European **Rev**iew for **Med**ical and **Pharmacol**ogical **Sci**ences | 2022; 26: 3950-3957

The efficacy of aerobic training on the pulmonary functions of hemophilic A patients: a randomized controlled trial

H.M. FARES[1], S.H. AHMED[2], E.S. FARHAT[3], M.S. ALSHAHRANI[4], W.K. ABDELBASSET[5,6]

[1]Department of Physical Therapy for Internal Medicine, Faculty of Physical Therapy, Ahram Canadian University, Cairo, Egypt
[2]Department of Internal Medicine, Clinical Hematology Unit, Faculty of Medicine, Cairo University, Giza, Egypt
[3]Department of Chest Diseases, Faculty of Medicine, Fayoum University, Fayoum, Egypt
[4]Department of Medical Rehabilitation Sciences, College of Applied Medical Sciences, King Khalid University, Abha, Saudi Arabia
[5]Department of Health and Rehabilitation Sciences, College of Applied Medical Sciences, Prince Sattam bin Abdulaziz University, Al-Kharj, Saudi Arabia
[6]Department of Physical Therapy, Kasr Al-Aini Hospital, Cairo University, Giza, Egypt

Abstract. – OBJECTIVE: The present study investigated the efficacy of a program of aerobic exercise on pulmonary functions in adult males with hemophilia A (HA).

PATIENTS AND METHODS: 40 patients with HA who met the eligibility criteria (40 HA; age range: 20-39 years) were invited to participate in the study. The patients were divided into two groups, 20 per each. Participants in the study group (A) underwent selected physical therapy program, along with aerobic training sessions on a cycle ergometer (50-60% heart rate reserve, moderate intensity), while the control group (B) underwent a selected physical therapy program only. The pulmonary functions (FVC, FEV_1, FEV_1/FVC, PEF, PIF, and MVV) were measured before and after treatment program.

RESULTS: There were noteworthy statistical differences between pre- and post-measurements in the study group in all measured variables ($p < 0.05$). There were also significant statistical differences between the study and control groups in all measured variables post treatment ($p < 0.05$).

CONCLUSIONS: This study has demonstrated that hemophilic A patients' pulmonary functions have improved significantly following aerobic exercise training. As a result, aerobic exercise can be used in addition to medical treatment for hemophilic A patients.

Key Words:
Aerobic exercises, Pulmonary functions, Hemophilia.

Introduction

Hemophilia is a rare X-linked congenital bleeding disorder characterized by a deficiency of coagulation factor VIII (FVIII) in hemophilia A and factor IX (FIX) in hemophilia B. Hemophilia A affects far more people than hemophilia B. Hemophilia A accounts for 80-85% of all hemophilic cases, according to estimates[1].

Hemophilia A is commonly known as classical hemophilia caused by a genetic mutation in the F8 gene on the X chromosome, which results in insufficient quantities of the clotting factor VIII[2]. It is mostly expressed in men, however some females who possess the gene may experience mild or, in rare cases, severe bleeding symptoms. Although there is no definite cure for hemophilia, effective medicines have been established; most affected individuals can live full, productive lives if proper medication and care are maintained[3].

When it comes to the bleeding characteristics of hemophilia, the range is extremely wide. It ranges from having little or no propensity to bleeding after minor trauma or with routine daily activities, to potentially life-threatening bleeds. Consequences of untreated hemophilia, which is typified by recurrent, acute joints bleeding and chronically synovitis include swelling, joint discomfort, muscle atrophy, and deformity[4]. Severe hemophilia is a life-threatening condition that can be fatal if left untreated. Flexion contracture,

Corresponding Author: Walid Kamal Abdelbasset, Ph.D; e-mail: walidkamal.wr@gmail.com

uneven gait, and diminished balance are some of the other clinical indications of frequent musculoskeletal bleeding; the confluence of these signs and symptoms can lead to decreased functional ability as well as a poor quality of life. Using the proper coagulation factor as a preventative measure can lessen the severity and frequency of bleeding[5].

Hemophilic children seem to be less physically active than healthy children, with a massive decrease in muscle strength, particularly in the lower limbs, as well as a substantial decrease in exercise capacity, which may be due to a lack of sufficient intensity in daily physical activities and a reduced ability to participate in intensive physical activities when compared with healthy controls children[6].

Participants in physical activity who have hemophilia can improve their quality of life, which was formerly restricted until 1970s, when the use of coagulation cascade was provided[7]. When it comes to hemophilia, exercise is highly encouraged as part of the existing level of care, and it is also widely promoted. While the relevance of physical therapy, physical exercise, training, and sports as part of the overall treatment plan in hemophilia individuals has long been recognized and accepted, it has only just begun to be fully recognized and implemented. While exercise presents particular challenges for hemophilia individuals, such as the danger of injury, and overloaded and potential bleeding, physical exercise and aerobic fitness can help to improve pulmonary function when performed correctly under the supervision of a hemophilia specialist[8].

The current study has been proposed to ascertain pulmonary functions in hemophilic patients in order to determine the impact of aerobic exercise on the pulmonary volumes of hemophilic A patients and to show that aerobic exercise should be an integral part of life for individuals with hemophilia. We hypothesized that encouraging hemophilic A patients to do aerobic exercise training improves the pulmonary function, assuming that habitual exercise training enhances many advantageous physical, psychological, and physiological influences in hemophilic A patients.

Patients and Methods

Study Design

Between May 2019 and September 2021, a randomized controlled trial study was conducted on two parallel groups, active and control, at the Red Crescent Hospital, Egyptian Ministry of Health. Based on their diagnosis, 40 males with mild or moderate hemophilia A (1-5% clotting factor activity) participated in this study, referring and then being followed by a hematologist. The aim and nature of the study were explained for each participant before initiating the study program.

Participants' Selection Criteria

Hemophilic patients were included in the study depending on the following criteria: (1) diagnosed with mild or moderate hemophilia A, (2) aged 20-39 years, (3) having no functional disturbances found by conditions other than hemophilia, and (4) being clinically stable having an ongoing prophylactic treatment (prophylaxis is the treatment by intravenous injection of a factor VIII concentrate to avoid any predictable hemorrhage aiming at maintaining ordinary musculoskeletal performance by averting blood loss and joint destructions. Treatment with 15-40 IU/kg per dose managed 3 times a week is the recommended prophylactic strategy.

Patients with a sustained joint bleeding in either knees or ankles 2 weeks after tests, any deformity that restrict with the training program and coexistence of further bleed diathesis (e.g., platelet function abnormalities, and von Willebrand disease) were also excluded.

All subjects' medical histories were meticulously documented, as well as their weights and heights, and the body mass index (BMI) was determined for each participant. Using a block randomization, the patients were divided into two groups, 20 per each. Allocation was concealed using sealed opaque envelopes. Participants in the study group (A) had to undergone elected physiotherapy program, along with aerobic training sessions on a cycle ergometer, while the control group (B) had to undergone only the elected physiotherapy program.

Evaluation Parameters

The following evaluation pulmonary functions parameters were measured before and after the intervention by a digital spirometer (Medical Graphics Corporation, St. Paul, Minnesota, MN, USA) in the sitting position: Forced Vital Capacity (FVC), Forced Expiratory Volume in 1st second (FEV_1), FEV_1/FVC ratio, Maximum Voluntary Ventilation (MVV), Peak Inspiratory Flow (PIF), and Peak Expiratory Flow (PEF).

Measurement of Respiratory Parameters

During the measurement, subjects were informed that a maximum attempt was mandatory for the accuracy of test outcome. Measurement was processed while the subject was sitting in a comfortable position. Each individual wore a mouthpiece that was unique to them. The patient's nose was sealed with a plug, and the mouthpiece was employed without a gap in the rim. The individual was audibly encouraged throughout the assessment.

FVC Measurement

An inhalation-exhalation test was used in which the patient breathed normally for three cycles, then quickly and deeply exhaled following a powerful and deep maximum inspiration. FEV_1 and FEV_1/FVC% values have been recorded during this assessment.

MVV Measurement

The subject completed the measurement with maximal fast and deep breathing for 12 seconds[9].

Treatment Programs

The experimental group (group A) performed aerobic exercise training bicycle ergometer (Corival 2015, Lode BV, Groningen, The Netherlands). Periodic adjustment of the intensity was done throughout the training period. The ergometer is an electronic braked cycle ergometer. It encloses an electronic meter demonstrating pedal rebellions per min, time function and total pedal rebellions. It also includes a pedal strap to fix the participant foot. The aerobic exercise session consisted of 5 min warm-up exercises in the form of a gentle stretch and pedaling on a bicycle ergometer starting at lower intensity, and then the active phase consisted of pedaling while gradually increasing resistance based on 50-60% heart rate reserve (moderate intensity). The treatment session was ended with cool down period in the form of unloaded cycling for other 5 min. The exercise was immediately stopped if the patient felt pain, fainting or shortness of breath.

The exercise duration was 30 minutes, three times a week for two successive months. Progression was done by gradually increasing the resistance by 5 watts every week, such that by the 8^{th} week, the subjects were exercising at 40 watts power.

For two months, the selected physical therapy program was also held three times a week. It included mobilization, coordination, as well as strengthening and flexibility exercises. Depending on the patient's condition, a 10-minute selected mobilization of the spine, hips, knees, ankles, shoulders, elbows, or wrists was performed from sitting and standing positions. Standing with feet in a narrow position, standing and walking in tandem, single leg stance (added difficulty by closing the eye or using a ball), one leg stands and doing motions like "8" with the other leg are all examples of coordination exercises.

Sample Size

Using data from a pilot study with 5 people per group, obtained with the G*Power statistical software (version 3.1.9.2; Franz Faul, Universitat Kiel, Germany) to calculate sample size, we discovered that this study required a sample size of 20 subjects per group. A power of 80, α-error of 0.05, effect size of 0.91, and DF of 38 were used in the calculation.

Statistical Analysis

Using an unpaired t-test, we were able to compare the features of the subjects in each group. A Chi-squared test was used to examine the distribution of severity among the various populations. To ensure that data were normal, the Shapiro-Wilk test was used. Groups were homogeneous after Levene's test for homogeneity of variances. A mixed-design MANOVA was used to compare effects on FVC, FEV_1, FEV_1/FVC, PEF, PIF, and MVV within and across groups. For following multiple comparisons, post-hoc tests were performed using the Bonferroni correction. All statistical tests were conducted with a significance level of $p < 0.05$. As a result, SPSS version 25 for Windows was used to carry out all statistical analyses (IBM Corp., Armonk, NY, USA).

Results

Subject Characteristics

In terms of subject characteristics, including demographics, activated partial thromboplastin clotting time (aPPT), factor VIII and severity distribution, there was no discernible difference between the groups ($p > 0.05$), as shown in Table I.

Effect of Treatment on FVC, FEV_1, FEV_1/FVC, PEF, PIF and MVV

An interaction between time and treatment was shown to be significant [$F_{(6,33)} = 23.01$, $p = 0.001$, $\eta^2 = 0.81$]. The main time effect [$F_{(6,33)}$ =

Table I. Comparison of subject characteristics between study and control groups.

	Mean ± SD		
	Study group	**Control group**	***p*-value**
Age (years)	28.3 ± 3.11	27.8 ± 4.29	0.67
Weight (kg)	83.25 ± 7.27	81.15 ± 6.05	0.33
Height (cm)	172.05 ± 6.24	170.35 ± 6.39	0.4
BMI (kg/m²)	28.12 ± 1.95	27.94 ± 1.04	0.73
aPTT	45.75 ± 3.11	47.15 ± 4.45	0.25
Factor VIII (%)	16.5 ± 3.64	15.8 ± 4.66	0.6
Severity			
Mild	14 (70%)	12 (60%)	0.51
Moderate	6 (30%)	8 (40%)	

BMI: Body Mass Index; aPTT: activated partial thromboplastin clotting time; SD: standard deviation; *p*-value: level of significance.

33.75, $p = 0.001$, $\eta^2 = 0.86$] was significant. In the main analysis, the treatment effect had a statistical significance [$F_{(6,33)} = 2.61$, $p = 0.03$, $\eta^2 = 0.32$].

Within Group Comparison

A significant rise in FVC, FEV1 and FEV_1/FVC was observed in the study group following therapy ($p = 0.001$), while the control group showed no significant change ($p > 0.05$) in these measurements. The study group's percent change in FVC, FEV_1, and FEV_1/FVC was 8.88, 15.87, and 6.32%, while the control group's percent change was 1.45, 1.53, and 0.27% (Table II).

In the study group, PEF, PIF, and MVV increased significantly after treatment compared to pre-treatment ($p = 0.001$), while the control group showed no significant change ($p > 0.05$). The study group's percent change in PEF, PIF, and MVV was 23.91%, the control group's was 5.49%, and both groups' were 0.35% (Table III).

Between Groups Comparison

Prior to therapy, there was no statistically significant difference between the groups ($p > 0.05$). The FVC ($p = 0.001$), FEV_1 ($p = 0.001$), and

Table II. Mean FVC, FEV_1 and FEV_1/FVC pre- and post-treatment of study and control groups.

	Study group Mean ± SD	Control group Mean ± SD	MD (95% CI)	*p*-value
FVC (L)				
Pre-treatment	4.05 ± 0.16	4.13 ± 0.17	-0.08 (-0.19: 0.02)	0.12
Post-treatment	4.41 ± 0.22	4.19 ± 0.16	0.22 (0.09: 0.35)	0.001
MD (95% CI)	-0.36 (-0.42: -0.29)	-0.06 (-0.12: 0.01)		
% of change	8.88	1.45		
p-value	0.001	0.11		
FEV_1 (L)				
Pre-treatment	3.15 ± 0.23	3.26 ± 0.25	-0.11 (-0.27: 0.04)	0.15
Post-treatment	3.65 ± 0.26	3.31 ± 0.26	0.34 (0.16: 0.5)	0.001
MD (95% CI)	-0.5 (-0.6: -0.39)	-0.05 (-0.15: 0.05)		
% of change	15.87	1.53		
p-value	0.001	0.33		
FEV_1/FVC (%)				
Pre-treatment	77.73 ± 5.03	78.84 ± 4.41	-1.11 (-4.14: 1.91)	0.46
Post-treatment	82.65 ± 3.49	79.05 ± 4.43	3.6 (1.03: 6.15)	0.007
MD (95% CI)	-4.92 (-6.78: -3.05)	-0.21 (-2.08: 1.65)		
% of change	6.32	0.27		
p-value	0.001	0.82		

SD: standard deviation; MD: mean difference; CI: confidence interval; *p*-value: level of significance; FVC: forced vital capacity; FEV_1: forced expiratory volume in one second.

Table III. Mean PEF, PIF and MVV pre and post treatment of study and control groups.

	Study group Mean ± SD	Control group Mean ± SD	MD (95% CI)	*p*-value
PEF (L/min)				
Pre-treatment	4.85 ± 0.38	4.92 ± 0.48	-0.07 (-0.31: 0.24)	0.59
Post-treatment	6.01 ± 0.78	5.19 ± 0.71	0.82 (0.33: 1.29)	0.001
MD (95% CI)	-1.16 (-1.49: -0.81)	-0.27 (-0.61: 0.07)		
% of change	23.91	5.49		
p-value	0.001	0.12		
PIF (L/min)				
Pre-treatment	4.77 ± 0.45	4.82 ± 0.41	-0.05 (-0.26: 0.28)	0.94
Post-treatment	5.61 ± 0.62	4.94 ± 0.42	0.67 (0.32: 1.01)	0.001
MD (95% CI)	-0.84 (-0.99: -0.66)	-0.12 (-0.27: 0.05)		
% of change	17.61	2.49		
p-value	0.001	0.17		
MVV (L/min)				
Pre-treatment	128.65 ± 3.45	127 ± 6.23	1.65 (-1.56: 4.88)	0.3
Post-treatment	135.4 ± 3.06	127.45 ± 6.28	7.95 (4.78: 11.11)	0.001
MD (95% CI)	-6.75 (-7.73: -5.76)	-0.45 (-1.44: 0.52)		
% of change	5.25	0.35		
p-value	0.001	0.51		

SD: Standard deviation; MD: Mean difference; CI: Confidence interval; *p*-value: level of significance; PEF: peak expiratory flow; PIF: peak inspiratory flow; MVV: maximum voluntary ventilation.

FEV_1/FVC ($p = 0.01$) of the study group were significantly higher than those of the control group after therapy ($p = 0.01$). According to Table II and III, there was a statistically significant rise in the study group's PEF, PIF, and MVV ($p = 0.001$) at the end of the study program.

Discussion

Patients with hemophilia are prone to a sedentary lifestyle, which can lead to health complications. Sedentary behavior has a variety of negative effects on the human body. Lipid metabolism, muscle glucose transporter activity, and carbohydrate metabolism are all harmed, as is lipoprotein lipase activity. As a result, there is an increased risk of death from any cause, cardiovascular disease, cancer, and metabolic diseases including diabetes, hypertension, and dyslipidemia, as well as musculoskeletal problems like arthralgia and osteoporosis, depression, and cognitive impairment. The public's health can be improved by eliminating sedentary habits and increasing physical activity, which may be able to counteract the negative effects of sedentary behavior, according to some research[10].

As a result of the danger of sports-related injuries, hemorrhage, and morbidity, individuals with hemophilia were prohibited from participating in sports. Studies[7] have shown that physical activity and proper sports activities (non-contact sports) improve physical, medical, and psychological functions in hemophilic individuals. Improved joint mobility and muscle strength are all linked to isometric, isotonic, and isokinetic activities, as well as better social relations.

Studies in hemophilic individuals have also revealed that exercise may increase coagulation parameters, such as endogenous FVIII activity and von Willebrand factor (VWF) after 10 min of maximal exercise, implying that adequate exercise may, to a certain extent, reduce the risk of bleeding[7].

In this current Egyptian's study, we compared pulmonary function in hemophilia A patients before and after training with moderate intensity aerobic exercise program, hypothesizing that encouraging hemophilic A patients for aerobic exercise training improves the pulmonary function.

Between May 2019 and September 2021, 40 hemophilic A men were investigated. The findings of this study clearly show that pulmonary function in males with hemophilia A significantly improved after therapy with an aerobic exercise program. The following parameters were improved in the aerobic exercise group: FVC, FEV_1, FEV_1/ FVC, PEF, PIF, and MVV. There were also significant differences between the study and control groups in all these parameters favoring the study group. Our findings revealed the existence of a beneficial relationship between aerobic exercise training and pulmonary function. Pulmonary functions have not been extensively studied in hemophilia patients.

In the current study, aerobic exercise training for two months has resulted in a considerable rise in pulmonary functions, which has led to an increase in respiratory muscle strength and/or endurance. This finding was consistent with the earlier published report's findings[11].

Mohamed and Sherief[12] used the same intensity (moderate intensity aerobic exercise training by bicycle ergometer) on a study conducted on 30 hemophilic boys.

This favorable link is consistent with other previously published studies[13] that concluded that athletes have higher levels of lung function than sedentary adults. Other reports[14,15] found that aerobic exercise training improved pulmonary function in a variety of patient groups, including asthma patients and overweight children and also in HIV patients.

The current finding was supported by İşleyen and Dağlıoğlu, who conducted a study on 24 male sedentary individuals between 18-23 years, participating in the aerobic exercise program for three days per week for 8 weeks. There were statistically significant improvements in VC, FVC, FEV_1, FEV_1/FVC % and MVV values of the experimental group. There was no significance in the other data[16].

A previous study[17] on 65 healthy adult volunteers in the age range of 20-35 years found that the mean values of the following parameters: FVC, FEV_1, FEF max, IC, and MVV were statistically significantly higher after performing aerobic exercise training than before. Conversely, Cheng et al came to the conclusion that the mean value of FEV_1/FVC is not statistically significant before and after performing aerobic exercise training[18].

According to Erickson et al[19], aerobic activity on a treadmill raised VO_2 max in aged subjects. They proposed that moderate-intensity aerobic exercise increased oxygen intake and activated dormant alveoli, and that repeated inspiration and expiration stimulation promoted alveolar compliance as a result of the FVC increased. More air may enter the alveoli when more inactive alveoli were activated, and enhanced alveolar compliance might be ascribed to improved lung elasticity and more air expiration. The FEV_1 is a common index of airflow resistance in the respiratory tract[20].

In the current study, FEV_1 considerably increased following aerobic exercise. This suggests that aerobic exercise enhances respiratory tract air flow. Bağıran et al stated that when a big lung volume is provided, the lung expands substantially and has a large contractile force, and the width of the respiratory tract is enlarged to lower air flow resistance[21]. As a result of our findings, we may conclude that FEV_1 improves as a result of lung expansion during aerobic activity, which introduces a higher volume of air into the airways and broadens the respiratory tract. The FEV_1/FVC ratio has been shown to be an indication of airway blockage[22].

Song and Kim[22] investigated the effect of exercise on FEV_1/FVC and discovered that strengthening respiratory and trunk muscles, as well as improving rib cage movement, had a beneficial influence on FEV_1/FVC. FVC/FEV_1%, which appeared to increase somewhat after exercise in the current study, with a significant difference. This finding also shows that the exercise used in this study was a muscle strengthening or rib cage expansion exercise combined with a direct stimulating activity for alveoli combined with high intensity aerobic exercise. After aerobic exercise training, the mean values of FEV_1 as a percentage of FVC (FEV_1/FVC%) and MVV were statistically significant when compared to before aerobic activity training[23]. These enhancements improve the participants' physical work capacity.

The current study's findings corroborated the viewpoint expressed by Ozdal et al[24], who affirmed that endurance training enhances lung capacity and sustained ventilation. The improved outcomes following aerobic exercise training are comparable with the findings of Kalkan and Daglioglu[25], who revealed that swimmers have better vital capacity and pulmonary function performance.

Some limitations were demonstrated in our current study. There is no statistical significance among distinct age categories. This could be owing to a limited number of individuals who have a specified age range. The relatively small cohort size is one of our study's shortcomings (although larger than previously reports conducted on patients with hemophilia). Future studies are required to assess hemophilic patients with older age where pulmonary function could be more impaired.

Conclusions

One can speculate from this study that encouraging hemophilic A patients for moderate intensity aerobic exercise training improves the pulmonary function, thus regular physical activity should be essential part of treatment strategy for hemophilic A patients, as it has many advantageous physical, psychological, and physiological aspects.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Data Availability

The authors declare that all relevant data supporting the findings of this study are available within the article.

Ethical Approval

This research has been accepted by the Research Ethics Committee of Cairo University's Faculty of Physical Therapy in Egypt (approval No.: 012/003312).

Informed Consent

Before enrollment, all subjects have sighed informed consents.

ORCID ID

Walid Kamal Abdelbasset: 0000-0003-4703-661X.

References

1) Srivastava A, Santagostino E, Dougall A, Kitchen S, Sutherland M, Pipe SW, Carcao M, Mahlangu J, Ragni MV, Windyga J, Llinás A, Goddard NJ, Mohan R, Poonnoose PM, Feldman BM, Lewis SZ, van den Berg HM, Pierce GF; WFH Guidelines for the Management of Hemophilia panelists and co-authors. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia 2020; 26 Suppl 6: 1-158.
2) Kumar R, Bouskill V, Schneiderman JE, Pluthero FG, Kahr WH, Craik A, Clark D, Whitney K, Zhang C, Rand ML, Carcao M. Impact of aerobic exercise on haemostatic indices in paediatric patients with haemophilia. Thromb Haemost 2016; 115: 1120-1128.
3) Putz P, Klinger M, Male C, Pabinger I. Lower physical activity and altered body composition in patients with haemophilia compared with healthy controls. Haemophilia 2021; 27: e260-e266.
4) Cuesta-Barriuso R, Gómez-Conesa A, López-Pina JA. Physiotherapy treatment in patients with hemophilia and chronic ankle arthropathy: a systematic review. Rehabil Res Pract 2013; 2013: 305249.
5) Shrestha A, Su J, Li N, Barnowski C, Jain N, Everson K, Jena AB, Batt K. Physical activity and bleeding outcomes among people with severe hemophilia on extended half-life or conventional recombinant factors. Res Pract Thromb Haemost 2020; 5: 94-103.
6) Engelbert RH, Plantinga M, Van der Net J, Van Genderen FR, Van den Berg MH, Helders PJ, Takken T. Aerobic capacity in children with hemophilia. J Pediatr 2008; 152: 833-838.
7) Negrier C, Seuser A, Forsyth A, Lobet S, Llinas A, Rosas M, Heijnen L. The benefits of exercise for patients with haemophilia and recommendations for safe and effective physical activity. Haemophilia 2013; 19: 487-498.
8) Czepa D, Von Mackensen S, Hilberg T. Haemophilia & Exercise Project (HEP): subjective and objective physical performance in adult haemophilia patients--results of a cross-sectional study. Haemophilia 2012; 18: 80-85.
9) Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, Casaburi R, Crapo R, Enright P, van der Grinten CP, Gustafsson P, Hankinson J, Jensen R, Johnson D, Macintyre N, McKay R, Miller MR, Navajas D, Pellegrino R, Viegi G. Standardisation of the measurement of lung volumes. Eur Respir J 2005; 26: 511-522.
10) Park JH, Moon JH, Kim HJ, Kong MH, Oh YH. Sedentary Lifestyle: Overview of Updated Evidence of Potential Health Risks. Korean J Fam Med 2020; 41: 365-373.
11) Moazami M, Farahati S. The effects of aerobic training on pulmonary function in post-menopausal women. Int J Sport Stud 2013; 3: 169-74.
12) Mohamed RA, Sherief AA. Bicycle ergometer versus treadmill on balance and gait parameters in children with hemophilia. Egypt J Med Hum Genet 2015; 16: 181-187.
13) Chaitra B, Narhare P, Puranik N, Maiyri V. Effect of aerobic exercise training on pulmonary function tests: A pragmatic randomized controlled trail. Int J Pharma Bio Sci 2011; 2: 455-60.
14) Kaufman C, Kelly AS, Kaiser DR, Steinberger J, Dengel DR. Aerobic exercise training improves ventilator efficiency in overweight children. Pediatr Exerc Sci 2007; 19: 82-92.
15) Aweto HA, Aiyegbusi AI, Ugonabo AJ, Adeyemo TA. Effects of Aerobic Exercise on the Pulmonary Functions, Respiratory Symptoms and Psychological Status of People Living With HIV. J Res Health Sci 2016; 16: 17-21.
16) İşleyen G, Dağlıoğlu Ö. The effect of aerobic exercise on pulmonary function and aerobic capacity in sedentary men. Int J Sports Exerc & Train Sci 2020; 6: 80-87.
17) Angane EY, Navare AA. Effects of aerobic exercise on pulmonary function tests in healthy adults. Int J Res Med Sci 2016; 4: 2059-2063.

18) Cheng YJ, Macera CA, Addy CL, Sy FS, Wieland D, Blair SN. Effects of physical activity on exercise tests and respiratory function. Br J Sports Med 2003; 37: 521-528.

19) Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, Kim JS, Heo S, Alves H, White SM, Wojcicki TR, Mailey E, Vieira VJ, Martin SA, Pence BD, Woods JA, McAuley E, Kramer AF. Exercise training increases size of hippocampus and improves memory. Proc Natl Acad Sci USA 2011; 108: 3017-3022.

20) Korean Academy of Cardiorespiratory Physical Therapy. Cardiovascular and Pulmonary: Physical Therapy Intervention; Panmun Education Publication Company: Seoul, Korea, 2014.

21) Bağıran, Y, Dağlıoğlu Ö, Bostancı Ö. The effect of respiratory muscle training on aerobic power and respiratory parameters in swimmers. Int J Sports Exer & Train Sci 2019; 5: 214-220.

22) Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, Coates A, van der Grinten CP, Gustafsson P, Hankinson J, Jensen R, Johnson DC, MacIntyre N, McKay R, Miller MR, Navajas D, Pedersen OF, Wanger J. Interpretative strategies for lung function tests. Eur Respir J 2005; 26: 948-968.

23) Song JW, Kim GD. Effects of core stability training on the pulmonary function and trunk muscle activity in chronic stroke patients. Asia-Pac J Multimed Serv converg Art Human Soc 2016; 6: 101-108.

24) Ozdal M, Daglioglu O, Demir T. Effect of aerobic training program on some circulatory and respiratory parameters of field hockey players. Int J Academ Res 2013; 5: 97-103.

25) Kalkan MK, Daglioglu O. The Effects of 8-Week Aerobic Training Program on Respiratory and Circulatory Parameters of Female Swimmers between 12-14 Years Old. J Edu Train Stud 2018; 6: 202-207.