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Comparative Effects of Strengthening Exercise Modalities on Biochemical and Functional Outcomes in Duchenne Muscular Dystrophy

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ABSTRACT: **Background:** Duchenne muscular dystrophy (DMD) is a progressive neuromuscular disorder characterized by declining muscle function and impaired physical performance. Exercise prescription in children with DMD requires careful consideration of the type and intensity of muscle loading. However, evidence regarding the comparative effects of different modes of strengthening exercise on metabolic and functional outcomes remains limited.

Objective: To compare the effects of concentric, isometric, and eccentric strengthening exercises on lipid profile, gait performance, and handgrip power in ambulatory children with DMD aged 6–10 years.

Methods: Eighty-three children with DMD were assessed for eligibility, of whom 23 were excluded according to the predefined eligibility criteria. Sixty children were randomly allocated equally to three intervention groups (n=20 each): concentric strengthening, isometric strengthening, and eccentric strengthening. The intervention was conducted for 3 months, three sessions per week, with each session lasting 40 minutes. The targeted muscles included the hip flexors and extensors, knee flexors and extensors, ankle dorsiflexors, wrist extensors, and finger flexors. Serum creatine kinase (CK), total cholesterol, triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were assessed as biochemical outcomes. Functional outcomes included the 6-Minute Walk Test (6MWT) and maximal static power as a measure of handgrip power. Within-group changes were analyzed using the Wilcoxon signed-rank test, while

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differences in change scores among the three groups were assessed using the Friedman test.

Results: Significant pre-to-post changes were observed in the concentric group for CK (P=0.018), total cholesterol (P=0.009), TG (P=0.022), HDL (P=0.044), LDL (P=0.031), 6MWT (P=0.035), and muscle power (P=0.001). The isometric group demonstrated significant changes in CK (P=0.012), total cholesterol (P=0.023), HDL (P=0.043), LDL (P=0.025), 6MWT (P=0.001), and MSPOW (P=0.041), but not TG (P=0.146). The eccentric group demonstrated significant changes in TG (P=0.028), HDL (P=0.029), LDL (P=0.037), 6MWT (P=0.001), and muscle power (P=0.007), whereas changes in CK (P=0.754) and total cholesterol (P=0.099) were not significant. Friedman test analysis demonstrated significant differences among the three groups in change scores for CK (χ^2=6.721, P=0.010), total cholesterol (χ^2=13.091, P<0.001), TG (χ^2=11.756, P=0.001), HDL (χ^2=12.902, P<0.001), LDL (χ^2=5.818, P=0.016), 6MWT (χ^2=30.422, P<0.001), and muscle power (χ^2=21.564, P<0.001).

Conclusion: Three months of concentric, isometric, or eccentric strengthening exercise were associated with significant changes in several lipid profile parameters, walking performance, and handgrip power in ambulatory children with DMD. The magnitude of pre-to-post change differed significantly among the three exercise modalities across all assessed outcomes. Further pairwise analysis is required to determine which specific exercise modalities differ from one another.

1. INTRODUCTION

Duchenne muscular dystrophy (DMD) is an X-linked progressive muscle disease due to mutations within the dystrophin gene [1]. Up till now, there is no cure, while corticosteroids can slow disease's progression [2] [3]. Management should target the essential consequences of the disease, including increased oxidative stress [4], increased protein degradation [5], and reduced protein synthesis [6].

DMD prevalence is about 1/3500-6000 boys worldwide, leading to severe loss of muscular mass and function, and death occurring frequently at the end of the second decade due to cardiac or respiratory failure [7].

Every type of muscle contains the vital protein dystrophin. Its crucial function is to optimize muscle contraction by attaching the N-terminus of the protein to the extracellular matrix and the actin microfilaments to the C-terminal end of the protein [8]. The lack of dystrophin in DMD will eventually cause the muscle tissue to become more permeable, which will release the muscle proteins [9].

A lack of functional dystrophin due to gene mutations in DMD result in fragile sarcolemma causing damage of skeletal muscles after contraction, leading to intrinsic myofibril necrosis. Necrosis is closely associated with increased oxidative stress and inflammation [10].

DMD boys usually appear normal during infancy, while in early childhood they become unable to climb stairs or get up from floor or run with frequent falling down. They are presented with pseudo hypertrophy of calf muscles. At the age of 7 to 12 years old, the patients become more deteriorated with developing scoliosis [11], and joint stiffness [12]. Also, they will have an obvious reduction in bone-mineral density resulting in osteoporosis [13].

As part of energy homeostasis, the enzyme creatine kinase (CK) converts creatine and ATP into phosphocreatine and ADP. CK is present in serum at 20 to 200 U/L under normal conditions due to myocyte turnover, but it is somewhat elevated in certain neurological diseases. It can reach several thousand units/L in DMD patients due to substantial muscle degeneration, and in extreme situations, it can reach 200,000 U/L [14]. Because of gradual muscle atrophy in advanced stages of DMD, CK levels can occasionally be deceiving because they are represented in serum within normal ranges [15].

Serum creatine kinase (CK) measuring is an important test in the investigation of patients with muscle weakness, myalgia, or myopathies. Elevated CK levels sometimes are incidental findings in patients without muscle related symptoms or with only

few nonspecific muscle symptoms (eg, spasms, cramps, fatigue) that don't significantly affect functions of daily living. This condition is referred to as "asymptomatic hyper- CK-emia." [16].

Metabolites in the blood or urine and the lipid profile are also crucial indicators of the condition of the muscles; as such, they can be examined to show the degree of muscular dystrophy and are ideal candidates for diagnosis [17]

Patients with DMD must get multidisciplinary care that is prudent and constantly patient-centered. Occupational therapy and physiotherapy are frequently considered routine care. Since physiotherapy has shown positive short-term outcomes, such as preserving these people's autonomy, it is considered essential to the success of treatment [18]. Another technique for treating DMD is physical activity [19]. Exercise has been shown in studies to prolong functional independence and reduce bone fractures, muscle degeneration, and contractures in people with DMD [20].

METHODS:

Subjects: 60 boys with DD, with inclusion criteria aging from 6 to 10, confirmed diagnosis of Duchenne muscular dystrophy, established by genetic testing and/or muscle biopsy in accordance with accepted diagnostic criteria, with the ability to walk independently without a wheelchair for routine ambulation, able to walk continuously for the duration required to perform the 6-Minute Walk Test (6MWT), with rest permitted according to the standardized testing protocol, able to follow simple verbal instructions and cooperate with the exercise and assessment procedures are randomly distributed into three equal experimental groups (A, B and C). Measurements were completed for serum creatine kinase and lipid profile levels, functional tasks and activity of daily living (gait and power of hand grip). Each subject supplied written assent, and a parent provided written approval for each study participant. The Pharos University in Alexandria Research Ethics Committee authorized every component of this study (Approval No.: PUA030234303090).

Participants were excluded if they lost independent ambulation or unable to perform the study's gait assessments, have fixed deformity of the upper or lower limb joints, or underwent any corrective surgery for upper or lower limb joints within the last 6 months, presence of another neuromuscular, neurological, orthopedic, or cardiopulmonary disorder that could independently affect gait, muscle strength, exercise tolerance, or lipid profile, severe mental retardation (IQ not less than 50). The study was continued for three successive months for each child

Randomization: As shown in figure (1), a total of 83 children with DMD were assessed for eligibility. Following application of the predefined inclusion and exclusion criteria, 23 children were excluded, while 60 eligible participants were enrolled in the study. The 60 participants were randomly allocated in a 1:1:1 ratio to one of three intervention groups, with 20 participants assigned to each group: the concentric strengthening group, the isometric strengthening group, and the eccentric strengthening group.

To guaranty equal distribution among the three intervention groups, a computer-generated random allocation sequence with permuted blocks was used for randomization. An independent researcher who was not engaged in participant recruiting, intervention administration, or outcome evaluation created the randomization sequence.

The group allocations were placed in opaque, sealed envelopes with sequential numbers to guaranty allocation concealment. An impartial researcher opened the subsequent envelope once the baseline evaluation was finished, and the subject was placed in the appropriate intervention group.

Because the nature of the exercise interventions did not allow participant or treating therapist blinding, the outcome assessor was blinded to group allocation. Participants were instructed not to disclose their assigned intervention to the assessor during outcome assessments.

Assessment methods:

Biochemical assessment. Venous blood samples were collected from the participants after an appropriate fasting period according to the laboratory protocol. Serum creatine kinase (CK), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and total cholesterol (TC) were measured using standard automated biochemical laboratory methods. CK was assessed as a biochemical marker of muscle membrane damage, while the lipid profile (LDL-C, HDL-C, TG, and TC) was evaluated to characterize the participants' metabolic profile. All analyses were performed using standardized laboratory procedures and the results were recorded in the units reported by the laboratory.

Six-Minute Walk Test (6MWT): The 6MWT was used to assess functional exercise capacity and walking endurance. The test was performed along a flat, straight, hard-surfaced walkway measuring 30 m (100 ft), with the turning points clearly marked. Before the test, the child was instructed to rest quietly for approximately 10 minutes. Baseline heart rate and peripheral oxygen saturation (SpO_2) were recorded before commencing the test. The child was then positioned at the starting line and instructed to walk back and forth along the marked walkway for 6 minutes at a self-selected pace, with the aim of covering as much distance as possible. Standardized verbal encouragement was provided at regular intervals. The child was permitted to slow down, stop, or rest when necessary and to resume walking as soon as able. The examiner recorded the total number of completed laps and the additional distance covered during the final partial lap. The primary outcome was the total distance walked in meters (6-minute walk distance; 6MWD). Heart rate and SpO_2 were monitored throughout the test, and the test was discontinued if the child developed significant symptoms, excessive fatigue, or other clinically concerning signs.

Muscle strength: Isometric handgrip strength of the dominant hand was assessed using a calibrated hand-held dynamometer. Before testing, the procedure was explained to each child in simple, age-appropriate language, and one familiarization trial was performed to ensure that the child understood the required movement and could maintain the standardized testing position. The dominant hand was determined according to the hand preferentially used by the child for common unilateral activities, such as writing, drawing, or throwing. The child was positioned in a comfortable sitting position on a chair with the back supported, both feet resting flat on the floor, and the hips and knees flexed to approximately 90°. The shoulder of the tested upper limb was positioned comfortably alongside the trunk, with the shoulder in a neutral position. The elbow was flexed to approximately 90°, and the forearm and wrist were maintained in a neutral position. The dynamometer handle was adjusted to an appropriate grip size for the child's hand so that the fingers could comfortably grasp the handle without excessive finger flexion or extension. The dynamometer was held firmly by the examiner and positioned so that the line of resistance was aligned with the child's handgrip force. Before each measurement, the child was instructed to squeeze the dynamometer gradually and then exert their strongest comfortable grip while maintaining the standardized posture. Verbal encouragement was provided consistently across trials using standardized instructions. The child was instructed to avoid compensatory movements, including shoulder elevation, trunk leaning, elbow extension, or excessive wrist flexion or extension. The examiner monitored the child's posture and stabilized the tested limb as necessary without restricting the child's ability to generate handgrip force.

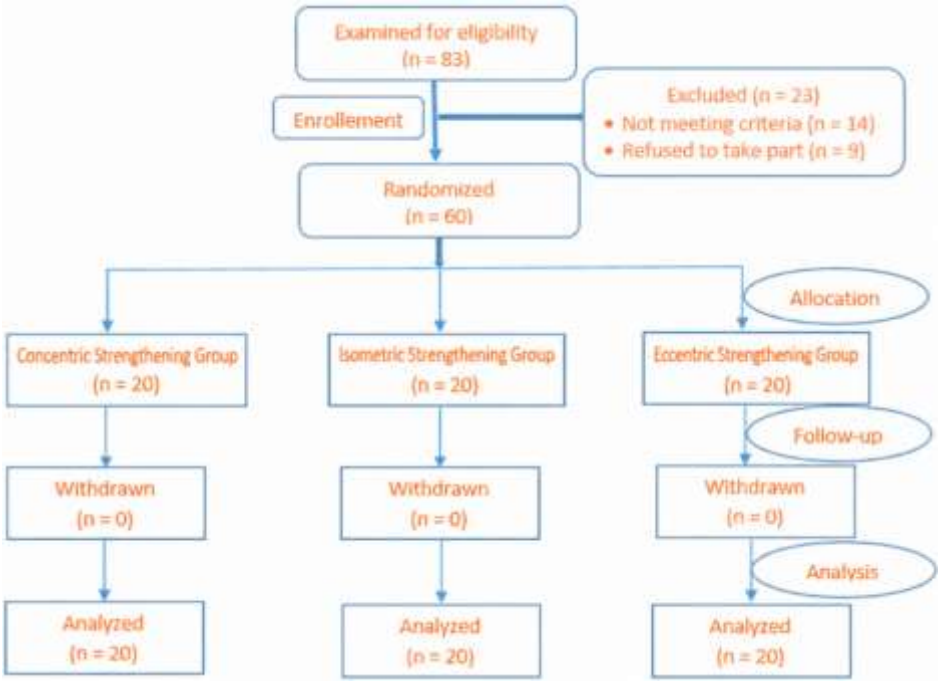


Fig. (1): Flowchart

Each child performed three isometric handgrip trials, with each contraction maintained for approximately 3–5 seconds, followed by an adequate rest interval of approximately 60 seconds between trials to minimize the effects of fatigue. Particular

care was taken to avoid repeated maximal efforts that could result in excessive muscle fatigue or overwork. Testing was discontinued if the child demonstrated pain, discomfort, cramping, marked fatigue, or inability to maintain the standardized position.

The peak force generated during each trial was recorded from the dynamometer. The highest value obtained from the three trials was used as the representative measure of dominant-hand isometric grip strength. Grip strength was recorded in Newtons (N). The same dynamometer, handle configuration, testing position, examiner, verbal instructions, and testing procedure were used for all participants to ensure consistency and improve the reliability of measurements.

Treatment methods:

A-Concentric strengthening exercises: involves the muscle producing tension and shortening to move a load

B-Isometric strengthening exercises: occur when a muscle produces tension without a change in muscle length. Isometric contractions involve sarcomere shortening and increasing muscle tension, but do not move a load

C-Eccentric strengthening exercises: occur when the muscle tension produced is less than the load and a muscle lengthens while under tension

Low-Intensity Exercise Protocol:

For three months in a row, the kids were trained three times a week on an inclination-free treadmill with speeds and durations according to their needs. Each training session lasted thirty minutes (21). Before the training program started, the kids were acclimated to the treadmill for seven days at a pace of four meters per minute in order to reduce the tension brought on by the unfamiliar surroundings.

The intervention targeted specific muscle groups in both the upper and lower limbs, including the wrist extensors and finger flexors in the upper limbs, and the ankle dorsiflexors, knee flexors and extensors, and hip flexors and extensors in the lower limbs.

Wrist extensors strengthening exercises:

The participant was seated beside a treatment table with the forearm supported in pronation, the elbow flexed to approximately 90°, and the wrist positioned beyond the table edge. The forearm was stabilized to minimize compensatory movements. For concentric strengthening, resistance was applied to the dorsal aspect of the hand toward wrist flexion while the participant actively extended the wrist. For isometric strengthening, the wrist was maintained in a neutral or slight extension position, and the participant exerted maximal effort against resistance without joint movement. For eccentric strengthening, the participant actively positioned the wrist in extension and slowly controlled its movement toward flexion against resistance.

Finger flexors strengthening exercises:

The participant was seated beside a treatment table with the forearm supported in a neutral or supinated position, the wrist in neutral, and the forearm stabilized to minimize compensatory movements. For concentric strengthening, resistance was applied to the palmar aspect of the fingers toward extension while the participant actively flexed the fingers through the available range. For isometric strengthening, the fingers were positioned in a comfortable degree of flexion, and the participant exerted force against resistance in the direction of extension without producing joint movement. For eccentric strengthening, the participant actively flexed the fingers against resistance and then slowly controlled their movement toward extension while maintaining muscle activation.

Ankle dorsiflexors strengthening exercises:

The participant was seated on a treatment table with the knee flexed to approximately 90°, the lower leg supported, and the foot positioned beyond the table edge for free ankle movement. The lower leg was stabilized to minimize compensatory movements. For concentric strengthening, resistance was applied to the dorsal surface of the foot toward plantarflexion while the participant actively dorsiflexed the ankle through the available range. For isometric strengthening, the ankle was positioned in neutral or slight plantarflexion, and the participant exerted force against resistance toward plantarflexion without producing

visible ankle movement. For eccentric strengthening, the participant actively dorsiflexed the ankle against resistance and then slowly controlled its movement toward plantarflexion while maintaining dorsiflexor activation.

Knee flexors strengthening exercises:

The participant was in a supported position while maintaining proper lower-limb alignment and minimizing compensatory movements. For concentric strengthening, the child was positioned prone with the pelvis stabilized and the knee initially extended. Light resistance was applied to the posterior aspect of the distal leg toward knee extension while the child actively flexed the knee through the available range. For isometric strengthening, the knee was positioned at approximately 30–45° of flexion, and the child attempted to flex the knee against stationary resistance toward extension without producing joint movement. For eccentric strengthening, the child actively flexed the knee against light resistance and then slowly controlled its movement toward extension while maintaining hamstring activation.

Knee extensors strengthening exercises:

The thigh was stabilized to minimize compensatory movements, and resistance was individualized according to the child's muscle strength and tolerance. For concentric strengthening, the child was seated with the hip flexed to approximately 90° and the knee at approximately 90° of flexion. Light resistance was applied to the anterior aspect of the distal leg toward knee flexion while the child actively extended the knee through the available range. For isometric strengthening, the knee was positioned at approximately 45–60° of flexion, and the child attempted to extend the knee against stationary resistance without producing joint movement. For eccentric strengthening, the child actively extended the knee against light resistance and then slowly controlled the movement toward flexion while maintaining quadriceps activation.

Hip flexors strengthening exercises:

The pelvis and trunk were stabilized to minimize compensatory movements, and resistance was individualized according to the child's muscle strength and tolerance. For concentric strengthening, the child was positioned supine with the hip and knee initially extended. Light resistance was applied to the anterior aspect of the distal thigh toward hip extension while the child actively flexed the hip through the available range. For isometric strengthening, the hip was positioned at approximately 30–45° of flexion, and the child attempted to further flex the hip against stationary resistance without producing joint movement. For eccentric strengthening, the child actively flexed the hip against light resistance and then slowly controlled the movement toward hip extension while maintaining hip-flexor activation.

Hip extensors strengthening exercises:

The pelvis and trunk were stabilized to minimize compensatory movements, and resistance was individualized according to the child's muscle strength and tolerance. For concentric strengthening, the child was positioned prone with the hips neutral and knees extended. Light resistance was applied to the posterior aspect of the distal thigh toward hip flexion while the child actively extended the hip through the available range. For isometric strengthening, the hip was positioned at approximately 10–15° of extension, and the child attempted to extend the hip against stationary resistance without producing joint movement. For eccentric strengthening, the child actively extended the hip against light resistance and then slowly controlled the movement toward hip flexion while maintaining hip-extensor activation.

Statistics:

Descriptive Statistics for Each Experimental Group: Descriptive statistics were used to summarize the baseline demographic and anthropometric characteristics of participants in the three experimental groups: the Concentric, Isometric, and Eccentric groups. The variables presented in this study were age, body weight, and height. Because the data are presented using the median together with the minimum and maximum values, the results are expressed as Median (Min–Max) rather than mean ± standard deviation.

The median represents the central value of each variable when the observations are arranged in ascending order. The minimum and maximum values indicate the observed range of the variable within each group and provide an indication of the variability of participants' characteristics.

Statistical Analysis between Pre- and Post-Intervention Within Each Group: The Wilcoxon Signed-Rank Test is a non-parametric statistical test used to determine whether there is a statistically significant difference between two related or paired

measurements obtained from the same participants. In the context of a pre–post intervention study, it is particularly appropriate for comparing measurements obtained before and after treatment within the same experimental group.

In this study, the test was used to evaluate whether each intervention produced a significant change in the measured outcomes by comparing the pre-treatment values with the corresponding post-treatment values for the same participants. Thus, the analysis was performed separately for each experimental group rather than comparing the groups with each other.

Statistical Analysis between Repeated Measurements in the Whole Sample: The Friedman Two-Way Analysis of Variance by Ranks is a non-parametric statistical test used to determine whether there are statistically significant differences among three or more related measurements obtained from the same participants. It is considered the non-parametric alternative to the one-way repeated-measures analysis of variance (repeated-measures ANOVA).

In the present study, the Friedman test was used to evaluate the overall change in the measured variables across repeated assessment points in the whole study sample, irrespective of the intervention group to which participants were assigned. This analysis was performed to determine whether the outcome measurements

RESULTS

Baseline Demographic and Anthropometric Characteristics

The baseline demographic and anthropometric characteristics of participants in the three experimental groups are presented in Table 1. Data are expressed as median and range (minimum–maximum). The median age was 7.5 years (6–10) in the concentric group, 8.0 years (6.5–10) in the isometric group, and 8.0 years (6–9) in the eccentric group. The median body weight was 28 kg (21–35), 29 kg (24–36), and 28 kg (24–33), respectively, while the median height was 122 cm (114–129), 123 cm (114–129), and 122 cm (112–127), respectively. Overall, the three groups showed similar baseline demographic and anthropometric characteristics.

Table 1. Baseline demographic and anthropometric characteristics of the study groups

Variable	Concentric, Median	Min	Max	Isometric, Median	Min	Max	Eccentric, Median	Min	Max
Age (years)	7.5	6	10	8	6.5	10	8	6	9
Weight (kg)	28	21	35	29	24	36	28	24	33
Height (cm)	122	114	129	123	114	129	122	112	127

Descriptive Statistics of Biochemical and Functional Outcomes by Group

The pre- and post-intervention descriptive statistics for the biochemical and functional outcome measures in the three experimental groups are presented in Table 2. Data are expressed as median and range (minimum–maximum).

In the concentric group, median CK decreased from 1990 (1600–2300) to 1890 (1560–2170), while total cholesterol decreased from 277 (240–300) to 275 (238–295) and TG from 200 (175–215) to 196 (172–211). HDL remained unchanged at a median of 46, although its range increased from 33–50 to 35–55. LDL decreased from 115 (90–135) to 112 (93–132). Functional outcomes also increased, with the median 6MWT distance increasing from 136 (92–154) to 140 (90–166) and MSPOW from 6.2 (4.2–7.2) to 6.9 (4.7–7.5).

In the isometric group, median CK decreased from 1950 (1700–2500) to 1910 (1660–2495), and total cholesterol decreased from 260 (230–300) to 255 (222–297). TG increased from 190 (180–220) to 194 (174–210), while HDL increased from 40 (30–50) to 43 (31–55). LDL increased from 102 (89–120) to 105 (90–117). The median 6MWT distance increased from 131 (108–142) to 138 (115–158), while MSPOW increased from 5.9 (4.3–7.4) to 6.1 (4.0–7.8).

In the eccentric group, median CK decreased from 2100 (1500–2260) to 2080 (1590–2350), total cholesterol decreased from 270 (250–310) to 266 (242–300), and TG decreased from 195 (165–215) to 193 (162–211). HDL increased from 40 (37–47) to 42 (37–52), whereas LDL decreased from 110 (89–120) to 108 (91–117). The median 6MWT distance increased from 137 (97–153) to 140 (101–157), and MSPOW increased from 6.5 (4.8–7.7) to 6.7 (5.0–7.8).

These descriptive findings indicate changes in several biochemical and functional outcomes after the intervention. Statistical significance of these pre- to post-intervention changes was assessed using within-group inferential analyses.

Table 2. Pre- and post-intervention descriptive statistics of biochemical and functional outcomes in the three experimental groups

Variable	Concentric Median	Min	Max	Isometric Median	Min	Max	Eccentric Median	Min	Max
Pre CK	1990	1600	2300	1950	1700	2500	2100	1500	2260
Post CK	1890	1560	2170	1910	1660	2495	2080	1590	2350
Pre Cholesterol	277	240	300	260	230	300	270	250	310
Post Cholesterol	275	238	295	255	222	297	266	242	300
Pre TG	200	175	215	190	180	220	195	165	215
Post TG	196	172	211	194	174	210	193	162	211
Pre HDL	46	33	50	40	30	50	40	37	47
Post HDL	46	35	55	43	31	55	42	37	52
Pre LDL	115	90	135	102	89	120	110	89	120
Post LDL	112	93	132	105	90	117	108	91	117
Pre 6MWT	136	92	154	131	108	142	137	97	153
Post 6MWT	140	90	166	138	115	158	140	101	157
Pre MSPOW	6.2	4.2	7.2	5.9	4.3	7.4	6.5	4.8	7.7
Post MSPOW	6.9	4.7	7.5	6.1	4.0	7.8	6.7	5.0	7.8

CK, creatine kinase; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; 6MWT, 6-minute walk test; MSPOW, muscle-specific power outcome.

Descriptive Statistics for the Whole Study Sample

The overall descriptive statistics for demographic, biochemical, and functional variables are presented in Table 3. Data are expressed as median and range (minimum–maximum). The median age of the whole sample was 8.0 years (6.0–10.0), with a median body weight of 28.0 kg (21.0–36.0) and median height of 123.0 cm (112.0–129.0).

For the biochemical outcomes, the median CK decreased from 2000.0 (1500.0–2500.0) before intervention to 1960.0 (1560.0–2495.0) after intervention. Median total cholesterol decreased from 270.0 (230.0–310.0) to 265.0 (222.0–300.0), while TG decreased from 195.0 (165.0–220.0) to 194.0 (162.0–211.0). In contrast, HDL increased from 40.0 (30.0–50.0) to 43.0 (31.0–55.0), whereas LDL decreased from 110.0 (89.0–135.0) to 108.0 (90.0–132.0).

Regarding functional outcomes, the median 6MWT distance increased from 133.0 (92.0–154.0) to 138.0 (90.0–166.0), and median MSPOW increased from 6.2 (4.2–7.7) to 6.5 (4.0–7.8). These values describe the overall direction of pre- to post-intervention changes across the complete study sample.

Table 3. Descriptive statistics of demographic, biochemical, and functional outcomes in the whole study sample

Variable	Median	Min	Max
Age (years)	8.0	6.0	10.0
Weight (kg)	28.0	21.0	36.0
Height (cm)	123.0	112.0	129.0
Pre CK	2000.0	1500.0	2500.0

Post CK	1960.0	1560.0	2495.0
Pre Cholesterol	270.0	230.0	310.0
Post Cholesterol	265.0	222.0	300.0
Pre TG	195.0	165.0	220.0
Post TG	194.0	162.0	211.0
Pre HDL	40.0	30.0	50.0
Post HDL	43.0	31.0	55.0
Pre LDL	110.0	89.0	135.0
Post LDL	108.0	90.0	132.0
Pre 6MWT	133.0	92.0	154.0
Post 6MWT	138.0	90.0	166.0
Pre MSPOW	6.2	4.2	7.7
Post MSPOW	6.5	4.0	7.8

CK, creatine kinase; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; 6MWT, 6-minute walk test; MSPOW, muscle-specific power outcome.

Within-Group Pre- to Post-Intervention Comparisons

Within-group changes in biochemical and functional outcomes were analyzed using the Wilcoxon signed-rank test. The results are presented in Table 4.

In the concentric group, statistically significant pre- to post-intervention differences were observed for CK ($p = 0.018$), total cholesterol ($p = 0.009$), TG ($p = 0.022$), HDL ($p = 0.044$), LDL ($p = 0.031$), 6MWT distance ($p = 0.035$), and MSPOW ($p = 0.001$).

In the isometric group, statistically significant differences were observed for CK ($p = 0.012$), total cholesterol ($p = 0.023$), HDL ($p = 0.043$), LDL ($p = 0.025$), 6MWT distance ($p = 0.001$), and MSPOW ($p = 0.041$). The change in TG was not statistically significant ($p = 0.146$).

In the eccentric group, statistically significant differences were observed for TG ($p = 0.028$), HDL ($p = 0.029$), LDL ($p = 0.037$), 6MWT distance ($p = 0.001$), and MSPOW ($p = 0.007$). Changes in CK ($p = 0.754$) and total cholesterol ($p = 0.099$) were not statistically significant.

Thus, statistically significant pre- to post-intervention changes were observed across all three groups for HDL, LDL, 6MWT distance, and MSPOW, whereas changes in CK, total cholesterol, and TG differed among the exercise modalities.

Table 4. Within-group comparison of pre- and post-intervention outcomes using the Wilcoxon signed rank test

Outcome	Concentric Z	p-value	Isometric Z	p-value	Eccentric Z	p-value
Post CK – Pre CK	−2.360	0.018	−2.520	0.012	−0.313	0.754
Post Cholesterol – Pre Cholesterol	−2.613	0.009	−2.280	0.023	−1.650	0.099
Post TG – Pre TG	−2.283	0.022	−1.452	0.146	−2.193	0.028
Post HDL – Pre HDL	−2.014	0.044	−2.022	0.043	−2.181	0.029
Post LDL – Pre LDL	−2.154	0.031	−2.243	0.025	−2.090	0.037
Post 6MWT – Pre 6MWT	−2.108	0.035	−3.419	0.001	−3.419	0.001
Post MSPOW – Pre MSPOW	−3.414	0.001	−2.046	0.041	−2.684	0.007

CK, creatine kinase; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; 6MWT, 6-minute walk test; MSPOW, muscle-specific power outcome.

Pre- to Post-Intervention Changes in the Whole Study Sample

Pre- and post-intervention measurements for the whole study sample were compared using the Friedman test. The statistical results are presented in Table 5.

Statistically significant differences were observed for all assessed variables: CK ($\chi^2 = 6.721$, $p = 0.010$), total cholesterol ($\chi^2 = 13.091$, $p < 0.001$), TG ($\chi^2 = 11.756$, $p = 0.001$), HDL ($\chi^2 = 12.902$, $p < 0.001$), LDL ($\chi^2 = 5.818$, $p = 0.016$), 6MWT distance ($\chi^2 = 30.422$, $p < 0.001$), and MSPOW ($\chi^2 = 21.564$, $p < 0.001$).

The direction of these changes corresponded to the descriptive findings presented in Table 3, with reductions in CK, total cholesterol, TG, and LDL and increases in HDL, 6MWT distance, and MSPOW from pre- to post-intervention measurements.

Table 5. Pre- to post-intervention comparison of biochemical and functional outcomes in the whole study sample

Outcome	Test statistic (χ^2)	p-value
Post CK – Pre CK	6.721	0.010
Post Cholesterol – Pre Cholesterol	13.091	<0.001
Post TG – Pre TG	11.756	0.001
Post HDL – Pre HDL	12.902	<0.001
Post LDL – Pre LDL	5.818	0.016
Post 6MWT – Pre 6MWT	30.422	<0.001
Post MSPOW – Pre MSPOW	21.564	<0.001

CK, creatine kinase; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; 6MWT, 6-minute walk test; MSPOW, muscle-specific power outcome.

All statistical analysis was done by IBM SPSS Statistics 27

DISCUSSION:

The present study investigated the comparative effects of concentric, isometric, and eccentric strengthening exercises on muscle integrity, biochemical markers, and functional performance in children with Duchenne muscular dystrophy (DMD).

The findings demonstrated that low-intensity exercise interventions produced significant functional improvements across all groups, accompanied by favorable biochemical adaptations. However, contraction mode influenced the magnitude and direction of these changes, with concentric and isometric exercises showing greater reductions in creatine kinase (CK) and more consistent metabolic improvements than eccentric exercise.

These findings provide important insight into the ongoing debate regarding the safety and efficacy of strengthening exercises in DMD. Historically, exercise in DMD has been controversial due to concerns about contraction-induced muscle damage (22). The present results support the emerging consensus that low-intensity, controlled strengthening exercises are not only safe but beneficial, particularly when avoiding excessive mechanical strain (23). This aligns with recent evidence suggesting that mild-to-moderate resistance or low-load training can improve strength and function without inducing muscle damage, as demonstrated in supervised isometric training programs showing no increase in CK or MRI-detected muscle injury (24). Similarly, a recent study showed that individualized low-resistance strengthening programs improved mobility, balance, and muscle strength in pediatric DMD without adverse effects, reinforcing the clinical relevance of the current findings (25).

A key observation in this study is the significant reduction in CK levels following concentric and isometric training, while eccentric training failed to produce similar changes. This can be interpreted through the pathophysiology of DMD, where dystrophin deficiency renders the sarcolemma highly susceptible to mechanical stress (26). Concentric and isometric contractions typically generate lower strain per muscle fiber compared to eccentric contractions, thereby reducing membrane disruption and leakage of intracellular enzymes such as CK. This interpretation is consistent with experimental and clinical

literature indicating that eccentric contractions impose higher mechanical stress and may exacerbate muscle damage in dystrophic muscle, even when performed at relatively low intensities. Conversely, isometric exercise has been reported as safe and feasible, with improvements in strength and function without signs of muscle injury (27).

However, the present findings partially contrast with some physiological studies suggesting that eccentric contractions may be metabolically efficient and produce less fatigue in healthy individuals, potentially allowing greater work output. This discrepancy highlights an important distinction: while eccentric exercise may be advantageous in healthy muscle, its application in dystrophic muscle is fundamentally different due to altered structural integrity, emphasizing the need for disease-specific exercise prescription (28).

Regarding lipid profile changes, the observed improvements (decreased cholesterol, triglycerides, LDL, and increased HDL) suggest that strengthening exercises may exert systemic metabolic benefits in children with DMD. These findings extend beyond muscle physiology and highlight the role of exercise in addressing secondary complications such as reduced physical activity and cardiometabolic risk (29). Previous literature supports the inclusion of low-intensity aerobic and resistance exercise to improve metabolic health and prevent deconditioning in DMD. Nevertheless, variability in triglyceride response—particularly the non-significant change in the isometric group—may reflect differences in energy expenditure and metabolic demand between contraction types. Isometric exercise, characterized by minimal movement and lower caloric expenditure, may produce less pronounced lipid metabolism adaptations compared to dynamic contractions (30).

Functionally, the significant improvements in the 6-minute walk test and handgrip strength across all groups reinforce the clinical value of structured exercise interventions. These findings are consistent with systematic reviews indicating that exercise training can enhance muscular strength and endurance in DMD, although the overall certainty of evidence remains low due to heterogeneity in study designs (31). Importantly, the fact that eccentric exercise improved functional outcomes despite limited biochemical benefits suggests that functional performance and muscle damage markers do not always change in parallel. This may reflect neuromuscular adaptations such as improved motor unit recruitment, coordination, and efficiency, rather than structural muscle changes alone (32).

At the same time, some studies report limited or inconsistent improvements in functional outcomes following exercise interventions in DMD, highlighting ongoing uncertainty in the field. These discrepancies may be attributed to differences in exercise intensity, duration, disease stage, and outcome measures (33, 34). The relatively short duration (8 weeks) in the current study may have been sufficient to detect functional gains but insufficient to observe long-term structural or disease-modifying effects (35).

LIMITATIONS

Several methodological limitations should be acknowledged. The relatively small sample size limits statistical power and the ability to detect subtle between-group differences. The absence of a non-exercise control group restricts causal inference regarding the effectiveness of the interventions. Additionally, the short intervention period does not allow assessment of long-term safety or disease progression. Variability in disease severity, corticosteroid use, and baseline functional status was not clearly controlled or stratified, which may have influenced responsiveness to exercise. Furthermore, reliance on CK as a primary biochemical marker may be insufficient, as CK levels can fluctuate with disease stage and may normalize in advanced stages despite ongoing muscle degeneration.

CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

From a pediatric physical therapy perspective, the findings support the preferential use of low-intensity concentric and isometric strengthening exercises as safe and effective modalities for improving function while minimizing muscle damage in children with DMD. Eccentric exercise, although beneficial for functional performance, should be applied cautiously and individualized based on disease stage and tolerance.

Future research should focus on large-scale randomized controlled trials with longer follow-up periods to establish optimal exercise prescriptions, including intensity, frequency, and contraction mode. Incorporating advanced outcome measures such as muscle MRI, inflammatory biomarkers, and patient-reported outcomes would provide a more comprehensive understanding of muscle adaptation. Additionally, exploring personalized rehabilitation approaches that integrate exercise with emerging

therapies (e.g., gene therapy, pharmacological treatments) may enhance overall disease management. Given the current variability in evidence, developing standardized clinical guidelines for exercise in DMD remains a critical priority.

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