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Research Article

Differential Effect of Progressive Resistance Training on Bone and Muscular Strength in Adults with Cerebral Palsy

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Abstract

Objective: To determine the effect of resistance training on Bone Mineral Density (BMD), and how it will affect musculoskeletal strength and postural stability in adults with Cerebral Palsy (CP) who have already progressed into muscle atrophy and osteoporosis.

Methods: Two independent group comparisons of CP and control, and two dependent group comparisons of CP before and after 3 months of progressive resistance training. Fourteen adults with CP with gender (10 women: 4 men), age (21-62 years), and Gross Motor Function Classification System (GMFCS) I-III, and fourteen gender-, age-, body weight- matched control subjects completed our study. BMD, structural/geometrical deformities (at the proximal region of the femur at the hip joint), maximal muscular strength (forearm and leg), postural stability, and body composition were measured.

Results: Adults with CP had skeletal deformities at the proximal femur, which was not altered after resistance training. Femoral BMD was significantly lower in adults with CP and improved significantly after 3 months of resistance training. BMD was not correlated with muscular strength in adults with CP before training; however, the initial level of BMD appeared to selectively influence muscular strength in adults with CP after training. Lean adults with CP improved muscular strength while overweight/obese adults with CP did not gain lower extremity strength after training.

Conclusion: 3 months of short-term resistance training increased femoral BMD significantly without structural alterations. Initial levels of BMD and overweight/obese state appear to influence the exercise training effect in adults with CP who have already developed muscle atrophy and osteoporosis.

Keywords: Balance; Bone mineral density; Femur geometry; Neurological disorder; Strength training

Abbreviations: CP: Cerebral Palsy; BMD: Bone Mineral Density; BMC: Bone Mineral Content; BMI: Body Mass Index; DXA: Dual Energy X-Ray Absorptiometry; GT: Greater Trochanter; LT: Lesser Trochanter

Introduction

Cerebral Palsy (CP) is a neurological disorder caused by lesions in the brain during fetal development or shortly after birth, and is characterized by impaired motor function, musculoskeletal deformity, and atrophy [1-4]. Although CP is a permanent and non-progressive neurological impairment, CP is associated with progressive clinical complications during development from child- to adulthood [3,4]. Individuals with CP experience a higher prevalence of cardiometabolic risk factors (e.g, obesity) and chronic diseases compared to the general population [5-7]. Acceleration of health risks is not a direct consequence of the neurological disorder but is linked to physical deconditioning from motor impairment experienced by individuals with CP [5,7]. Exercise is an essential component in the management of muscle weakness, obesity, and many chronic diseases in the general population [8,9]. Reduced physical activity may be associated with cardiometabolic risk factors and other secondary conditions in the CP population [10-12].

Motor impairments contribute to muscle weakness in individuals with CP, which are also impacted by atypical architectural growth in skeletal muscle fibers [13-15]. Muscle weakness begins in childhood; the musculoskeletal development of CP children will be slower than typically developing peers [3,4,11]. Due to physical deconditioning, accelerated muscle atrophy may lead to higher incidence of falls with compromised balance and functional mobility in the CP population [13,14,16,17]. Research to date is equivocal as to whether resistance training has a positive effect on musculoskeletal function in the CP population [18-21]. Also, there is public misbelief that resistance training may worsen the spasticity in individuals with CP. It is uncertain whether the muscular function and functional mobility is improved from resistance training in adults with CP who have already developed atrophy.

Individuals with CP develop osteoporosis at an earlier age compared to the general population which has adverse effects on the muscular system and results in an increased likelihood of fractures [6,22]. Resistance training improves Bone Mineral Density (BMD) as well as reduce fall and fracture risks [23,24]. Optimizing bone health and achieving adequate BMD are critical in preventing fractures as well as improving the quality of life and well-being [25,26]. However, it is still uncertain whether resistance training alters BMD in adults CP who have already developed osteoporosis. Previously our laboratory reported that the degree of skeletal deformities is more important than the severity of BMD in the lower extremities in adults with CP in relation to muscular strength and postural stability [27]. Exercise training may not improve musculoskeletal deformities; equivocal results were reported on whether resistance training affects improving muscular function in CP [18-22]. Therefore, the purpose of this study was to investigate the effect of resistance training on BMD, and how it would affect musculoskeletal strength and postural stability in adults with CP who have already progressed into muscle atrophy and osteoporosis. We hypothesized that 1) skeletal deformities specific to the proximal femur will not be improved from resistance training, 2) resistance training will increase BMD and muscular strength, 3) BMD and muscular strength in lower extremities will correlate with postural stability in adults with CP after resistance training.

Methods

Subjects

A total of 28 participants (14 adults diagnosed with CP and 14 gender-, age-matched controls) were recruited through CP centers in San José and the Greater Bay Area. Adults with CP participated in a three-month resistance training program. Individuals with CP who were within the classification levels I-III of the Gross Motor Function Classification System were included in the study to ensure that subjects could perform resistance training regimen. All experimental procedures and protocols, informed consent and medical health history forms were approved by the San José State University IRB.

Exercise Intervention

The intervention included three months of progressive resistance training following a general recommendation from American College of Sports Medicine Guidelines (ACSM) [28]. The intervention included 2 to 3 times per week with 1.5 hours per session with 10 minutes of warm-up and cool-down period. Additional stretching exercises were included if CP participants experienced greater spasticity prior to joining the exercise session to prevent any potential muscle injuries. All exercise regimens were individualized and designed with a variety of exercises to strengthen muscles in the upper and lower extremities, core, and whole-body (e.g, bicep curls, grip squeeze, hamstring curls, leg extensions, push-ups, squats, etc.). Each exercise was performed between 2 to 3 sets for 10 to 15 repetitions. The workload (i.e, intensity and numbers of repetitions) was increased or adjusted over time as the participants progressed over the course of 3 months after a thorough bi-weekly evaluation. This exercise intervention plan was registered and approved in ClinicalTrials.gov (NCT05070117).

Experimental Measurements/Procedures

All measurements were taken the same way during pre-visit (CPpre, before exercise training) and post-visit (CPpost, 3-months after exercise training) in adults with CP, and one visit for the controls. Anthropometric measurements (i.e, weight, height, waist, and hip circumferences) were obtained. Whole-body Dual Energy X-Ray Absorptiometry (DXA) was used to measure the bone, muscle, and fat mass. Regional DXA scans at the femoral neck and total area of the proximal femur were performed to measure Bone Mineral Content (BMC) and BMD. All DXA scans were performed by the same, trained DXA technologist who is certified by the State of California. Handgrip dynamometer was used to perform maximal forearm strength. Muscular strength in hamstrings and quadriceps (as a form of peak torque, work, and power) were performed during a full range of knee extension and flexion using a Humac Norm Isokinetic Dynamometer system. Participants performed two sets of three repetitions of full range of knee extension/flexion at three different velocities (90, 150, and 210 degree/seconds). Postural stability and balance were assessed using a Biodex Balance System© and a Berg Balance test. A modified protocol using the limits of stability test from the

Biodex Balance System was performed as previously described [17]. BMD analysis on DXA software were performed using a customized function to identify structural features of proximal femur. Skeletal deformities at the proximal femur were identified by geometrically measuring angles, lengths and diameters of the femoral neck and head, and shaft as previously described [17].

Statistical Analysis

All data are presented as means±standard error of estimate. Comparisons among the control group and CP group before and after exercise training on main variables were made using Analysis of variance (ANOVA). Pearson correlations were calculated to indicate the relationship of leg muscular strength, BMD, and regional fat (%). Statistical analyses were conducted using IBM SPSS Statistics V.24. Statistical significance was set at $p<0.05$.

Results

Anthropometric Differences

Control and CP groups had similar characteristics except for height. Even though waist and hip circumference measures were not significantly different between groups, the waist-to-hip ratio was greater in the CP group than in the control (Table 1). All CP participants had spastic CP. Two participants had mixed types with spastic and dyskinetic CP. No anthropometric changes were observed after 3 months of exercise training.

	Control	CPpre	CPpost
Age (years)	35.5 ± 4.1	38.4 ± 4.1	38.4 ± 4.2
Sex (men/women)	(5/9)	(5/9)	(5/9)
Weight (kg)	66.9 ± 3.4	65.9 ± 5.2	64.1 ± 6.2
Height (cm)	168.1 ± 2.4	157.4 ± 2.8 *	157.1 ± 3.0 *
BMI (kg/m^2)	23.5 ± 0.9	26.8 ± 2.4	26.4 ± 2.8
Waist (cm)	78.6 ± 2.4	88.9 ± 4.9	86.7 ± 5.0
Hip (cm)	95.6 ± 1.7	96.0 ± 4.4	95.9 ± 4.2
W-H ratio	0.82 ± 0.1	0.88 ± 0.1 *	0.90 ± 0.1 *
Whole Body Fat (%)	27.2 ± 2.1	35.4 ± 3.0 *	32.3 ± 3.6
Whole Lean Mass (%)	69.0 ± 2.0	61.9 ± 2.8 *	65.1 ± 3.3
Whole Bone Content (%)	4.1 ± 0.1	3.6 ± 0.2 *	3.7 ± 0.3
Types (spastic/mixed)	-	(12/2)	(12/2)
GMFCS level (I/II/III)	-	(2/7/5)	(2/7/5)
Unilateral/Bilateral	-	(2/12)	(2/12)
Use of Botulinum toxin	-	1	1

Values are Mean ± SEM. *represents P < 0.05 vs Control. CPpre; Cerebral Palsy before training, CPpost; Cerebral Palsy after training, BMI; body mass index, Waist; waist circumference, Hip; hip circumference, GMFCS; gross motor function classification system

Table 1: Subject characteristics.

Impact of Resistance Training

The CP group had significantly smaller geometrical features than the control group. There were no changes in skeletal geometries after 3-month resistance training in the CP group (Table 2). BMD at the femur was significantly lower in the CPpre than in the control group; however, it improved dramatically after exercise training in the CP group (Table 2 and Figure 1). There were no longer significant differences detected in the CP group compared to controls after exercise training (Table 2, Figure 1A). Following the World Health Organization criteria for defining osteoporosis (BMD that lies 2.5 standard deviations or more below the average value for young healthy individuals), ten out of fourteen CP participants had osteoporosis before they started the resistance training. T-scores for eight of these CP participants dramatically improved after training; thus, they were no longer osteoporotic.

	CPpre				CPpost			
Bone strength	**BMC (g)**	**BMD (g/cm²)**	**T-score**	**Z-score**	**BMC (g)**	**BMD (g/cm²)**	**T-score**	**Z-score**
Left Femur								
neck	3.71 ± 0.5	0.75 ± 0.07	–2.13 ± 0.5	–2.05 ± 0.5	4.14 ± 0.36*	0.87 ± 0.04*	–1.34 ± 0.23*	–1.33 ± 0.22*
total	22.49 ± 2.2	0.78 ± 0.06	–2.11 ± 0.4	–2.14 ± 0.5	29.39 ± 2.13*	0.91 ± 0.04*	–0.98 ± 0.32*	–1.08 ± 0.29*
Bone Geometry	**Proximal GT (degree)**	**Distal GT (degree)**	**Proximal LT (degree)**	**Shaft (cm)**	**Proximal GT (degree)**	**Distal GT (degree)**	**Proximal LT (degree)**	**Shaft (cm)**
	69.0 ± 1.1	16.6 ± 1.3	59.8 ± 2.0	2.2 ± 0.1	69.2 ± 1.1	13.1 ± 2.1	64.2 ± 2.4	2.3 ± 0.1
	Head length (cm)	**Head diameter (cm)**	**Neck length (cm)**	**Neck diameter (cm)**	**Head length (cm)**	**Head diameter (cm)**	**Neck length (cm)**	**Neck diameter (cm)**
	3.2 ± 0.1	4.1 ± 0.1	1.4 ± 0.1	3.2 ± 0.1	3.1 ± 0.1	4.3 ± 0.1	1.3 ± 0.1	3.2 ± 0.1
Values are Mean ± SEM. * represents P < 0.05 vs CPpre. CPpre; Cerebral Palsy Before Training, Cppost; Cerebral Palsy after Training, BMC; Bone Mineral Content, BMD; Bone Mineral Density, GT; Greater Trochanter, LT; Lesser Trochanter								

Table 2: Characteristics of skeletal strength and structure of the proximal femur at the hip joint in CP adults before and after resistance training.

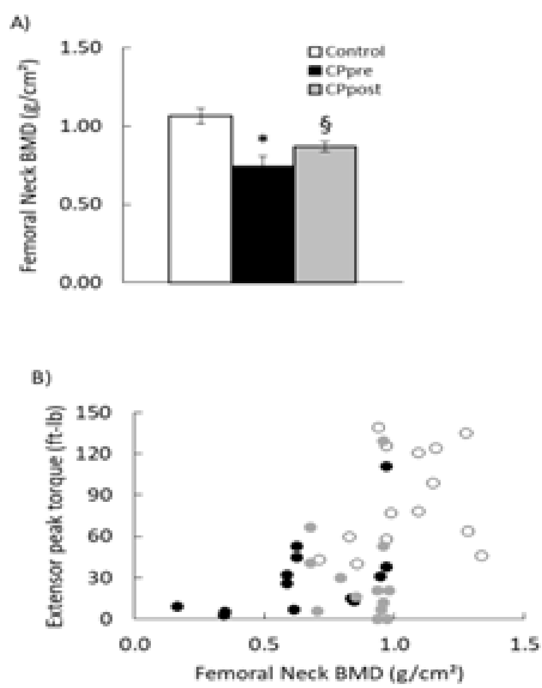

Figure 1: Summary of data showing the group differences in Bone Mineral Density (BMD) on the femoral neck of the proximal femur (panel A) and the relationship between femoral neck BMD and peak torque at 90 degrees/sec during knee extension in control and CP groups before (CPpre) and after (CPpost) 3-month of resistance training (panel B). * represents P<0.05 vs. control. § represents P<0.05 vs. CPpre. CP; cerebral palsy.

The CPpre demonstrated significant weakness across all measures of muscular strength for both the forearm and the knee extensors/flexors at 90, 150, and 210 degrees/sec compared to controls (Supplement Table 1). After exercise training, no significant improvements were observed. Postural stability was significantly lower in all directions of stabilization and time to complete the test in the CPpre compared to the control. There were no significant improvements in postural stability after 3-month resistance training in the CP group (Supplement Table 2). Berg Balance Score was significantly lower in the CP group compared to the control; this score was improved in the CP group after exercise training.

	CPpre			**CPpost**		
Handgrip strength (kg)	15.1 ± 3.8			19.7 ± 3.8		
Leg strength	**Peak torque (ft-lb)**	**Work (ft-lb)**	**Power (W)**	**Peak torque (ft-lb)**	**Work (ft-lb)**	**Power (W)**
Knee extension						
90˚/sec	28.1 ± 7.7	23.2 ± 8.5	35.9 ± 12.5	35.8 ± 10.1	29.1 ± 10.9	39.8 ± 13.7
150˚/sec	20.4 ± 5.9 ƚ	16.7 ± 6.8 ƚ	34.3 ± 14.8 ƚ	24.8 ± 7.9 ƚ	19.4 ± 8.4 ƚ	38.0 ± 15.8
210˚/sec	15.2 ± 4.7ƚ	11.6 ± 5.3 ƚ	27.0 ± 11.8 ƚ	19.3 ± 5.6 ƚ	13.5 ± 5.7 ƚ	31.6 ± 12.5 ƚ
Knee flexion						
90˚/sec	13.2 ±3.8	11.7 ± 4.9	18.0 ± 8.4	15.9 ± 5.9	14.4 ± 7.1	19.3 ± 9.1
150˚/sec	11.2 ± 3.4	9.3 ± 4.3	18.3 ± 9.0	12.1 ± 4.1	9.2 ± 4.9	16.6 ± 9.5
210˚/sec	9.8 ± 2.9 ƚ	7.4 ± 3.5 ƚ	16.5 ± 8.1 ƚ	10.5 ± 3.1 ƚ	7.0 ± 3.4 ƚ	16.8 ± 8.9
Values are Mean ± SEM. ƚ represents P < 0.05 vs. 90 degree/sec. CPpre; Cerebral Palsy before training, CPpost; Cerebral Palsy after training						

Supplement Table 1. Summary of muscular strength of forearm during isometric maximal handgrip contraction and of legs during knee extension and flexion in CP adults before and after 3-months of resistance training.

	CPpre	**CPpost**
Forward	42.7 ± 6.5	42.1 ± 7.1
Forward goal (%)	65.3 ± 9.2	64.1 ± 10.9
Backward	40.0 ± 8.5	40.9 ± 8.4
Backward goal (%)	120.2 ± 28.6	136.1 ± 28.1
Left	32.8 ± 6.5	36.4 ± 7.2
Left goal (%)	50.8 ± 9.1	55.7 ± 11.0
Right	38.1 ± 6.6	39.6 ± 6.9
Right goal (%)	58.1 ± 8.9	61.8 ± 10.3
Overall score	28.6 ± 5.6	30.3 ± 5.3
Overall goal (%)	45.7 ± 7.8	46.4 ± 8.1
Time to complete (sec)	80.7 ± 16.3	62.2 ± 10.6
Values are mean ± SEM. CPpre; Cerebral Palsy before training, CPpost; Cerebral Palsy after training, Forward; forward lean, Backward; backward lean, Left; left lean, Right; right lean		

Supplement Table 2: Summary of postural stability for directional movement during limit of stability test in adults with CP before and after 3-month of resistance training.

Responders vs. Non-responders on BMD

We divided CP participants into two sub-groups by selecting individuals who exhibited a significant improvement on BMD at the femoral neck (responders, Figure 2A) and those who did not improve (non-responders, Figure 2D). Interestingly, muscular strength was not improved by resistance training in the responder group even though their postural stability was slightly improved only with time to complete the test (Figure B and C). The non-responder group exhibited the opposite effect. Without any changes in BMD with resistance training, they gained muscular strength; this did not seem to affect overall postural stability (Figure D-F).

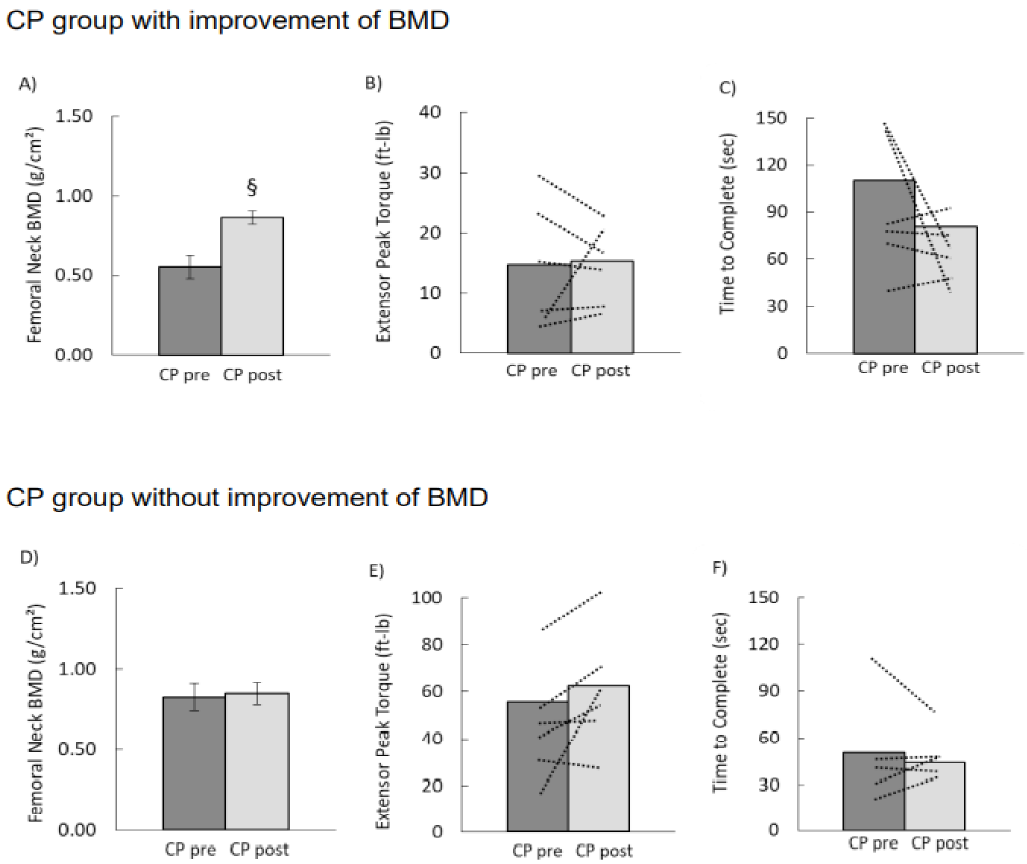

Figure 2: Summary and individual data showing BMD at femoral neck, peak torque at 90 degrees/sec during knee extension and postural stability (time to complete, sec) of two subgroups of CP participants with a significant improvement in BMD (panel A-C) and without improvement in BMD (panel D-F) after 3-month of resistance training. § represents $P<0.05$ vs. CPpre. CP; Cerebral Palsy, BMD; Bone Mineral Density.

Responders vs. Non-responders on BMI

Figures 3A and 3B show the overall body fat and the relationship between regional leg fat and extensor peak torque in all groups. Compared to the control, CPpre had a significantly higher leg fat percentage (Figure 3A). After resistance training, this statistical effect was minimized with a slight reduction of leg fat in CP. Due to the linear inverse relationship that was observed between total leg fat and muscular strength (Figure 3B), we attempted to explore whether overall body fat may affect the training effect in CP participants. We identified two sub-groups in CP participants by selecting individuals based on their initial health status with BMI (lean, BMI<25kg/m² and overweight/obese, BMI≥25kg/m²). Figures 4A and B showed that those who were lean had mild but consistent improvement on both muscular strength and postural balance. However, the sub CPpost group who were overweight and obese did not show any improvement in muscular strength or postural stability (Figure 4C-4D).

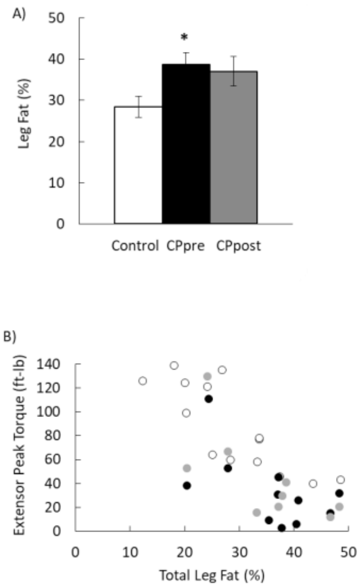

Figure 3: Summary of data showing the group differences in regional leg fat (%, panel A) and the relationship between regional leg fat and peak torque at 90 degrees/sec during knee extension in control and CP groups before (CPpre) and after (CPpost) 3-month of resistance training (panel B). * represents P<0.05 vs. control. CP; cerebral palsy.

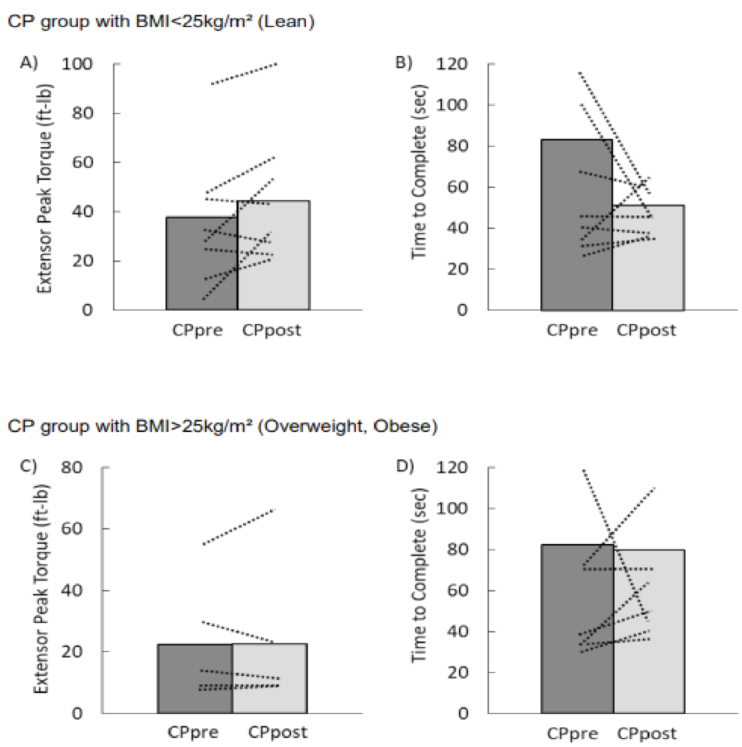

Figure 4: Summary and individual data showing peak torque at 90 degrees/sec during knee extension and postural stability (time to complete, sec) of two subgroups of CP participants who were a lean and normal (BMI <25kg/m², panel A, B) and with overweight and obese (BMI >25kg/m², panel D-F) after 3-month of resistance training. CP; cerebral palsy, BMI; body mass index.

Discussion

The purpose of this study was to investigate the effect of resistance training on BMD, and how it would affect musculoskeletal strength and postural stability in adults with CP who have already progressed into muscle atrophy and osteoporosis. The resistance training did not impact structural alterations at the proximal femur of CP participants although BMD showed significant improvement. Highlights of our main findings are as follows: (1) adults with CP had skeletal deformities at the proximal femur, which was not altered after resistance training; (2) femoral BMD was significantly lower in adults with CP, and improved significantly after 3 months of resistance training; (3) BMD was not correlated with muscular strength in adults with CP before training; however, the initial level of BMD appeared to selectively influence muscular strength in adults with CP after training; (4) lean adults with CP improved muscular strength while overweight/obese adults with CP did not gain lower extremity strength after training. We found that the structural deformities at the proximal femur in adults with CP were not altered even though BMD increased significantly from short-term resistance training. This finding may reflect differences between adults and children or adolescents. Previous studies suggested that the skeletal muscle morphology and architecture (e.g, muscle size, cross-sectional area, fascicle length, etc.) were improved after progressive resistance training in children and adolescents with CP [28]. However, at a microscopic level, skeletal muscle in individuals with CP has altered protein transcription processes and sarcomere length [29]. It is also evident that altered muscle architecture and size in CP have similar patterns observed with disuse and aging in the general population [30]. Children and adolescents with CP may benefit from resistance training more than the adult population.

One of the most notable findings was the improvement of BMD after resistance training in osteoporotic adults with CP. Ten out of fourteen CP participants had osteoporosis before they started the resistance training. T-scores for eight of these CP participants dramatically improved after training; thus, they were no longer osteoporotic. However, we identified two separate groups within our participants after training, those who improved BMD significantly and those who did not (responders vs. non-responders). Even though resistance training impacted on BMD, it did not directly improve muscular strength and functional mobility. Rather, those CP participants who started with very low BMD were the ones who showed a strong improvement on BMD after resistance training; they did not improve muscular strength or postural balance at all. Meanwhile, those who started with relatively high BMD had small or no increases in BMD after training but were likely to demonstrate improvement in muscular strength and postural balance. This observation is important because adults with CP may require an initial health status assessment (e.g, higher baseline BMD) and a certain length of training period to see a training effect on the musculoskeletal system. The effectiveness of progressive resistance training is confirmed by many studies in the elderly suggesting an increase in site-specific improvements in bone density, most notably at the neck of the femur, which was maintained in the short to medium term [23,31,32]. We observed the short-term training effect on adults with CP only for BMD without any dramatic alterations in bone structure, muscular strength, and/or postural stability. Our study suggests a potential for a long-term effect of exercise training on physical mobility in the CP population who are at high risk of falls and fractures.

Previously, our laboratory suggested that postural stability and functional mobility among adults with CP were due to greater leg muscular strength, while healthy adults showed similar stability measures that were independent of leg strength [17]. We believed that our data supported the promise for further improvement of functional mobility in adults with CP. Our results suggest that positive effects from exercise training may be highly dependent on an individual's other initial health status (e.g, the severity of musculoskeletal contractures, level of musculoskeletal strength, etc.). This could be the reason why previous studies have reported equivocal results of resistance training on gaining muscular strength and functional mobility in the CP population. We believe that resistance training for CP participants may have a selective effect on improving muscular strength; it may depend on the initial status of body composition. Lean CP adults ($BMI<25kg/m^2$) showed noticeable increases in leg muscular strength with training: overweight CP adults ($BMI\geq25kg/m^2$) did not improve muscular strength after training. A resistance training regimen alone will not have an impact on weight loss. None of our CP participants lost weight after training even though body composition was altered with decreased body fat and higher lean muscle mass and bone content. Our data also showed that there was a weak inverse relationship between leg muscular strength and leg fat in CP groups with and without resistance training. A combination of aerobic exercise training with resistance training may improve body composition by reducing fat and increasing muscular strength, which may improve functional capacity in adults with CP more effectively.

Study Limitations

Findings should be interpreted in the context of study limitations. We had a small sample size of fourteen subjects in the CP group. The adequacy of the sample size of the study depends on the magnitude of the expected effect size when comparing characteristics between and within two or more groups of subjects [33]. Because our study showed very significant group differences in the main outcomes, we felt confident in reporting our results despite our small sample. However, future studies with a larger sample size may reveal additional insights about correlations between individual variables in the current study. It is possible that some of our findings were driven by other factors. Our exercise plans were individualized and differed among participants. We included and/or excluded certain exercises if participants could not perform with correct movement patterns and/or biomechanics. Our exercise plan consisted of various exercise types that targeted gross muscle groups, which may have influenced varying results between participants. Some of the exercises were focused on improving knee flexors and extensors selectively (or hip flexors and extensors). Our participants consistently improved muscular strength in knee extensors more than in knee flexors. This could be due to the individualized exercises performed in our CP participants. For future studies involving resistance training plans, it will be worth including one on one assistance with physical therapists or personal trainers to make sure both extensors and flexors are included in the individualized program.

Different types of CP (spastic, dyskinetic, ataxic) may affect the effectiveness of exercise training or the progression of the outcome. Most of our participants had spasticity of varying degrees of pain at the beginning of the participation. The relationships between muscle weakness and spasticity have been widely debated by clinicians and researchers for decades with some claiming that no relationships exist. However, clinical practices in individuals with CP have focused on the management of spasticity to reduce muscle tightness and pain. While we extended our warm-up period if our CP participants described additional spasticity on the day of exercise training, we did not record or control the degrees of pain from spasticity throughout the intervention. Thus, we cannot conclude if our resistance training regimen had a positive effect on spasticity by reducing pain. Further studies with a larger population with different types of CP are required to extend our findings and to investigate the true effects of exercise in adults with CP.

Conclusion

Three months of progressive resistance training did not impact structural alterations at the proximal femur of CP participants although femoral BMD showed significant improvement. BMD was not correlated with muscular strength in adults with CP before training; however, the initial level of BMD appeared to selectively influence muscular strength in adults with CP after resistance training. Meanwhile, lean adults with CP improved muscular strength while overweight/obese adults with CP did not gain muscular strength after training. Thus, we conclude that resistance training appears to have a differential effect on altering physiological and physical functioning in CP adults who have already developed muscle atrophy and osteoporosis.

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