed using the Modified Downs and Black Checklist. The 27-item scale was used to assess the methodological quality of randomized and non-randomized experiments and consists of 5 subscales: (1) Reporting, (2) External validity, (3) Internal validity-bias, (4) Internal validity-confounding, and (5) Power. All items were scored as 0 or 1, except for 1 item in the reporting subscale which was scored as 0-2. The final maximum score available was 28. Study quality was categorized based on the final score as excellent (26-28), good (20-25), fair (15-19) or poor (≤14).

3. Results

3.1. Retrieve Results

A total of 1313 articles were retrieved from database searches. After, excluding duplicates and screening titles and abstracts, 48 full text articles were assessed for eligibility. Finally, four articles were eligible for inclusion after viewing the full text according to the inclusion criteria. Fig.1

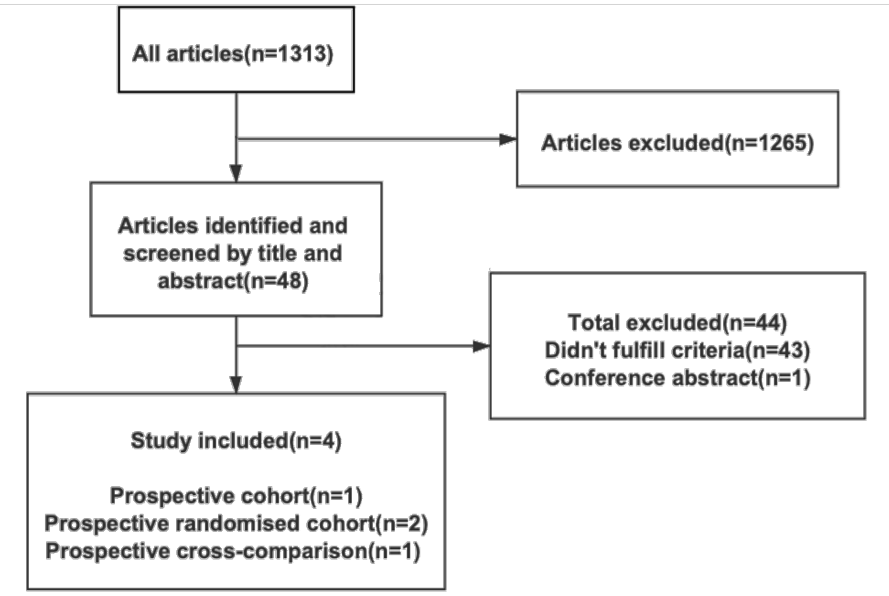

Figure 1. Flow diagram of the literature search.

3.2. Study Design

Included in the four papers were two randomized cohort studies [16,17], one cohort follow-up study [18] and one cross-comparison study [19]. Of these four studies of lower limb strength training, three evaluations were home-based [17-19] while the other was conducted in a tertiary centre [16].

3.3. Participants

In the included literature, there were 49 participants (30 males and 19 females) with a mean age ranging from 8-13 years. All participants were at I–III level of the Gross Motor Function Classification System(GMFCS) and all had a diagnosis of cerebral palsy (36 for diplegia and 13 for hemiplegia). The characteristics of the participants are summarized in Table 1.

Table 1. Study design and participants characteristics.

Study	Design	Subject(s)	Sex(m/f)	Mean age	Cerebral Palsy type	GMFCS Level
Williams et al.(2013)	Cross-comparison design	15	10/5	8y5mo	15 diplegia	I-II (n=NR)
McNee et al.(2009)	Prospective cohort	13	7/6	10y11mo	8 diplegia 5 hemiplegia	I=6; II=5; III=2
Moreau et al.(2013)	Prospective randomized cohort	16	10/6	13y8mo	8 diplegia 8 hemiplegia	I=9; II=1; III=6
Stackhouse et al.(2007)	Prospective randomized cohort	5	3/2	10y5mo	5 diplegia	II-III (n=NR)

m = male; f = female; NR = not reported.

3.4. Type of Intervention

According to Table 2, the interventions of these four studies ranged between 8-12 weeks, with a frequency of 3-4 sessions per week and a total of 24-40 sessions. Williams et al. combined strength training with Botulinum toxin A (BoNT-A) injection therapy; McNee et al. developed unilateral heel raises and Thera-Band exercises (full extension of the knee); Moreau et al. used high velocity concentric training and traditional strength training; and finally, Stackhouse et al. performed isometric strength training over a prescribed joint angle.

Table 2. Description of intervention from included studies.

Study	Intervention type	Training location	Mode of exercise	Frequency duration Total sessions	Supervision & adherence	Load	Progression
Williams et al.(2013)	Lower limb strength training	Home	Manual resistance; Thera Band resistance;	3*week, 10 weeks, 30 sessions	One session per fortnight supervised by exercise physiologist	NR Exercises completed in sets of 10	Fortnightly increase in repetitions and load
McNee et al.(2009)	Lower limb strength training	3*sessions at home; 1*session at tertiary center	Single-leg heel-raises; Seated Thera Band calf press with knee extended	4*week 10 weeks 40 sessions	One session per week supervised by physiotherapist; 70% adherence	3-4 sets * 6-12 repetitions; Maximum Thera Band used if could not complete heel raises	Weight added in completion of 12 repetitions; Heavier Thera Band
Moreau et al.(2013)	Lower limb progressive resistanc	Tertiary center	High velocity concentric; Traditional strength training	3*week, 8-10 weeks, 24 session	Supervised; 94% adherence	6 sets * 5 repetitions; 80% of maximum torque	Weekly to match highest torque value achieved in previous week

	e training					output at 30°/s	
Stackhouse et al.(2007)	Lower limb strength training	Home; 1*session at tertiary centre	Isometric strength training on custom build exercise board	3*week, 12 weeks 36 sessions	Parent/ guardian supervision; 100% adherence	1 set * 15 MVICs lasting 15s each	NR

NR=not reported; MVIC= maximum voluntary isometric contraction.

3.5. Qualitative Assessment

Methodological quality is assessed using the Modified Downs and Black Checklist. A total of 27 items were included in five sections: reporting, external validity, internal validity (bias), internal validity (confounding) and power. Three studies scored 16 [16,17,19] and one study scored 18 [18] (out of a total score of 28), which categorized them as “fair” quality. The methodological quality assessment is shown in Table 3.

	Modified Downs and Black Scale					
Study	**Reporting/ 11**	**External Validity/3**	**Bias/7**	**Confounders /6**	**Power/1**	**Total/28**
Williams et al.(2013)	6	1	5	3	1	16
McNee et al.(2009)	9	1	4	3	1	18
Moreau et al.(2013)	7	1	5	3	0	16
Stackhouse et al.(2007)	7	1	5	3	0	16

3.6. Outcome Measures

Outcome measurements from the four studies are summarized in Table 4. Williams et al. measured muscle volume using magnetic resonance imaging(MRI), while McNee et al. used three-dimensional ultrasound (3DUS) to measure it. Moreau et al. used two-dimensional ultrasound (2DUS) measured cross-sectional area, muscle thickness, fascicle length, and fascicle angle, while Stackhouse et al. measured cross-sectional area using MRI.

3.7. Outcomes

In the study by Williams et al. the intervention group showed significant increases in muscle volume in the quadriceps ($p < 0.001$, ES = 0.53) and plantar flexors ($p < 0.001$, ES = 0.40) after progressive strength training. Strength training increased progressively with increasing repetitions and load level, manual resistance and the use of Thera bands. Children completed three maximum isometric contractions and successive maximum isokinetic contractions. In isometric muscle peak torque (PT/BW)($p = 0.012$, ES = 0.53) ($p = 0.003$, ES = 0.66), isokinetic PT/BW ($p = 0.047$, ES = 0.43) ($p = 0.002$, ES = 0.73) and muscle power ($p = 0.008$, ES = 0.59) ($p = 0.031$, ES = 0.52), both knee flexor (KF) and knee extensor (KE) strength were significantly increased in the intervention group.

The muscle volume of the medial and lateral gastrocnemius was significantly greater after the intervention than at baseline in the McNee et al. study, with increasing of 30.5% ($p<0.001$) and 19.7% ($p=0.007$) respectively. Participants performed plantar flexor(PF) strengthening exercises, increasing the load by backpack weights and using the Thera Bnad to provide resistance to the PF. There was a significant increase in the number of heel raises performed by the participants. There was no statistically significant increase in ankle dorsiflexion range, although there was also a slight increase.

In the Moreau et al. study, participants completed any exercise from self-paced walking, unresisted stationary cycling and stretching according to an individualised training programme. The CSA of the rectus femoris (RF) increased statistically significantly in both groups, but only the muscle thickness of the vastus lateralis (VL) ($p=0.011$) increased in the strength training (ST) group. RF fascicle length increased significantly in the high velocity training (VT) group (+1.23 cm; 95% confidence interval [CI] = 0.12-2.34, *P* =0.044), but decreased in the ST group (-0.76 cm; 95% CI = -0.07 to -1.46, *P* =0.049). The VT group of concentric knee extension maximal-effort contractions gradually increases in speed over the course of each week if the participant is able to complete the previous training at a faster pace. VL fascicle length decreased after training in both groups. Isokinetic strength at all four angles of the KE increased in both groups after the intervention, as did the muscle volume of the KE.

In the neuroelectric stimulation (NMES) group, strength training is performed on the quadriceps and triceps muscles by using transcutaneous implanted electrodes. Participants performed electrically induced contractions on specific exercise plates and adherence could be detected by the stimulator. CSA of the quadriceps was more variable in the NMES group, but PF did not change significantly in either group. Isometric strength of the results of the KE had a small increase in the study by Stackhouse et al. The results of all four trials are summarized in Table 4.

Table 4. Effect sizes for muscle morphology and architecture outcomes by subgroup.

Study	Outcome	Measurement method	Muscle/s	Intervention Subgroup	Mean difference	Effect Size	95% C.I.	*p Value*
Williams et al.(2013)	Muscle volume Isometric strength Isokinetic strength Muscle Power	MRI Isokinetic dynamometer Isokinetic Dynamometer Isokinetic dynamometer	Quadriceps Quadriceps Plantar flexors Plantar flexors Knee extension Knee flexion Knee extension 60°/s Knee flexion 60°/s Knee extension 60°/s Knee flexion 60°/s	Pre-BoNT-A Post-BoNT-A Pre-BoNT-A Post-BoNT-A Pre-BoNT-A Post-BoNT-A Pre-BoNT-A Post-BoNT-A Pre-BoNT-A Post-BoNT-A Pre-BoNT-A Post-BoNT-A Pre-BoNT-A Post-BoNT-A Pre-BoNT-A Post-BoNT-A	0.98 0.83 0.85 0.77 0.29 0.18 0.20 0.17 0.27 0.21 0.18 0.04 3.44 4.49 4.19 2.59	0.31 0.27 0.51 0.37 0.43 0.16 0.58 0.40 0.52 0.28 0.68 0.13 0.61 0.41 1.06 0.38	-0.44 to 1.05 -0.48 to 1.01 -0.25 to 1.26 -0.37 to 1.12 -0.32 to 1.17 -0.54 to 0.85 -0.17 to 1.34 -0.30 to 1.10 -0.23 to 1.27 -0.41 to 0.98 -0.08 to 1.44 -0.56 to 0.82 -0.15 to 1.36 -0.34 to 1.16 0.27 to 1.85 -0.37 to 1.30	0.001 <0.001 <0.001 <0.001 0.210 0.102 0.233 0.010 0.114 0.033 0.053 0.076 0.164 0.033 0.004 0.002
McNee et al.(2009)	Muscle volume Heel raises	3DUS -	Medial gastrocnemius	- - -	0.30 0.20 9.00	0.46 0.44 0.80	-0.32 to 1.24 -0.34 to 1.22 0.0 to 1.59	0.001 0.006 <0.001

			lateral					
			gastrocnemi					
			us					
			Planter					
			flexion					
							-0.81 to	
			Rectus				1.04	
			Femoris				-0.81 to	
			Rectus				1.30	
			Femoris				-0.69 to	
			Vastus				1.17	
			Lateralis				-0.44 to	
	Cross-							
			Vastus				1.71	
	sectional	2DUS						
			Lateralis				-0.59 to	
	area							
			Rectus	VT	0.26	0.12	1.37	0.029
		2DUS						
			Femoris	ST	0.57	0.25	-1.24 to	0.009
	Muscle							
			Rectus	VT	0.08	0.24	0.86	>0.05
	thickness	2DUS						
			Femoris	ST	0.07	0.63	-1.37 to	0.011
			Vastus	VT	1.23	0.34	0.50	0.044
	Fascicle							
			Lateralis	ST	-0.76	-0.19	-1.31 to	0.049
	length							
			Vastus	VT	-0.64	-0.44	0.80	>0.05
		Isokinetic						
			Lateralis	ST	-0.26	-0.26	0.16 to	>0.05
Moreau et		dynamomet						
			Knee	VT	0.72	1.15	2.15	<0.05
al.(2013)		er						
			extension	ST	0.86	1.20	0.06 to	<0.05
	Isokinetic							
			30°/s	VT	0.63	1.00	2.33	<0.05
	strength							
				ST	0.68	1.56	0.02 to	<0.05
			Knee	VT	0.60	1.04	1.98	<0.05
			extension	ST	0.65	1.51	0.36 to	<0.05
			60°/s	VT	0.71	1.47	2.75	<0.05
				ST	0.58	1.01	0.56 to	<0.05
			Knee	VT	1.34	0.46	2.02	0.023
		Isokinetic						
			extension	ST	0.56	0.19	0.33 to	>0.05
		dynamomet						
			90°/s				2.70	
	Muscle	er						
							0.43 to	
	Power							
			Knee				2.51	
			extension				-0.11 to	
			120°/s				2.12	
							-0.48 to	
			Knee				1.40	
			extension				-0.86 to	
							1.24	
							-1.13 to	
			Quadriceps					
	Cross-						1.35	
		MRI	Plantar					
	sectional			-	2.35	0.11	-0.88 to	>0.05
Stackhous			flexors					
	area			-	0.47	0.38	1.63	>0.05
e et		Isokinetic	Knee					
				-	0.51	0.49	-0.77 to	>0.05
al.(2007)		Dynamomet	extension					
	Isometric			-	-0.28	-0.44	1.75	>0.05
		er	Plantar					
	strength						-1.70 to	
			flexion					
							0.81	

Pre-BoNT-A = trained prior to receiving intramuscular botulinum toxin type-A; Post-BoNT-A = trained following intramuscular botulinum toxin type-A injection; VT = high velocity training group performed training repetitions at movement velocities up to 120° s^{-1}; ST = traditional strength training group performed all training repetitions at movement velocity of 30° s^{-1}; 2DUS = two-dimensional ultrasound; 3DUS = three-dimensional ultrasound.

4. Discussion

The aim of this systematic review was to investigate the effects of strength training on muscle volume, strength and function in the lower limbs of children and adolescents with CP. All four of the included papers showed a positive effect of strength training on lower limb muscle volume and strength in children with CP. However, the final effect sizes differed because of the interventions and loads.

4.1. The Impact of Strength Training on Muscle Volume and Muscle Power

In the study by Williams et al., BoNT-A injections were combined with strength training. After ten weeks of training, children in the intervention group showed targeted strength gains in each muscle. Muscle strength also increased significantly in the PF (ES0.43-0.55) and tibialis anterior (TA) (ES0.27-0.31), but there were also differences in change between groups. This is because the gastrocnemius and hamstring (HS) are usually the targets of BoNT-A injections. Spasticity was significantly reduced after BoNT-A injection and therefore strength in the gastrocnemius and HS increased after strength training. The Pre-BoNT-A group had a greater effect on muscle volume in the results compared to the Post-BoNT-A group. This may be because the Post-BoNT-A group seemed to be able to take advantage of the increased muscle volume immediately, whereas the Pre-BoNT-A group needed to wait until after the real strength increase to mask the spasticity. The greatest effect on motor development in children with CP would be spasticity, whereas BoNT-A injections blocked the release of acetylcholine at the neuromuscular junction, reducing muscle spasticity and promoting joint movement [20].

Muscle hypertrophy following strength training is also consistent with the findings of McNee et al., suggesting that CP children's muscles can acquire growth due to the stimulus of strength training. After 10 weeks of plantar flexor training, both the medial gastrocnemius (0.46) and lateral gastrocnemius (0.44) increased in muscle volume. However, a control group was lacking, so it was not possible to determine whether the increase in muscle volume and strength was due to natural growth or the result of strength training. However, the effect of muscle strength gains following strength training was better in children and adolescents with CP than in typically developing individuals, possibly due to poorer initial strength in children with CP. There is an evidence that function and strength are associated with spasticity [21] and that strength is significantly reduced in children with CP [22], and is present in all muscles around the joints [23]. Therefore, muscles, spasticity and strength should be correlated with each other. Morphological results suggest a potential role for strength training in altering the rate of muscle growth. According to Williams et al.'s study, the goal attainment scale scores of the participating children all increased with the combination of neural and musculature, showing that the aim of increasing muscle volume and muscle strength through strength training is also to improve muscle function.

4.2. The Impact of Strength Training on Muscle Morphology and Function

Williams, Moreau and Stackhouse et al. all produced results for strength training at isometric strength, isokinetic strength and CSA. In the study by Moreau et al. training at higher shortening velocities resulted in an increase in fascicle length and CSA in the RF and a decrease in fascicle length in the strength training group. However, there was a small negative effect on the vastus lateralis. Isokinetic strength of the knee extensors increased between both groups. Of the four studies, this was the only one that examined the effectiveness of strength training on fascicle length. Strength training at slow speeds did not have much effect on the change in length of the fascicle length. It has been observed that children with spastic cerebral palsy exhibit abnormal lengthening of the gastrocnemius muscle during standing. These persistent lengthening of the gastrocnemius may lead to permanent muscle damage, which can affect gait posture [24].

According to the study of Stackhouse et al., there was a significant change in CSA of the quadriceps, but little effect on the PF. There was also a large increase in knee extensor strength. This may be due to the sample size of only five individuals and the fact that the intervention was only a maximal voluntary isometric contraction. NMES is widely used in rehabilitation to restore muscle mass and function in patients. It has been shown that brief low voltage transcutaneous stimulation will reduce quadriceps atrophy secondary to knee immobilisation and prevent a decline in muscle protein synthesis [25].

Factors such as range of motion, speed of movement and contraction pattern may all have an effect in terms of muscle adaptation after training. It has been suggested that lack of exercise in patients with neuromuscular disease leads to poorer physical condition, and poorer physical condition can be a vicious cycle that hinders motor function [26]. Chronic pain is a significant problem in adolescents with neuromuscular disease, and pain can also hinder motor performance. Studies have shown that individualised progressive resistance training can increase a patient's strength, but the increased strength does not result in an objective improvement in mobility [15].

4.3. Limitations

The frequency, intensity and load of the interventions varied across the four included studies and there is a relative lack of description in the literature to compare the correlations between studies. Differences in measurement methods within the studies also produced differences in findings and there was also a lack of elaboration on the reliability of the results. The different interventions and complementary therapies make it difficult to draw valid conclusions from the only four studies.

The lack of intensity and duration of strength interventions in the study and the small sample size are also limitations of this paper. Different muscle groups may produce different muscle adaptations after sustained prolonged strength training, or produce different rates of muscle growth due to age and gender.

The inclusion of participants belonging to different types of CP, as well as the large range of GMFCS levels spanned between levels I-III. The results were also biased by the different levels of motor ability, cognition, coordination and movement completion in children with CP at each level, which ultimately also produced different effects on strength training.

4.4. Future Research

Due to the diversity of CP types and the adaptations of different muscles at different ages, genders, and intervention sessions, the inclusion of participants and interventions should be kept relatively consistent in future studies to assess changes in muscle morphology and strength in children and adolescents with CP from strength training. The natural increase in muscle volume and strength over time in children and adolescents during their formative years should also be taken into account. As the field of medical advances, future studies should incorporate the use of equipment instruments to measure more neuromuscular properties. A full understanding of the different effects and impact of strength training interventions on different parts of the muscles of CP patients should be studied.

5. Conclusion

This systematic review presents the preliminary evidence of the effects of strength training on lower limb muscle volume, strength and function in children and adolescents with CP, suggesting positive effects on skeletal muscle strength and morphology following resistance training. In addition, limitations arise because of the limited sample size and variability in intervention design.

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