

ORIGINAL RESEARCH ARTICLE

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# Aerobic training versus strength exercises on muscle strength and quality of life for children with acute lymphoblastic leukemia

Doaa Mohamed<sup>1,2\*</sup> , Faten Abd Alazim<sup>1</sup>, Elham Salem<sup>1</sup>, Nesreen Ali<sup>3,4</sup> and Dina Elgalaly<sup>5</sup>

## Abstract

**Background:** The treatment for children and adolescents with acute lymphoblastic leukemia (ALL) can lead to multiple adverse effects, including poor physical capacity and muscle weakness. This study aimed to determine which is more effective, aerobic exercises or modified strength training program, on muscle strength and quality of life (QOL) for children with ALL.

**Results:** In terms of muscle strength, there was a significant difference ( $P < 0.05$ ) in selected group of muscles elbow flexors, shoulder abductors, hip flexors, knee extensors, and ankle dorsiflexors at both sides in group B compared with group A, whereas there was no significant difference ( $P > 0.05$ ) between groups on QOL.

**Conclusion:** The outcomes of the study showed that there was a significant difference in the selected group of muscles at both sides in group B compared with group A; thus, the modified strength training program is more effective for muscle strength of children with ALL than aerobic training, but there was no significant difference between them on QOL.

**Trial registration:** The clinical trial registered in clinicaltrials.gov with an identifier number [NCT03147365](https://clinicaltrials.gov/ct2/show/study/NCT03147365)

## Background

Acute lymphoblastic leukemia (ALL) is an aggressive neoplasia, and ~ 60% of cases occur at age less than 20 years [1]. The treatment protocol is divided into three phases: remission induction, consolidation, and maintenance. The maintenance phase is the longest period of the treatment (2–3 years); the aim of this phase is to prevent disease relapse. It is also the stage in which children already have greater clinical stability and have passed through the other stages [2]. Pharmacological treatment, especially vincristine and dexamethasone, had bad effect on the whole skeletal and neuromuscular system, and the muscles that were most affected were shoulder

abductors, elbow flexors, hip flexors, knee extensors, and dorsal flexors [3, 4].

Risk classification of patients with ALL was performed on the basis of age, initial presenting white blood cell count, the genetic and immune phenotypic characteristics of the leukemic blast, and individual response to therapy. B cell precursor patients between 1 and 10 years of age and leukocyte count less than  $50 \times 10^9/l$ , DNA index more than or equal to 1.16, or reciprocal translocation of genetic material between chromosome 12 and chromosome 21, t(12; 21), and with a fusion gene called ETV6-RUNX1, were provisionally classified as low-risk ALL. Cases with reciprocal translocation of genetic material between chromosome 9 and chromosome 22, t(9;22), and with a fusion gene called BCR-ABL1 were considered to have high-risk ALL, whereas the remaining cases were provisionally classified as standard (intermediate)-risk ALL. The final risk status was determined by minimal residual disease (MRD) levels. Any

\* Correspondence: [dr.doaa.n26@gmail.com](mailto:dr.doaa.n26@gmail.com)

<sup>1</sup>Department of Physical Therapy for Growth Development Disorders in Children and its Surgery, Faculty of Physical Therapy, Cairo University, Giza, Egypt

<sup>2</sup>Almonoufia, Egypt

Full list of author information is available at the end of the article



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patient with more than or equal to 1% bone marrow MRD on day 19 of remission induction or 0.1–0.99% MRD after completion of 6-week induction therapy was considered to have standard-risk ALL. MRD more than or equal to 1% after the completion of induction therapy denoted high-risk ALL [5].

There is growing evidence for the positive effects of aerobic exercise training and strength exercises on physical fitness, fatigue, and physical well-being of children during and after treatment for ALL [6–10], but the literature describing the effects of aerobic exercise on muscle strength is very limited; therefore, the current study is one of the very few studies that have shown the effect of aerobic exercises on muscle strength and aimed at determining which is more effective, aerobic exercises or a modified strength training program, on muscle strength and quality of life (QOL) for children with ALL.

## Methods

### Study design

A randomized clinical trial was conducted. The study was approved by (CCHE57357) Ethics and Committee Review Board, and it was part of the trial which was registered in [clinicaltrials.gov](https://clinicaltrials.gov) with an identifier number NCT03147365. Before initiating the study, all of the patients' parents provided a written informed consent after they were provided with a complete verbal and written explanation about the study's objectives, as well as the risks and benefits that were involved. All patients were evaluated using a hand-held dynamometer for muscle strength and the pediatric quality-of-life inventory questionnaire (PedsQL) for QOL at baseline and after 12 weeks, and then they were divided randomly into two groups who received 12 weeks of a training program (aerobic training for group A and strength exercises for group B). All patients received two sessions/week for 12 weeks.

### Patients

Thirty-four eligible patients (boys and girls) were recruited from the Outpatient Oncology Clinic of CCHE57357 from March 2017 to May 2019. The inclusion criteria for this study were as follows: (a) age range from 8 to 12 years; (b) children during the maintenance phase of the treatment and time elapsed since the start of the phase more than 20 weeks; (c) preserved cardiac structure and function, as assessed by an ECG; (d) height, weight, and BMI within normal ranges; and (e) able to walk. The exclusion criteria for this study were as follows: (a) platelet levels less than 50,000/ $\mu\text{l}$ ; (b) hemoglobin less than 8 g/dl; (c) pain in bone; (d) acute or chronic bone, joint, or muscular abnormalities; and (e) patient relapse. Nineteen patients were at low risk, and 15 patients were at standard risk. The patients with low-risk ALL received vincristine and steroid monthly

(VCR 2 mg/m<sup>2</sup> and dexamethasone 8 mg/m<sup>2</sup> for 5 days/month) until the 67th week, and then, the dose of dexamethasone was decreased to 6 mg/m<sup>2</sup> 5 days/month. The patients with standard risk received vincristine and steroid monthly (VCR 2 mg/m<sup>2</sup> and dexamethasone 12 mg/m<sup>2</sup> for 5 days/month) until the 67th week, and then, the dose of dexamethasone was decreased to 6 mg/m<sup>2</sup> 5 days/month, and they received the 6-mercaptopurine and methotrexate like the low-risk group according to the treatment protocol of CCHE57357 (SJude therapy Total XV) [5].

As shown in the flow chart in Fig. 1, the study began 40 eligible patients and five patients drop out due to far distance. Thirty-five patients were divided randomly using the Block Stratified Randomized Software program (windows version 6.0 of randomization program (Rand.exe), block sizes 4, 8, 2, 6, and 10, and in this randomized program, it is difficult to place samples in both groups equally with the same numbers when there are multiple stratified variables [11]) into group A, which included 19 children (10 boys and nine girls); then, one patient returned to intensive chemotherapy and had to be excluded during the program. Therefore, group A completed the study with 18 patients. Group B began and completed the study with 16 children (11 boys and five girls).

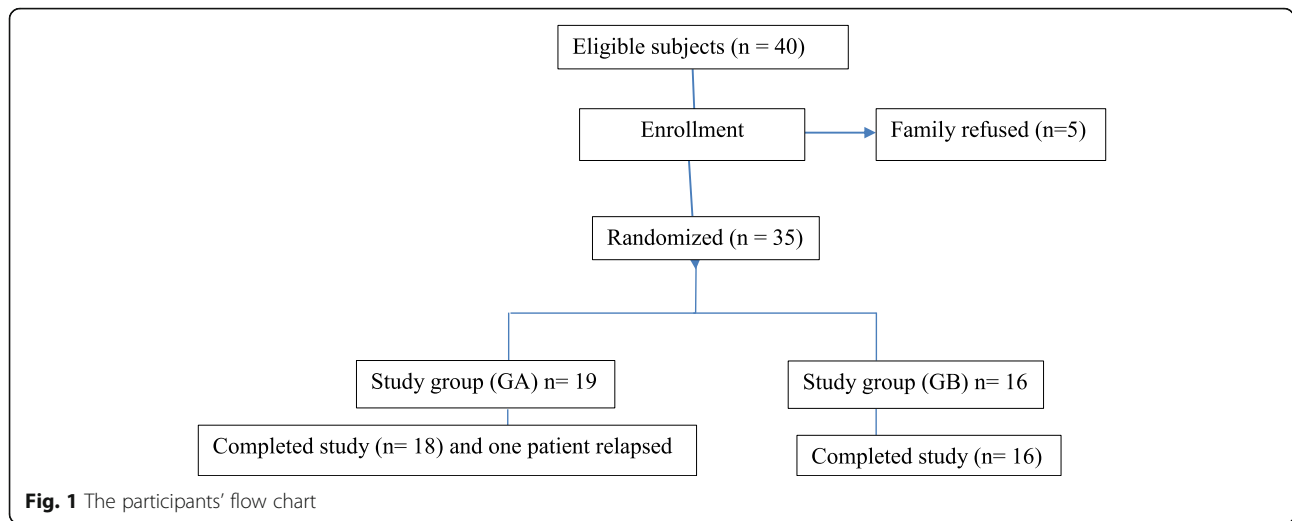
### Procedure

Demographic data of all patients were collected from the patient medical charts, and then, complete assessment of the muscle strength and QOL was performed in the Physical Therapy Department. Assessment for the two groups was performed twice during the program (before and after the program). For the safety of the exercise training, structure and function of the heart were assisted by ECG or take approval of cardiologist before the start of training for the first 3 weeks.

### Measurement procedures

#### Muscle strength

This was assessed using a hand-held dynamometer (Lafayette manual muscle tester 01163). Five muscle groups were measured for both sides of the body: shoulder abductors, elbow flexors, knee extensors, foot dorsal flexors, and hip flexors. Each group of muscles was measured three times during each test session, and then, the average was determined for analysis. A transducer was positioned on the limb, and the child performed maximal efforts for 5 s with a 30-s rest between trials. The objective of the test was for the examiner to overcome or "break" the children's resistance. When the resistance "break" occurs, the Manual Muscle Tester records the peak force and the time required to achieve the break. Most comfortable and stable positions were adopted to achieve optimal



conditions for maximum muscle strength efforts. Five different muscle groups were tested bilaterally according to the order, and the procedures are described in Table 1 according to Bohannon [12] and vander Ploeg et al. [13]. The reliability of the hand-held dynamometer was 0.80–0.96 for lower extremity muscle actions and 0.44–0.92 for upper extremity muscle actions and the validity was. Sensitivity varied from 73 to 87%, whereas specificity varied from 54 to 80%. At the sensitivity = 100% cut-off point, specificity varied from 0 to 48% [14].

**Quality of life**

This was assessed using the validated Brazilian PedsQL inventory [15]; it included three domains, which were the generic core scale, version 4, the multidimensional fatigue scale, and the cancer module, version 3. To reverse the score, the 0–4 scale items were transformed into 0–100 as follows: 0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0. The mean was calculated as the sum of the items over the number of items answered (this accounts for missing data) if more than 50% of the items in the scale are missing. To do this, number of missing values in the scale is counted. Next, the item scores are summed and divided by the number of items in the

scale. The questionnaire is scored out of 100, with a higher score indicating better health-related QOL. The reliability of the PedsQL inventory was 0.88 for the Children Self-Report, and the questionnaire has been tested for construct validity for healthy children ( $P = 0.0001$  for the total score and generic core scale,  $P = 0.005$  for the multidimensional fatigue scale, and  $P = 0.024$  for the cancer model) [16].

**Treatment procedures**

**Aerobic training**

According to San Juan et al. [17] and Abd El Bakya and Adel Elhakkb [18], the patients of group A received aerobic exercises using a RAM model (770 CF) electronic treadmill (two sessions/week, with each session lasting from 20 to 35 min). The patients were started with at least 50% of maximum heart rate (HRmax), which was measured with  $220 - \text{age}$ , and 70% HRmax at the end of the 12th week of the program. The exercise program was divided into a warm-up period (5 min at a speed of 1–1.5 km/h with zero inclination), followed by moderate intensity of aerobic exercises, and finishing with a cool-down period (5 min, and the speed was gradually decreased until reaching zero). The patients started the

**Table 1** Muscle groups test for limb/joint positions and dynamometer placement

Muscle group	Position	Limb/joint positions	Dynamometer placement
Elbow flexors	Supine	Shoulder will be abducted 30°, elbow will be flexed 90°, and forearm will be supinated.	Just proximal to wrist on flexor surface of forearm
Shoulder abductors	Supine	Shoulder will be abducted 45°, and elbow will be extended	Just proximal to lateral epicondyle of humerus
Hip flexors	Supine	Hip will be flexed 90°, knee will be relaxed, and ankle will be supported.	Just proximal to knee on anterior surface of thigh
Knee extensors	Sitting	Knee will be flexed 90°	Just proximal to ankle on anterior surface of leg
Foot dorsiflexors	Sitting	Knee will be flexed 90°, and foot will be in neutral position	Just proximal to metatarsophalangeal joints on dorsal surface of foot

aerobic exercise period in the form of walking on a treadmill for 10 min and at a speed of 2.5 km/h for 3 weeks, and then, aerobic exercises were increased by 5 min, 0.5 km/h speed, and slope of the treadmill every 3 weeks to reach 30 min, 4 km/h speed, and 7% slope at the end of the 12th week of the program. Their heart rates were recorded during the exercise sessions using a portable HR monitor.

#### **Modified strength exercise program**

According to Perodi et al. [9], patients of group B received a modified strength exercise program that included strengthening exercises for shoulder abductors, elbow flexors (using a pulley-assisted machine with a suitable weight of 4 kg), and knee extensors (using a quadriceps chair provided with weight 5 kg), and seated row exercise using a Tunturi rowing machine. The exercise sessions lasted ~ 20–35 min/session. The patients were started with at least 50% of HRmax and reached 77–90% HRmax at the end of the 12th week of the program. For each exercise, the children performed one set of 6–10 repetitions (total of ~ 20-s duration), followed by 1–2 min of stretching exercise as an adaptation to the high-intensity resistance training. When the patient was able to perform 10 repetitions in the last training set for two consecutive workouts, progression of the training program increased gradually until four sets of 6–10 RM were reached at the end of 12 weeks.

#### **Sample size calculation**

The sample size (34 patients) was calculated on the basis of a pilot study on 10 participants (five in each group) for all dependent variables to obtain a power of 0.95 with a significance level of 0.05 and an effect size of 0.867 with a two-tailed for a comparison of two independent groups; 17 participants in each group is the total sample size estimation using G\*power 3.1 software (Institute for Experimental Psychology; HeinrichHeine-Universität niversitätsstraße, Düsseldorf, Germany).

#### **Statistical analysis**

All statistical measures were performed using the statistical package for social science program, version 23, for Windows. Before the final analysis, data were screened for normality assumption and the presence of extreme scores. This exploration was performed as a prerequisite

for the parametric calculation of the analysis of difference and analysis of relationship measures. Descriptive analysis using histograms with the normal distribution curve showed that the data were normally distributed and did not violate the parametric assumption. In addition, testing for the homogeneity of covariance using Box's test showed that there was no significant difference with *P* values of more than 0.05. Normality test of data using the Shapiro–Wilk test was used, which showed that the data were normally distributed for all the dependent variables. All these findings allowed the researchers to carry out a parametric analysis. Therefore, 2 × 2 mixed design multivariate analysis of variance was used to compare the tested variables of interest in the different tested groups and measurement periods. The alpha level was set at 0.05.

#### **Results**

Table 2 summarizes the demographic characteristics of the participants in both groups. A total of 34 patients (21 boys and 14 girls) with ALL were involved in this study. The independent *t* test showed that there was no significant difference (*P* < 0.05) between the patients in both the groups in age (*P* = 0.189), weight (*P* = 0.935), height (*P* = 0.57), BMI (*P* = 0.895), and the elapsed time since the patients' last chemotherapeutic treatment (*P* = 0.873). Table 3 presents the descriptive statistics for medical properties of the participants in both groups. Statistical analysis using mixed-design multivariate analysis of variance indicated that there were significant within-patient effects (*F* = 136,891, *P* = 0.0001) and treatment × time effects (*F* = 15,632, *P* = 0.0001). Also, there was a significance between patient effect (*F* = 7.827, *P* = 0.0001).

#### **Muscle strength**

The comparison of muscle strength pretreatment among groups A and B showed that there was no significant difference in all assessed groups of muscles among groups A and B as shown in Table 4. Regarding with in group, there was a significant difference in shoulder abductors, hip flexors, knee extensors, and foot dorsal flexors at both sides in the post treatment condition compared with before treatment in both groups, whereas at the right elbow flexors, there was a significant difference in the post treatment condition compared with before treatment only in group B. However, at the left elbow flexors, there was a significant difference in the post

**Table 2** Demographic characteristics of the patients in both groups

Variables	Group A	Group B	<i>t</i> test	<i>P</i> values
Age (year)	10.61 ± 1.03	10.06 ± 1.34	1.343	0.189
BMI (kg/m <sup>2</sup> )	19.45 ± 3.27	18.69 ± 3.03	0.702	0.488
Time of maintenance (week)	73.16 ± 31.83	71.43 ± 30.6	0.161	0.873

Data are presented as the mean ± SD

**Table 3** Medical characteristics of the patients in both groups

Variables	Hemoglobin(g/dl) Mean ± SD	Platelet count (× 10 <sup>9</sup> /L) Mean ± SD	White blood cells (× 10 <sup>9</sup> /l) Mean ± SD	Red blood cells (× 10 <sup>12</sup> /l) Mean ± SD	O <sub>2</sub> saturation Mean ± SD
Group A	10.50 ± 1.63	140 ± 80.23	2.3 ± 2.22	3 ± 0.54	0.97 ± 0.009
Group B	10.15 ± 1.63	150 ± 124.69	2.8 ± 1.05	3.85 ± 0.57	0.97 ± 0.009

Data are presented as the mean ± SD

treatment condition compared with before treatment in both groups (Table 5). In comparing the mean values after treatment among groups, there was a significant difference in all the muscle groups assessed at both sides in group B compared with group A as shown in Table 6.

**Quality of life**

Comparison of the mean value of QOL before treatment among groups A and B showed that there was no significant difference between the generic code scale, the multidimensional fatigue scale, and the cancer module (Table 7), whereas within groups, there was a significant increase in the three scales in the after treatment compared with before pretreatment (Table 8). Also, there was no significant difference in three scales in the post treatment condition among groups A and B (Table 9).

**Discussion**

The present study included ALL, which constitutes a major classification among leukemia types. This was supported by Park et al. [19], who reported that ALL is the most common leukemia type in pediatric patients. Choosing the age of children between 8 and 12 years old was in agreement with Tanir and Kuguoglu [10] who reported that child started to have a good performance like adult between the age of 8 and 12 years.

Before beginning treatment, homogeneity of the two groups was confirmed for all parameters (muscle strength and QOL), which indicated poor performance and reduced QOL in children with ALL because of

treatment procedures. This may be explained by the numerous side effects to cancer treatment, which often include anemia (low hemoglobin in the blood), decreasing blood oxygen transport and decreasing red blood cells as shown in Table 3; it can also affect cardiac function, which reduces cardiac output, and skeletal muscle mass, leading to muscle atrophy. Chemotherapy also induces gastrointestinal toxicities that can interfere with nutrition. Thus, in addition to having low levels of cardiorespiratory fitness and muscle strength, individuals under cancer treatment can experience fatigue even during normal activities of daily living [20, 21].

For the muscle strength, a study carried out by Yeh et al. [7] supported our results, as they reported positive results for a 6-week supervised aerobic exercise program among children with ALL, especially in terms of knee extensors and ankle flexors.

From secondary supported studies for our results, Abd El Bakya and Adel Elhakk [18] reported that there was a significant improvement in both physical fitness and fatigue levels in children who survived ALL with the inclusion of a 16-week aerobic exercise training program with a home exercise program. Moreover, Adamsen et al. [22] showed that a high-intensity exercise program for 6 weeks led to an improvement in VO2 max by 16% in patients with cancer, including leukemia.

Juel et al. [23] suggested that the increase in aerobic capacity and physical fitness with an aerobic exercise program may be because of the effect of aerobic exercise on respiratory function and the stroke volume of the

**Table 4** Comparison mean value of muscle strength before treatment among groups (A and B)

Variables	Group (A)	Group (B)	Δ	P value	Sig
Right elbow flexors	8.89 ± 2.07	8.32 ± 2.68	.569	.491	NS
Left elbow flexors	8.12 ± 1.53	8.94 ± 2.13	-.816	.207	NS
Right shoulder abductors	7.36 ± 1.18	7.29 ± 1.07	.068	.862	NS
Left shoulder abductors	6.97 ± 0.78	7.35 ± 1.05	-.484	.194	NS
Right hip flexors	8.43 ± 1.26	8.84 ± 1.57	-.410	.406	NS
Left hip flexors	8.83 ± 2.44	8.68 ± 1.8	.146	.846	NS
Right knee extensors	6.77 ± 1.15	6.85 ± 1.33	-.484	.194	NS
Left knee extensors	10.46 ± 1.38	10.2 ± 1.71	.267	.620	NS
Right ankle dorsiflexors	8.38 ± 1.77	8.42 ± 1.8	-.042	.946	NS
left ankle dorsiflexors	8.59 ± 2.14	8.65 ± 1.68	-.056	.934	NS

Δ Mean difference pre group A–pre group B

**Table 5** Comparison mean value of muscle strength before and after treatment for both groups A and B

Variables	Group	Pre-treatment	Post-treatment	Δ	% of improvement	P value	Sig
Right elbow flexors	Group A	8.89 ± 2.07	9.67 ± 1.04	− .783	8.7%	.198	NS
	Group B	8.32 ± 2.68	11.99 ± 1.96	− 3.669*	44.1%	.0001	S
Left Elbow flexors	Group A	8.12 ± 1.53	10.97 ± 1.21	− 2.844*	35%	.0001	S
	Group B	8.94 ± 2.13	13.33 ± 2.26	− 4.394*	49.1%	.0001	S
Right shoulder abductors	Group A	7.36 ± 1.18	10.46 ± 1.17	− 3.106*	42.1%	.0001	S
	Group B	7.29 ± 1.07	12.46 ± 1.35	− 5.167*	71.6%	.0001	S
Left shoulder abductors	Group A	6.97 ± 0.78	9.72 ± 0.81	− 2.750*	39.4%	.0001	S
	Group B	7.35 ± 1.05	10.43 ± 1.32	− 3.083*	41.9%	.0001	S
Right hip flexors	Group A	8.43 ± 1.26	9.33 ± 1.22	− .900*	10.6%	.004	S
	Group B	8.84 ± 1.57	12.11 ± 2.01	− 3.275*	36.9%	.0001	S
Left hip flexors	Group A	8.83 ± 2.44	10.38 ± 1.49	− 1.550*	17.5%	.002	S
	Group B	8.68 ± 1.8	11.98 ± 1.7	− 3.294*	37.2	.0001	S
Right knee extensors	Group A	6.77 ± 1.15	9.2 ± 0.7	− 2.433*	35.8%	.0001	S
	Group B	6.85 ± 1.33	10.33 ± 1.02	− 3.075*	50.8%	.0001	S
Left knee extensors	Group A	10.46 ± 1.38	11.42 ± 1.66	− .956*	9.1%	.001	S
	Group B	10.2 ± 1.71	13.21 ± 1.56	− 3.013*	29.5%	.0001	S
Right ankle dorsiflexors	Group A	8.38 ± 1.77	13.21 ± 1.56	− 3.033*	54.6%	.0001	S
	Group B	8.42 ± 1.8	13.11 ± 1.79	− 4.688*	55.7%	.0001	S
Left ankle dorsiflexors	Group A	8.59 ± 2.14	10.98 ± 1.47	− 2.394*	27.8%	.0001	S
	Group B	8.65 ± 1.68	13.39 ± 1.53	− 4.744*	54.7%	.0001	S

Values of variables are expressed as mean ± SD. Δ(mean difference pre–post) within group  
 \*Significant at the alpha level ( $P < 0.05$ )

heart. These respiratory adaptations help facilitation of oxygen supply to tissues, which leads to an improvement in respiratory fitness. It also increases storage of energy molecules such as fats and carbohydrates within the muscles, and this leads to increased endurance and enhanced neovascularization of the muscle sarcomeres to increase blood flow through the muscles. These reasons may explain our results, which

show that aerobic exercise improves muscle strength when compared before and after treatment in group A in muscle strength.

However, Shore and Shepard [24] showed no significant difference between the exercise performances of two groups [a group that received aerobic exercise ( $n = 6$ ) and a group of healthy children ( $n = 11$ )]. This outcome may have stemmed from the limited number in

**Table 6** Comparison of mean values of muscle strength after treatment among groups A and B

Variables	Group A	Group B	Δ	P value	Sig
Right elbow flexors	9.67 ± 1.04	11.99 ± 1.96	− 2.316*	.0001	S
Left elbow flexors	10.97 ± 1.21	13.33 ± 2.26	− 2.365*	.0001	S
Right shoulder abductors	10.46 ± 1.17	12.46 ± 1.35	− 2.004*	.0001	S
Left shoulder abductors	9.72 ± 0.81	10.43 ± 1.32	− 1.992*	.0001	S
Right hip flexors	9.33 ± 1.22	12.11 ± 2.01	− 2.785*	.0001	S
Left hip flexors	10.38 ± 1.49	11.98 ± 1.7	− 1.134*	.001	S
Right knee extensors	9.2 ± 0.7	10.33 ± 1.02	− 1.126*	.001	S
Left knee extensors	11.42 ± 1.66	13.21 ± 1.56	− 1.791*	.001	S
Right ankle dorsiflexors	11.41 ± 1.65	13.11 ± 1.79	− 1.704*	.001	S
Left ankle dorsiflexors	10.98 ± 1.47	13.39 ± 1.53	− 2.410*	.0001	S

Values of variables are expressed as mean ± SD. Δ(mean difference pre–post) within group  
 \*Significant at the alpha level ( $P < 0.05$ )

**Table 7** Comparison of mean values of quality of life before treatment among groups A and B

Variables	Group A	Group B	Δ	P value	Sig
Generic code scale	70.91 ± 10.96	70.29 ± 7.84	.623	.852	NS
Multidimensional fatigue scale	71.75 ± 11.62	72.33 ± 8.61	-.582	.871	NS
Cancer module	65.96 ± 8.13	70.01 ± 6.03	-4.058	.112	NS

Δ(mean difference pre group A–pre group B)

the group sample, whereas the sample of the present study included 34 patients.

Moreover, Takken et al. [3] found no cardiopulmonary response to our same program period-based exercise training program in nine children with ALL (aged 6–14 years) as assessed by standardized cardiopulmonary exercise testing. This inconsistency across the literatures might be related to the variability in the population’s age, evaluation time after chemotherapy treatment, the number in the group sample, the intensity, and duration of the intervention.

A study carried out by Marchese et al. [25] supported our results, as they reported positive results of a 4-month intervention (strength exercises) in children with ALL, especially ankle dorsiflexion and knee extension strength.

Moreover, Perodi et al. [9], who used the same modified strength program of the current study for 12 weeks, showed that there was an improvement in the strength of the muscles and had investigated the effects of exercise on the immune system of children with ALL. In another exercise intervention, back and leg strength was assessed using a hand-held dynamometer and general body fitness by the timed up and down stairs test and the 9-min run-walk test. This study showed that this intervention was successful in improving back and leg strength [10], and our study was in agreement with these results. Marchese et al. [26] supported the use of a hand-held dynamometer as a reliable tool for measuring strength in children with ALL 4 years of age and older.

The results of the current study confirmed the findings of San Juan et al. [27], who subjected seven children (4–7 years) to a 16-week conditioning program that included resistance training. The results showed improvements in functional mobility and both upper and lower

limbs strength. McArdle et al. [28] suggested that muscular strength and endurance result from increasing the frequency, duration, and intensity of training. In exercise physiology, this is known as the overload principle. An exercise overload specific to the activity must be applied to enhance physiologic improvement and bring about a training effect. Desired training effects include increases in muscle strength, size, and endurance.

After the intervention, study group B had higher muscle strength scores than study group A. These may have been because the two types of exercise differ by the duration and intensity of muscular contractions involved, as well as by how energy is generated within the muscle. According to McArdle et al. [28], aerobic exercise recruits slow oxidative (type I) fibers, whereas resistance exercise recruits fast glycolytic (type II) fibers and increases in strength and power require exercises of short duration and high intensity, such as resistance exercises.

Another important finding of this study was a significant reduction in the overall fatigue level and improvement in QOL when compared before and after measurements within group. Khodashenas et al. [8] confirmed these results by examining the efficacy of a 12-week aerobic training program (which included walking, running, and different forms of playing) on QOL among childhood with ALL. In addition, Beulertz et al. [29] evaluated the effects of a 6-month, group-based, resistance exercise program for a mixed childhood cancer population on motor performance, level of activity, and QOL. The results of the current study confirmed the findings of

Jarden et al. [6] reported that various physical therapy techniques are used to reduce fatigue and improve

**Table 8** Comparison of the mean values of quality of life before and after treatment for both groups A and B

Variables	Group	Pre-treatment	Post-treatment	Δ	% of improvement	P value	Sig
Generic code scale	Group A	70.91 ± 10.96	76.02 ± 11.01	- 5.111*	7.2%	.0001	S
	Group B	70.29 ± 7.84	77.35 ± 8.51	- 7.056*	10%	.0001	S
Multidimensional fatigue scale	Group A	71.75 ± 11.62	76.41 ± 11.35	- 4.656*	6.4%	.0001	S
	Group B	72.33 ± 8.61	78.41 ± 8.58	- 6.075*	8.4%	.0001	S
Cancer module	Group A	65.96 ± 8.13	69.08 ± 9.24	- 3.122*	4.7%	.0001	S
	Group B	70.01 ± 6.03	72.3 ± 5.86	- 2.281*	3.2%	.001	S

Values of variables are expressed as mean ± SD. Δ(mean difference pre–post) within group

\*Significant at the alpha level ( $P < 0.05$ )

**Table 9** Comparison of the mean values of quality of life after treatment among groups A and B

Variables	Group A	Group B	$\Delta$	P value	Sig
Generic code scale	76.02 $\pm$ 11.01	77.35 $\pm$ 8.51	- 1.322	.701	NS
Multidimensional fatigue scale	76.41 $\pm$ 11.35	78.41 $\pm$ 8.58	- 2.001	.570	NS
Cancer module	69.08 $\pm$ 9.24	72.3 $\pm$ 5.86	- 3.217	.241	NS

$\Delta$ (mean difference post group A–post group B)

muscle strength in cancer patients such as aerobic exercises, stretching, or strengthening exercises. Mock [30] has suggested that endorphins, a class of depressants, are secreted through pituitary gland stimulation resulting from strength exercise, thereby improving the responsiveness of the central nervous system and the body's tolerance to strong stimulation.

Simultaneously, the nervous system produced micro stimulation during exercise, which relieves muscle tension, anxiety, and depression. In addition, exercise enhances metabolism to promote the clearance of metabolic waste and accumulated adrenaline. Exercise also promotes blood circulation, resulting in improved organ function. Thus, exercise has beneficial effects on patients' cardiorespiratory fitness, muscle strength, fatigue, negative moods, and activities of daily living. These explained the improvements in QOL in both groups without significant difference among them.

The current study has several limitations: first, the relatively small sample size. Therefore, a large sample size should be studied. Second, the patients were recruited from only one regional center, thereby limiting generalization. Third, some patients are from far places so it was very difficult to come regularly that is why they refused to participate in the study so further researches are needed for knowing parents and children about the benefits of physical exercise and increasing number of patients who participate in the study, and moreover impact on quality of gait and running style and programs for a younger age group.

## Conclusion

The outcomes of the study showed that there was a significant difference in the selected group of muscles at both sides in group B compared with group A; thus, the modified strength training program is more effective for muscle strength of children with ALL than aerobic training, but there was no significant difference between the two interventions on QOL.

## Abbreviations

ALL: Acute lymphoblastic leukemia; CCHE: Cancer Children Hospital Egypt; DNA: Deoxyribonucleic acid; EMD: Electromechanical delay; HRmax: Maximum heart rate; NS: Non-significant; PedsQL™: Pediatric Quality of Life Inventory; P value: Probability value; QOL: Quality of life; RM: Repetition maximum; S: Significant; Se: Sensitivity; Sp: Specificity; SPSS: Statistical package of social studies; VO2max: Maximum volume of oxygen uptake

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## Authors' contributions

All authors have read and approved the final manuscript. Prof. Dr. Faten Abd Alazim and Prof. Dr. Elham Elsayed substantively revised the study and supported and guided me throughout the procedure of the study. Dr. Nesreen Ali contributed to the anatomical and pathological part of the disease and clarified the treatment protocol and reviewed it in the study. Dr. Dina Elgalaly contributed to the design of the work and analysis data. Doaa Mouhamed would be DM. Faten Abd Alazim would be FA. Elham Elsayed Salem would be E S. Nesreen Ali would be NA. Dina Elgalaly would be DE.

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## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Ethics approval and consent to participate

This study was approved by the ethical committee, Faculty of Physical Therapy, Cairo University on 28 February 2016 No: P.T.REC/012/001232. It was also approved by SMAC (Scientific and Medical Advisory Committee), CCHE 57357, Cairo on 23 Mar 2016 as (appendix V). It was also approved by IRB ethical committee on 2 February 2017 and renew every year.

All of the subjects' parents provided a written informed consent after being provided with a complete verbal and written explanation about the study's objectives, as well as the risks and benefits that were involved.

## Consent for publication

Not applicable

## Competing interests

The authors have no conflicts of interest to disclose.

## Author details

<sup>1</sup>Department of Physical Therapy for Growth Development Disorders in Children and its Surgery, Faculty of Physical Therapy, Cairo University, Giza, Egypt. <sup>2</sup>Almonoufia, Egypt. <sup>3</sup>Pediatric Oncology and Hematology at National Cancer Institute, Cairo University, Cairo, Egypt. <sup>4</sup>Pediatric Oncology and Hematology, Children Cancer Hospital Egypt, Cairo 57357, Egypt. <sup>5</sup>Clinical Research, Children Cancer Hospital Egypt, Cairo 57357, Egypt.

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