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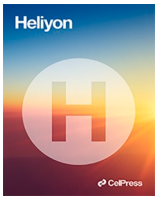

Research article

Efficacy of accommodating variable-resistance training on muscle architecture, peak torque, and functional performance in patients with juvenile idiopathic arthritis: A randomized controlled trial

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A R T I C L E I N F O

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A B S T R A C T

Purpose: This study sought to find out if a 6-week accommodating variable-resistance (AcVR) training might enhance muscle architecture, peak torque, and functional performance in patients with juvenile idiopathic arthritis (Juv-IA).

Methods: Fifty-eight patients with polyarticular Juv-IA (aged 12–18 years) were involved in a randomized controlled trial. They were allocated into two groups: the AcVR group (n = 29; underwent AcVR training, and the control group (n = 29; received the usual exercise regimen). Interventions were applied three times a week over six consecutive weeks. Measurements were done at baseline and after the intervention. The primary outcome measures were muscle architecture and peak torque, with functional capacity being the secondary measure.

Results: Compared to the control group, the AcVR group showed favorable pre-to-post changes in muscle architecture [fascicle length (P = 0.0007, η_p^2 = .18), pennation angle (P = 0.0004, η_p^2 = .20), and muscle thickness (P = 0.001, η_p^2 = .17)]. Further, the AcVR group revealed a greater increase in peak concentric torque of knee extensors at angular speeds of 120°/sec [right side (P = 0.0032, η_p^2 = .08); left side (P = 0.039, η_p^2 = .07)] and 180°/sec [right side (P = 0.01, η_p^2 = .11); left side (P = 0.014, η_p^2 = .10)]. Furthermore, The AcVR group achieved more conducive changes in functional performance [6-min walk test (P = 0.003, η_p^2 = .15), timed up and down stair test (P = 0.009, η_p^2 = .12), and 4 × 10 m shuttle run test (P = 0.036, η_p^2 = .08)].

Conclusion: A 6-week AcVR training is potentially effective for improving muscle architectural qualities, enhancing peak muscle torque, and boosting functional performance in patients with Juv-IA without experiencing any detrimental side effects.

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1. Introduction

Juvenile idiopathic arthritis (Juv-IA) is a chronic rheumatologic condition with an uncertain cause or trigger, typically manifests in children/adolescents under the age of 16 years. Persistent arthritis (i.e., joint pain, swelling, inflammation, and stiffness) for a minimum duration of six weeks and, occasionally, extra-articular symptoms are traits of Juv-IA [1]. The condition is estimated to affect about 1.6–23 children out of every 100,000 across the globe, with girls being more vulnerable [2]. The International League of Associations for Rheumatology (ILAR) has identified six distinct, mutually-exclusive subtypes of Juv-IA; these are the undifferentiated, systemic, poly-articular, oligo-articular, enthesitis-related, and psoriatic arthritis [3].

Patients with Juv-IA tend to be less active because of the condition, which also has detrimental effects on muscle structure and function [4]. Despite having no evident neuromuscular abnormalities, patients with Juv-IA might experience muscle hypotrophy and weakness. The physically-hypoactive behavior brought on by the condition may cause a widespread loss of muscle mass and strength, while also the pain-induced reflex inhibition may cause localized hypotrophy and weakening of the muscles next to the inflamed joint [4,5]. These mass/strength alterations are known to be associated with various architectural impairments such as reduced fascicle length, pennation angle, and muscle thickness [6]. Additionally, changes in muscle mass caused by persistent inflammation may lead to expansion of the adipose tissue between muscle bundles (i.e., intermuscular adipose tissue: Inter-MAT) [7]. Patients with Juv-IA are regarded to have poor functional performance, meaning that they struggle more with daily tasks than healthy peers do [8]. Given the fact that functional capacity is dependent on the acting muscles [9], muscular health-focused therapy approaches are essential for those patients and might improve their functional performance.

Numerous treatment strategies focused on exercise have been utilized to improve joint mobility, muscle mass/strength, bone mineral properties, and physical fitness in patients with Juv-IA [10–13]. The current exercise interventions for patients with Juv-IA focus primarily on the use of flexibility exercise (range-of-motion and muscle lengthening), active-free/functional activities, low-intensity strengthening, postural reeducation, aerobic training, and, to a lesser extent, forceful resistance training due to apprehension about either aggravating the arthritis or causing harm to the muscles or bones [14]. Research has shown that patients with Juv-IA can engage in several types of exercise without the risk of flare-ups [15]. Resistance training in particular, although has not been thoroughly studied in patients with Juv-IA, has been reported as a safe, practicable, and acceptable training approach (as demonstrated by the lack of pain aggravation or any other unfavorable incidents), and may even have positive effects [16,17]. The rationale for the prospective benefits of resistance training for patients with Juv-IA comes from previous research in adults/children with arthritic or other rheumatic conditions [10,12,17–19]. Resistance training in adults with rheumatoid arthritis has been shown to enhance strength by a factor of four relative to the baseline, reduce pain by 53%, and improve the 50-foot walking time (all were meaningful compared to controls) [19]. Resistance training has also been proven to be helpful for children with idiopathic arthritis, dermatomyositis, systemic lupus erythematosus, and fibromyalgia [10,12,17,18,20,21].

Unlike typical resistance training, accommodating variable-resistance (AcVR) training is an instrumented exercise approach that maintains the motion of the limb at a constant speed across a predefined range of motion while applying resistance proportional to the force exerted by the trained muscle. That is, increasing volitional efforts or acceleration would be correspondingly countered by increased resistance [22]. Besides, the AcVR training provides a controlled environment that reduces the possibility of loading the patients over their tolerance and enables the exercise to be conducted at the individual's maximum strength level at each joint angle, while also allowing for precise measurement of the muscle performance [23]. Despite the fact that AcVR training has some inherent advantages, its implications for patients with Juv-IA haven't been adequately studied as of yet. The primary objective of the present study was, therefore, to explore the effects of a 6-week AcVR training on muscle architecture (pennation angle, fascicle length, and muscle thickness) and peak concentric torque of knee extensors, while also monitoring the functional capacity in a convenience sample of patients with Juv-IA. It has been hypothesized that, in comparison with the usual exercise intervention, the AcVR training would induce favorable changes in the aforementioned outcomes.

2. Methods

2.1. Design and ethics

The was a dual-arm, randomized controlled clinical trial (ClinicalTrials.gov Identifier: NCT05805969) undertaken at the Physical Rehabilitation Center and Laboratories of Prince Sattam bin Abdulaziz University (Al-Kharj, KSA) from November 2021 to January 2023. A single-blind protocol was adopted, keeping the intervention allocation undisclosed to the outcome assessor. The trial was authorized by the Physical Therapy Research Ethics Committee at the university, which issued the following approval number: RHPT/0021/0036. The experimental procedures were carried out in compliance with the ethical standards of the 1975 Declaration of Helsinki. Patients and their legal guardians signed a consent form after being thoroughly informed about all aspects of the study by the principal investigator.

2.2. Participants

Fifty-eight patients were recruited from the Pediatric Rheumatology clinics at King Khalid Hospital and two other referral hospitals in Riyadh, KSA. They were diagnosed with Juv-IA according to the ILAR's criteria [3], had poly-articular onset with bilateral knee involvement, were between 12 and 18 years old, were on stable doses of medications for a minimum of three months before entry, were not in need to change types or adjust dosages during the study, and were not engaging in regular exercise regimens other than the

physical therapy sessions or school-based physical education classes. Patients who had irreversible lower limb contractures, joint/muscle surgery in the past six months, radiographic evidence of advanced Juv-IA (i.e., fibrous/osseous ankylosis, fractures, bone erosion, or joint malalignment), cardio-respiratory comorbidities, or discouraged from engagement in strength training by the attending Pediatric Rheumatologist were excluded.

2.3. Sample size estimation

The effective sample size required to get results that are clinically meaningful was determined considering estimates of 95% confidence intervals (1.51–8.79 Nm) for a mean difference (5.12 Nm) of the peak concentric torque of knee extensors at an angular speed of 120°/second (being a primary outcome measure) and a tolerance probability of 90%. These data were obtained from a preliminary investigation in which 10 Juv-IA patients received the same treatment as in this full-scale study. Forty-eight patients (24 per group) were needed to produce a two-sided 95% confidence interval with a distance from the difference in means to the limits that is less than or equal to 3.62 Nm if the pooled standard deviation is 5.51 Nm. The sample size was expanded to 58 patients (29 per group) in anticipation of a 20% dropout rate. The analysis was conducted using version 16.0.1 of the PASS software (NCSS, Kaysville, UT, USA).

2.4. Allocation to interventions

Two independent researchers who were not informed of the patients' involvement in the trial performed a simple randomization of enrolled patients. Fifty-eight random numbers were created by one researcher through an online random number generator (https://www.graphpad.com/quickcalcs/randomN1/; GraphPad Software Inc, La Jolla, CA, USA). The second researcher then associated each random number with a patient from another list of names organized according to the order in which they were enrolled. Following that, the randomization lists were transferred into two secured, opaque envelopes, which were then given to the lead researcher. Patients were divided into two equal groups: the AcVR group, which included patients whose names were associated with the first 29 randomly created numbers, and the control group, which included patients whose names were associated with the remaining 29 random numbers.

3. Interventions

3.1. AcVR training

A pediatric-physical therapist led the AcVR training program, which was carried out on the HUMAC NORM isokinetic dynamometer (Humac Norm 2009, CSMI, MA, USA) three times a week (with 48-h recovery intervals) for six consecutive weeks. The training was executed in keeping with the guidelines and safety standards set forth by the American Academy of Pediatrics [24] and the National Strength and Conditioning Association [25]. All participants attended a familiarization session where they were fully instructed about how the training should be conducted. To optimize performance and allow a gradual transition to the training demands (physiological, biomechanical, bio-energetic), 10 min were devoted to warm-up (by way of three 15-s stretches for the lower limb muscles and low-resistance exercise on a bicycle ergometer) ahead of the AcVR training. The AcVR workout protocol included maximum voluntary concentric knee flexor/extensor actions. Participants were comfortably positioned on a fully-adaptable dynamometer chair, with the backrest inclined rearward at a 10° angle from the vertical plane. To provide stability and eliminate the involvement of muscles other than those of interest, Velcro straps were snugly applied around the thigh, waist, and upper torso. The rotating axis of the dynamometer was aligned to the lateral femoral condyle such that during knee flexion and extension motions, they are co-axial. The resistance pad was placed on the lower leg (3 cm proximal to the malleoli) at the distal end of the dynamometer's lever arm and fastened by a posterior Velcro strap. A knee flexion range of movement between 10^{o} and 90^{o} was utilized for the training. Participants were trained bilaterally, and the AcVR workout included three sets of five to 10 repetitions of maximum-effort concentric action at angular speeds of 240, 180, and 120°/second. All participants had a 2–3-min rest interval between training sets, with repetitions being performed consecutively without pausing. Standardized verbal instructions were delivered throughout the training, and real-time feedback on performance (i.e., torque development curve) was also supplied via the computer interface. After the AcVR training, the lower limb muscles were stretched out again for 15 s as a kind of cooling down.

3.2. Usual exercise regimen

Control participants underwent the usual exercise regimen as detailed in a prior study [12,26]. They attended three sessions per week over six weeks, with each session lasting around 45 min. Exercises were overseen by a pediatric physical therapist and were broken up into three stages. i) Warming-up for 10 min; wherein arm swings, joint mobility exercises, static/dynamic stretches of major muscle groups, and free walking or running have been performed. ii) Core exercise set; continued for 30 min and included flexibility exercises (manual stretching of tight muscles, then performing active range-of-motion activities), strengthening exercise–progressively transitioned from an isometric to an active to a low- to moderate-intensity resistance form, proprioceptive and weight-bearing exercises (stepping in different directions while bearing the bodyweight on lower limbs or employing a leg press machine while not bearing bodyweight), and aerobic exercises on a cycle ergometer or a treadmill as preferable. iii) Cooling down for 5 min by way of brisk walking or jogging and stretching exercises.

4. Measurements

Measurements were done at baseline and after the intervention period of six weeks by the same assessor, who was unaware of the intervention allocation on either occasion. The primary outcome measures were muscle architecture and peak torque, with functional capacity being the secondary measure.

4.1. Primary outcome measures

4.1.1. Muscle architecture

The architectural features of the vastus lateralis muscle (specifically, fascicle length, pennation angle, and muscle thickness) at the dominant limb were examined through a two-dimensional, B-mode ultrasonography (GE Logiq 500 Pro, Milwaukee, Wisconsin) with a 10-cm linear array transducer (10 MHz, 74-mm depth). We particularly gathered data from the vastus lateralis since it is commonly assumed that architectural changes in this muscle are characteristic of those in the entire quadriceps [27]. Participants were laid in a supine position, their muscles relaxed, and their legs were fully extended. A water-soluble gel was applied to the transducer to promote acoustic coupling and reduce deformations that may result from applying too much pressure on the underlying muscle. Scanning was performed with the transducer pointed perpendicular to the skin and parallel to the muscular fascicles. Images were captured in the middle of the muscle halfway between the greater trochanter and the lateral femoral condyle. Scanning sites were imprinted onto a pliable plastic sheet for the purpose of ensuring that follow-up scans were taken from the same spot as the baseline. The fascicle length was determined by measuring the distance between the superficial and deep aponeurosis along the fascicular path. The pennation angle was defined as the angle formed between the deep aponeurosis and the fascicular path. The muscle thickness was determined as the perpendicular distance between the superficial and deep aponeurosis of the muscle [28,29].

4.1.2. Peak torque

The peak torque during concentric action of knee extensors (Nm) was measured bilaterally using an isokinetic dynamometer (Humac Norm 2009, CSMI, MA, USA) and a positioning protocol similar to that used for the AcVR training. The test was conducted in accordance with the manufacturer's guidelines for measuring lower limb strength. Prior to data collection, the dynamometer was calibrated, and participants warmed up by performing 10 knee flexion/extension movements with a sub-maximal effort at a speed of 240°/second. The peak torque was recorded within the 0-90^{o} knee flexion range at two angular speeds: 120 and 180°/second. Participants were verbally urged to put up their best effort while simultaneously receiving real-time visual feedback on a computer interface during the test. Three test trials with 120-s rest intervals were allowed. In each trial, the isolated concentric knee extension mode was used to carry out three consecutive maximum contractions. The average score was computed and employed for the data analysis.

4.2. Secondary outcome measures

4.2.1. Functional performance

The walking capacity/endurance, functional mobility that requires strength, and movement speed/ability were assessed utilizing the 6-min walk test (6MWT) [30], timed up and down stairs (TUDS) [31], and the 4 × 10 m shuttle run test (4x10mSRT) [32], respectively. A 15–20-min rest period was allowed.

In the 6MWT, participants had 6 min to walk at their normal pace as far as they could down a straight, level, 30-m-long pathway with clearly designated turnaround points. In conformity with the American Thoracic Society's guidelines [33], the assessor directed and motivated participants every minute using a standard language. A stopwatch was used to keep track of the passing of time, and a measuring wheel was used to measure distance in feet before being converted to meters. Covering longer distances during the 6MWT indicates better performance [30].

During the TUDS test, participants were required to climb a 14-step staircase (20 cm height each step), turn around at the top, and go all the way down to hit the landing as quickly but cautiously as possible. They were allowed to use any strategy they preferred to get up and down the stairs, including step-to or foot-over-foot sequences, stepping-skips, run-ups, and other variations, and were given verbal cues like "ready," "set," and "go". A stopwatch was used to measure the task's completion time (in seconds). Each data point corresponds to the duration of a single test trial. Lower test scores (i.e., shorter durations) suggest improved functional mobility [31].

For the 10mSRT, participants were asked to run as rapidly as they could for four rounds back and forth along a 10-m running track (with starting and end points visibly delineated by two parallel lines). As soon as each participant crossed the starting line with one foot in the fourth round, the nearby rater stopped the timer. The duration of the task, measured in seconds, was noted. Three testing trials with 1–2-min rest intervals were permitted, and the most effective trial (i.e., the shortest duration) was documented [32] and employed for the statistical analyses.

4.2.2. Statistical analysis

Statistical analyses were performed using Statistica software, version 13.3.0 (Statsoft, TIBCO Software, CA, USA). The data distributions were checked for normality using the Kolmogorov-Smirnov test, and logarithmic transformations were utilized as appropriate. All dependent variables were analyzed on an intention-to-treat basis. The intergroup pre-to-post change differences (i.e., treatment-by-time interaction effect) were computed through the mixed-model ANOVA test, which comprised one between-group factor (treatment: AcVR/control) and one within-group factor (time: pre/post). In case the mixed ANOVA analysis indicated a

significant difference, further analysis using the dependent *t*-test was conducted to evaluate the within-group changes. The amount of the reported between- and within-group differences (i.e., effect size) were respectively computed through the eta-squared partial (η_p^2) and Hedge's *g* formulae. A $P < 0.05$ was the standard for significance for all analyses.

5. Results

5.1. Enrollment and retention

Seventy-nine patients were potentially eligible. Of them, 58 patients met the requirements for inclusion and moved on to the trial's next stages. Five patients—two from the AcVR group and three from the control group—were lost to follow-up measurements or failed to complete the prescribed intervention due to schedule issues or unreported personal reasons. To retain the entire data set, a regression imputation model was employed to replace the missing data in keeping with the intention-to-treat principle.

5.2. Tolerability, safety, and adherence to intervention

All participants in the AcVR group found the training to be tolerable and were capable of undertaking the proposed training (i.e., completing the required number of sets and repetitions) in all scheduled sessions. No adverse effects were reported by participants except for three participants who occasionally mentioned fatigue perception of variable degrees without the program being discontinued (that is, the 2-3-min rest interval between exercise sets and the 48-h recovery period between sessions were likely sufficient to allow for adequate recuperation and preparation for the subsequent training session). The adherence to intervention rate (i.e., the percentage of the 18 scheduled training sessions that the participants actually completed over the course of the six-week period) was comparable in both groups ($P = 0.13$). In the AcVR group, the median (IQR) adherence to intervention rate was 94.4% (88.9%–100%), while in the control group, it was 88.9% (88.9%–94.4%).

5.3. Baseline homogeneity

The baseline demographic, anthropometric, and clinical characteristics of the participants in the study groups are shown in Table 1. The AcVR and control groups were comparable ($P > 0.05$) in terms of age, anthropometrics, pubertal status, and Juv-IA-related clinical characteristics (disease duration, age of onset, involved joints, or medication dosages).

5.4. Post-intervention differences

The between-group change differences in vastus lateralis muscle architecture from the pre-to post-treatment occasion are outlined in Table 2. A significant large treatment-by-time interaction effect was detected on the fascicle length ($F_{1,56} = 12.65$, $P = 0.0007$, $\eta_p^2 = .18$), pennation angle ($F_{1,56} = 14.00$, $P = 0.0004$, $\eta_p^2 = .20$), and muscle thickness ($F_{1,56} = 11.19$, $P = 0.001$, $\eta_p^2 = .17$). Compared to the control group, the AcVR group showed more conducive changes in all architectural features.

The pre-to-post change difference in knee extensors' peak torque during concentric action between the AcVR and control groups is listed in Table 3. A significant moderate-to-large treatment-by-time interaction effect was revealed on the peak torque at both the angular speed of 120°/sec [right side ($F_{1,56} = 4.86$, $P = 0.0032$, $\eta_p^2 = .08$); left side ($F_{1,56} = 4.74$, $P = 0.039$, $\eta_p^2 = .07$)] and 180°/sec [right side ($F_{1,56} = 7.16$, $P = 0.01$, $\eta_p^2 = .11$); left side ($F_{1,56} = 6.50$, $P = 0.014$, $\eta_p^2 = .10$)]. The AcVR group had a larger increase in muscle torque as compared to the control group.

The change differences in functional performance between the AcVR and control groups are presented in Table 3. The analysis

Table 1
Demographic, anthropometric, and clinical baseline characteristics of participants in the AcVR and Control Groups.

	AcVR group ($n = 29$)	Control group ($n = 29$)	***P*-value**
Age, *year*	15.10 ± 2	14.3 ± 1.7	0.12¥
Weight, *Kg*	49.72 ± 11.94	47.34 ± 8.73	0.39¥
Stature, *m*	1.49 ± 0.15	1.48 ± 0.12	0.73¥
Body mass index, Kg/m^2	21.97 ± 1.68	21.41 ± 1.53	0.19¥
Gender (b/g), *n (%)*	11 (37.9)/18 (62.1)	13 (44.8)/16 (55.2)	0.79‡
Pubertal maturation, (y/n), *n (%)*	24 (82.8)/5 (17.2)	21 (72.4)/8 (27.6)	0.53‡
Disease duration, years	9.9 ± 2.2	9.4 ± 1. 7	0.33¥
Age of onset, *years*	5.2 ± 0.8	4.97 ± 1.1	0.33¥
Involved joints, *n*	8.24 ± 1.27	7.79 ± 0.98	0.14¥
RF (±), *n (%)*	4 (13.8)/25 (86.2)	6 (20.7)/23 (9.3)	0.73‡
Methotrexate dose, *mg/wk.*	17.14 ± 3.99	15.86 ± 2.95	0.17¥
Corticosteroids dosage, *mg qod*	166.38 ± 68.10	145.86 ± 57.12	0.22¥
Steroid injection frequency, *n*	15.83 ± 7.64	14.69 ± 4.55	0.49¥

Data are listed as mean ± StDev if numerical and as frequency (proportion, %) if qualitative.
Abbreviations: AcVR: accommodating variable resistance, y/n: yes/no b/y: boys/girls, RF: rheumatic factor.
¥ independent samples *t*-test, ‡ Fisher's exact test.

Table 2
The between- and within-group change differences in vastus lateralis muscle architecture.

	AcVR group ($n = 29$)	Control group ($n = 29$)	**ANOVA interaction**	
			P-value	η^2_p
Fascicle length, mm				
Pre	60.47 ± 5.38	59.72 ± 4.91	0.0007*	0.18
Post	63.96 ± 6.47	61.15 ± 5.02		
P-value	<0.0001*	0.0002*		
Hedges' *g* (95% CI)	0.57 (0.36–0.80)	0.28 (0.14–0.43)		
Pinnation angle, degree				
Pre	15.37 ± 1.40	15.42 ± 1.15	0.0004*	0.20
Post	17.28 ± 1.61	16.27 ± 1.01		
P-value	<0.0001*	0.0003*		
Hedges' *g* (95% CI)	1.23 (0.87–1.65)	0.76 (0.35–1.21)		
Muscle thickness, mm				
Pre	17.83 ± 2.02	17.37 ± 1.54	0.001*	0.17
Post	19.69 ± 2.54	18.18 ± 1.77		
P-value	<0.0001*	<0.0001*		
Hedges' *g* (95% CI)	0.79 (0.48–1.13)	0.48 (0.29–0.68)		

The variables are displayed as (mean ± SD).
Hedges' *g*: effect size for the within group difference, $\eta^2_{Partial}$: effect size for the between-group difference.
* Significant at $P < 0.05$.
AcVR: accommodating variable-resistance.

Table 3
Pre-to-post change differences in peak torque (Nm) and functional performance measures between the study groups.

	AcVR group ($n = 29$)	Control group ($n = 29$)	**ANOVA interaction**	
			P-value	η^2_p
RT knee extensors – 120°/sec				
Pre	38.10 ± 5.46	37.81 ± 5.72	0.032*	0.08
Post	43.47 ± 4.52	40.03 ± 6.59		
P-value	<0.0001*	0.035*		
Hedges' g (95% CI)	1.04 (0.58–1.55)	0.35 (0.03–0.69)		
LT knee extensors – 120°/sec				
Pre	35.85 ± 5.72	34.10 ± 5.03	0.039*	0.07
Post	39.58 ± 4.81	36.20 ± 5.84		
P-value	<0.0001*	0.0006*		
Hedges' g (95% CI)	0.69 (0.43–0.98)	0.37 (0.16–0.60)		
RT knee extensors – 180°/sec				
Pre	33.60 ± 3.95	31.80 ± 3.66	0.01*	0.11
Post	37.73 ± 3.45	33.82 ± 3.40		
P-value	<0.0001*	0.0005*		
Hedges' g (95% CI)	1.08 (0.72–1.50)	0.56 (0.25–0.89)		
LT knee extensors – 180°/sec				
Pre	32.60 ± 3.64	31.33 ± 2.92	0.014*	0.10
Post	36.77 ± 3.65	33.46 ± 3.50		
P-value	<0.0001*	0.0006*		
Hedges' g (95% CI)	1.11 (0.70–1.57)	0.56 (0.21–0.93)		
6MWT, m				
Pre	477.55 ± 90.94	470.54 ± 77.62	0.003*	0.15
Post	550.79 ± 82.13	506.59 ± 70.62		
P-value	<0.0001*	0.0006*		
Hedges' g (95% CI)	0.82 (0.57–1.12)	0.47 (0.21–0.76)		
4x10mSRT, sec				
Pre	11.28 ± 2.13	11.79 ± 1.92	0.009*	0.12
Post	9.14 ± 2.23	10.80 ± 1.30		
P-value	<0.0001*	<0.0001*		
Hedges' g (95% CI)	0.95 (0.54–1.41)	0.59 (0.32–0.88)		
TUDS, sec				
Pre	18.69 ± 4.54	19.78 ± 4.67	0.036*	0.08
Post	13.58 ± 3.92	16.41 ± 3.75		
P-value	<0.0001*	0.0001*		
Hedges' g (95% CI)	1.17 (0.84–1.56)	0.77 (0.40–1.18)		

The variables are displayed as (mean ± SD).
Hedges' *g*: effect size for the within-group difference, $\eta^2_{Partial}$: effect size for the between-group difference.
* Significant at $P < 0.05$.
AcVR: accommodating variable-resistance, 6MWT: 6-min walk test, 4x10mSRT: 4 × 10 m Shuttle Run test, TUDS: timed up and down stair test.

indicated a significant moderate to large treatment-by-time interaction effect on the 6MWT ($F_{1,56} = 9.96$, $P = 0.003$, $\eta_p^2 = .15$), TUDS ($F_{1,56} = 7.32$, $P = 0.009$, $\eta_p^2 = .12$), and 4x10mSRT ($F_{1,56} = 4.59$, $P = 0.036$, $\eta_p^2 = .08$). The AcVR group walked further distance in the 6MWT and performed faster during the TUDS and 4x10mSRT compared with the control group.

6. Discussion

The main objective of this study was to assess the potential benefits of AcVR training for muscle architecture, peak torque, and functional performance in a cohort of patients with Juv-IA. A six-week training period was adopted in this experiment since earlier studies showed that children and adolescents could benefit from training for as little as four weeks [34]. The results of this study indicated that the AcVR training led to significant alterations of muscle architecture (i.e., reflected by increased vastus lateralis muscle fascicle length, pennation angle, and thickness) and meaningful enhancement of peak concentric torque of knee extensor muscles. Additionally, the AcVR training resulted in more conducive changes in the functional capacity as AcVR training participants covered more ground during the 6MWT and outperformed the control participants in the TUDS and 4x10mSRT.

The scope of the present study did not allow for identifying the precise mechanisms of how the AcVR training influenced the outcomes directly. There exist, however, potentially reliable neurophysiological and mechanical explanations for the favorable changes demonstrated herein. The concentric load imposed by muscles during the AcVR training might have changed the muscle excitability (i.e., evoked stronger signals from the muscle spindles, and consequently increased the efferent neural drive, boosted motor units' recruitment, and enhanced the rate of force/torque generation). The changes in the architectural properties (fascicle length, pennation angle, and muscle thickness) might, thus, have occurred as consequential morphological/structural adaptations that matched the evolving mechanical properties of the muscle [35]. On the other side, the increased peak torque of knee extensors during the concentric action could be attributed to the positive changes in the spatial arrangement of muscle fiber architecture (i.e., parallel muscle fiber orientation relative to the force-generating axis) and increased muscle fiber cross-sectional area, both of which are proportionally associated with an enhanced rate of force development [36,37]. According to a previous study that supports this assertion, increases in muscle fascicle length and pennation angle allow for an increase in the contractile components and may even facilitate the development of more cross bridges. These developments result in an increase in maximal force-generating capacity when more cross-bridges are activated concurrently during muscular contraction [38]. Taking into account the relationship between the morpho-mechanical characteristics of the acting muscle and functional capacity [9], it is also reasonable to assume that the improved muscle architecture and increased muscle strength have contributed to the enhanced performance during the 6MWT, TUDS, and 4x10mSRT.

To our knowledge, this deems the first investigation trying to uncover how AcVR training affects muscle architecture in patients with Juv-IA. It might therefore be more challenging to contrast the findings of this research with those of similar investigations. We reasoned that assessing interventions at the muscular level might be crucial because muscle involvement is a putative long-term predictor of health (physical health, in particular) in patients with inflammatory disorders [7], and further because prior studies have only demonstrated that resistive exercises may improve strength and function without showcasing the potential changes in muscle morphometric characteristics [10,12], which, as is widely understood, are related to muscular efficiency and functional performance [6]. Our revelation that most of the architectural features changed in favor of AcVR training expands the body of research supporting the advantages of such a training paradigm (i.e., resistive exercises) for patients with Juv-IA [10,12,16,17]. Patients in the AcVR training group showed remarkable increases in vastus lateralis muscle fascicle length, pennation angle, and muscle thickness. These increases may reflect the dose-response relationship that was appropriate for the training protocol adopted in this investigation. In other words, the training doses (i.e., its volume, intensity, and duration) were barely sufficient to bring about noticeable architectural alterations. Nonetheless, additional studies are still needed to establish the viability of the AcVR training.

Van Oort et al. [16], evaluated the effects of a six-week resistance training program on muscle strength, thickness, and functional ability in patients with Juv-IA (age: 8–18 years). The training has been proven safe and feasible and resulted in significant improvements in the measured outcomes. Elnaggar et al. [10,12], evaluated the role of different forms of resistance training alone or in combination with other modalities for the muscle peak concentric torque and functionality in patients with poly-articular Juv-IA. They deduced that the training was well tolerated, produced noticeable improvements in the knee extensor peak torque during concentric actions, and enhanced functional capacities. Sule and Fontaine [17], explored the impact of a 12-week slow-speed resistance training on body composition, aerobic fitness, peak isometric torque, fatigue, and functional capacity in a cohort of patients with poly-articular Juv-IA. The reported improvement in fatigue and improved energy although no significant changes were detected in other variables. The non-significant changes have been attributed to poor adherence to the training since only 53% of participants in the exercise group completed the assigned intervention and they even met only 1–2 sessions a week, which was less than the recommended rate (2–3 times/week) for resistance exercises. In view of the foregoing, it is possible to argue that the current findings significantly add to that of past research in this area that linked resistance training with significant improvements in muscular strength and functional capacity based on data from patients with Juv-IA.

The fact that this study was the first to validate the efficacy of AcVR training in patients with Juv-IA is one of its key advantages. Further, by employing a fairly large sample size and a power that was reasonably high (90%), the study design (i.e., randomized, assessor-blinded controlled study) might have boosted the likelihood of arriving at a reliable conclusion regarding the effects and clinical relevance of the intervention. Furthermore, as muscle architecture and strength are potentially significant determinants of functional performance [9], this study considered these variables among the outcome measures, which might help provide a full picture of the prospective causal association of functional performance with muscle architecture and strength.

Even though the AcVR training yielded favorable results, there exist certain limitations on how broadly these results can be applied.

This study was limited to patients with polyarticular Juv-IA whose conditions were clinically stable. Therefore, to give more conclusive data, the upcoming studies should examine AcVR training responses in larger samples with representation from all Juv-IA subtypes. Participants in this study were of a particular age range (12–18 years). The significance of AcVR training for patients with Juv-IA in younger or older age groups will require additional research to be determined with greater certainty. Whether the training effects will sustain beyond the post-treatment occasion when no more training is given, is another unresolved issue in this study. So, determining the sustainability of those effects will require more investigations that consider the long-term follow-up at 3-, 6-, or 12-month terms. The laboratory markers of disease inflammations (such as C-reactive protein or erythrocyte sedimentation rate) were not examined in this investigation. These findings might have helped in figuring out if the AcVR training had any anti-inflammatory effects.

6.1. Implications for clinical practice

Evidence suggests that patients with Juv-IA often experience alterations in muscle morphology, a decline in muscle strength, and a deterioration in their ability to execute functional tasks [4–8]. These observations emphasize the importance of incorporating targeted exercise interventions into the management of Juv-IA to remedy these deficits. The current results imply that the use of AcVR training can help with addressing the observed muscle morphology changes, impaired strength, and functional performance deficits in patients with Juv-IA. Accordingly, physical rehabilitation professionals working with this patient population could broaden the care plan and incorporate AcVR training based on empirical evidence.

7. Conclusion

The results of the present study provide evidence that AcVR training, when incorporated into the usual physical rehabilitation, may produce favorable adaptations of muscle architecture, enhance peak muscle torque, and boost functional competence in patients with Juv-IA. Nevertheless, additional investigations are warranted to validate the evidence concerning the role of AcVR training for such a patient population.

Ethics statement

The trial was authorized by the Physical Therapy Research Ethics Committee at the university, which issued the following approval number: RHPT/0021/0036.

The experimental procedures were carried out in compliance with the ethical standards of the 1975 Declaration of Helsinki.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e27693.

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