

Research Paper

Aerobic and Anaerobic Exercise Benefits for Lupus: Fatigue, Fitness, and Life Quality



Somayeh Hashemi¹, Sahar Farahbakhsh², AliAsghar Fallahi^{1*}, Farhad Daryanoosh¹, Mohammad Ali Babaei Beigi³, Narges Jamshidian Tehrani⁴

1. Department of Exercise Sciences, Faculty of Education and Psychology, Shiraz University, Shiraz, Iran.

2. Department of Occupational Therapy, School of Rehabilitation Sciences, Zanjan University of Medical Sciences, Zanjan, Iran.

3. Department of Cardiology, School of Medical Sciences, Shiraz University of Medical Sciences, Shiraz, Iran.

4. Organ Transplant Center, Abu_alisina Hospital, Shiraz University of Medical Science, Shiraz, Iran.



Citation Hashemi S, Farahbakhsh S, Fallahi A, Daryanoosh F, Babaei Beigi MA, Jamshidian Tehrani N. Aerobic and Anaerobic Exercise Benefits for Lupus: Fatigue, Fitness, and Life Quality. *Iranian Rehabilitation Journal*. 2024; 22(3):499-508. <http://dx.doi.org/10.32598/irj.22.3.2081.1>

doi <http://dx.doi.org/10.32598/irj.22.3.2081.1>

Article info:

Received: 03 May 2023

Accepted: 05 Sep 2023

Available Online: 01 Sep 2024

ABSTRACT

Objectives: This study evaluates the effects of combining aerobic running and anaerobic Pilates exercises to reduce fatigue improve cardiovascular and muscular fitness, and enhance the quality of life (QoL) in systemic lupus erythematosus (SLE) patients.

Methods: A total of 19 SLE patients with index SLE disease activity index (SLEDAI) scores ≤ 4 were randomly assigned into an intervention group (n=10), undertaking the combined exercise program, and a control group (n=9), undertaking normal activities of daily living only. The combined exercise program lasted 8 weeks and consisted of three 1-h weekly sessions. In both groups, functional capacity, cardiovascular fitness, muscle endurance capacity and QoL were assessed before and following the programmed activity or ADL only. The data were analyzed by the SPSS software, version 18 at the significance level of 0.05.

Results: The results confirm that this combined exercise program provides significant benefits over activities of daily living concerning pre-test and post-test difference scores for functional capacity (VO_{2peak} 1.86 \pm 1.45 vs -0.95 \pm 1.43 mL/min/kg, $P < 0.01$). Significant benefits were also observed for the number of sit-ups achieved (11.30 \pm 9.91 vs 0.5 \pm 1.06, $P < 0.01$), sit and reach improvements (6.92 \pm 5.09 vs 0.5 \pm 0.92 cm, $P < 0.05$), subjective fatigue (-3.38 \pm 5.59 vs 1.75 \pm 1.48, $P < 0.05$), and regarding the overall mean of summed QoL subscales scores (10.80 \pm 4.90 vs 0.06 \pm 1.56).

Discussion: Combining aerobic and anaerobic exercises can mitigate subjective fatigue and significantly improve functional capacity, myocardial metabolism, muscular endurance, flexibility, and QoL in SLE patients.

Keywords:

Systemic lupus erythematosus (SLE), Exercise capacity, Muscular endurance, Heart rate recovery, Rate pressure product (RPP)

* Corresponding Author:

AliAsghar Fallahi, Assistant Professor.

Address: Department of Exercise Sciences, Faculty of Education and Psychology, Shiraz University, Shiraz, Iran.

Tel: +98 (990) 9152455

E-mail: aliiasgharfallahi@gmail.com



Copyright © 2024 The Author(s);

This is an open access article distributed under the terms of the Creative Commons Attribution License (CC-BY-NC: <https://creativecommons.org/licenses/by-nc/4.0/legalcode.en>), which permits use, distribution, and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Highlights

- Anaerobic (delivered by Pilates) and aerobic exercise reduce fatigue in systemic lupus erythematosus (SLE) patients.
- This study emphasized the importance of combined aerobic and anaerobic exercise in improving quality of life (QoL) among SLE patients.
- Cardiovascular and muscular fitness can be improved in SLE patients by doing combined aerobic and anaerobic exercises.

Plain Language Summary

Lupus disease affects the cardiovascular and muscular system, feeling fatigued, and QoL. Accordingly, concerning the results of the present study, combined aerobic and anaerobic exercise can improve cardiovascular and muscular fitness and QoL and mitigate fatigue in lupus patients.

Introduction

Systemic lupus erythematosus (SLE) is a serious autoimmune disease that can affect many major organ systems [1, 2]. While less serious, reduced cardiovascular fitness and impaired muscular strength, endurance, and flexibility are all also common consequences [2, 3]. Chronic generalized fatigue is similarly a frequent and troublesome complaint that affects some 80% of patients [4]. These cardiovascular and muscular deficits, which would impair quality of life (QoL), reflect the adverse consequences of disease-related involvement of pro-inflammatory cytokines, including IL-6, IL-1 and IL-1b [5], which could all impact directly muscle function [6].

However, as these cardiovascular and musculoskeletal abnormalities can also occur in association with a disease-induced sedentary lifestyle, to cause further loss of skeletal and cardiac muscle fitness, a vicious cycle of functional disability, chronic fatigue, and reduced QoL may be generated, irrespective of SLE disease activity [2]. If such a cycle continues, a progressive decline in functional capacity would result and contribute to hastened cardiovascular complications unrelated to disease activity [2, 7, 8]. Other cardiovascular problems apparent in SLE patients include a reduced ability to increase heart rates (HRs) commensurate with demand (i.e. an incompetent chronoscope reserve), a delayed HR recovery (i.e. a prolonged elevation of HR following physical activity), and indicative of impoverished cardiovascular fitness [9-11].

Although many studies demonstrate that SLE is associated with poor cardiovascular and musculoskeletal fitness levels, none appear to have investigated the effects of non-pharmacological rehabilitation to overcome or reverse these deficits [2]. Hence, the effectiveness of exercise programs to reduce fatigue symptoms in SLE patients remains unclear [2]. Ramsey-Goldman et al. (2000) indicated that aerobic range of motion and muscle strengthening exercises appear safe and did not worsen SLE disease activity, and patients did show some improvements in fatigue, functional status, cardiovascular fitness, and muscle strength [12].

Assessment of the responses of these cardiovascular abnormalities to treatment by exercise regimes has been considerably limited, the results suggesting that outcomes relating to fatigue, functional status, cardiovascular fitness, and muscle strength were similar whatever exercise regime was used [13]. However, most of the activity protocols used in these previous studies utilized aerobic exercises only, i.e. with no resistance training component employed to improve muscle strength [7]. As muscle weakness and atrophy could contribute directly to reduced physical fitness and impoverished muscular endurance [2] and thus an increased perception of fatigue, the inclusion of muscle strengthening exercises through resistance training should also be contemplated for use in studies designed to reverse SLE-induced muscular deficits.

The need for this study is that SLE patients often experience fatigue, reduced cardiovascular and muscular fitness, and decreased QoL. These symptoms can be exacerbated by the use of medications and the disease itself. Therefore, there is a need to identify safe and effective interventions that can improve these outcomes.

Previous studies have shown that exercise can be beneficial for SLE patients [14, 15], but there is limited research on the effects of combined aerobic and anaerobic exercise. This article fills this gap by summarizing the existing literature and providing recommendations for exercise programs that can be tailored to individual patient needs.

This original study was performed to evaluate the effects of a fitness regime combining aerobic and resistance training exercises to reduce fatigue and improve cardiovascular fitness and QoL in SLE patients. The philosophical assumptions of this study are based on the principles of pragmatism and positivism. In this study, a pragmatic approach was taken by implementing a combined exercise protocol and evaluating its effects on SLE patients. A positivist approach was taken by conducting the article and analyzing the results to conclude the effectiveness of combined aerobic and anaerobic exercise for SLE patients.

Materials and Methods

This study utilized a pre-test-post-test design to evaluate the effects of a combined aerobic and anaerobic exercise program on fatigue, cardiovascular fitness and QoL in SLE patients. Patient selection adhered to the [American College of Rheumatology \(ACR\)](#) diagnostic criteria for SLE [16]. To ensure consistency, patients with SLE disease activity index (SLEDAI) scores exceeding 4 were excluded. This criterion controlled disease severity and provided a comparable stage of the disease. SLEDAI scores were also used for stratification and matching to minimize potential confounding due to disease activity. Stratification was performed based on age and disease severity, followed by exact matching to pair participants in intervention and control groups. Randomization further facilitated an equitable distribution of confounders, enhancing internal validity. Comprehensive exclusion criteria were established to account for potential independent variables. Patients with concurrent systemic or rheumatic disorders affecting physical function, those engaged in regular exercise, and subjects with mental health issues or severe cardiovascular disease were excluded [16, 17]. Cardiologists and rheumatologists evaluated cardiovascular fitness. To mitigate bias in self-reported QoL assessments, exercise interventions and outcome assessments were conducted separately. This minimized inadvertent influence on participants' QoL perceptions due to participation in the exercise program. Insights from previous studies and expert consultations informed the exercise program's design, ensuring balanced participants' fitness levels and health status [12, 14, 15].

In summary, meticulous identification and control of intervening variables were paramount. Stratification, matching, randomization and exclusion criteria collectively ensured methodological rigor. This systematic approach facilitated accurate evaluation of the exercise program's effects on fatigue, cardiovascular fitness, and QoL, independent of confounding variables.

Pilot study

Before the commencement of the main study, five of the recruited patients participated in a one-month pilot exercise program, to confirm the feasibility of using resistance training exercise patterns in SLE patients. The intensity and type of endurance and sometimes anaerobic Pilates exercise activities were assessed to inform the design of the exercise training protocol to be used in the main study. Because of the generally poor fitness levels of lupus patients, including poor cardiovascular fitness, the exercise regime selected for the main study was a 1-h-long exercise program combining aerobic and sometimes anaerobic activities, the latter made possible by using body weight as the resistive load during Pilates [18]. The patients used in the pilot study were not used in the main study. The 19 remaining patients were randomly assigned to participate in either a supervised exercise group, undertaking a program consisting of combined aerobic and sometimes anaerobic (Pilates) resistance training activities (the active group [n=10]), or to undertake normal ADL-only (the control group [n=9]). All patients gave their written informed consent before their participation.

Cardiovascular fitness assessments

Throughout this research, all cardiovascular assessments were performed in the [Imam Reza Hospital of Shiraz University of Medical Sciences](#), under the supervision of experienced cardiologists and specialist cardiac nurses. Assessments were undertaken on a Trackmaster stress-testing system (full vision USA treadmill tmx425). The protocol used to assess patients' cardiovascular status was a standard Bruce protocol undertaken up to the end of stage 3 (Table 1) [19]. Before each Bruce testing session, the patients were mandated to avoid caffeinated drinks, including tea, for 8-10 h. HR, blood pressure (BP), equal RPP ($HR \times BP$) and 12 lead electrocardiograms were all assessed before, during and at 5 min after the Bruce protocol. The time of each exercise testing session for each individual was between 15.00 and 18.00, to avoid heat and hydration issues. Assessments of cardiovascular fitness used functional capacity (i.e. VO_{2peak}) and HR recovery (HRR). The HRR values at 1, 2 and 3

min following cessation of the 9-min Bruce protocol (i.e. HRR1, HRR2 and HRR3) were obtained by subtracting the HR at 1, 2 and 3 min from the maximum HR during the Bruce protocol.

Muscular endurance and flexibility assessments

Anterior abdominal wall muscular endurance was assessed by counting the maximum number of sit-up repeats possible in one go, i.e. without time limits and rest stops. Meanwhile, muscular flexibility was assessed by the measured improvement in the sit and reach stretch test [20, 21].

Exercise training program

The combined activity program was an 8-week supervised exercise training that was performed for 1 h thrice weekly. Before and following each training session, an exercise physiologist or physiotherapist checked the patients' HR and BP. In the first week the exercises were undertaken for about 40 min to allow acclimatization, but thereafter increased to a standard 60 min. Once fully initiated, each session of the exercise program consisted of 4 stages as follows: a) Warm-up for 10 min; b) Aerobic exercise program including 10 min cycling and 10 min running on a treadmill, both at an intensity of 50%-60% of maximum, as pre-determined in their previous VO_{2peak} measurements; c) 20 min Pilates training using body weight as the resistive load (Table 2) and cool down for 10 min. The Borg scale was used to assess patients' perception of effort during the aerobic exercises being used in stage B. During each session of this training program, the participants' HRs were assessed by polar-frequency meter monitoring (polar Kempele, Finland) and patients were given verbal and visual feedback to enable them to accurately set their HR to the desired 50%-60% of maximum exercise intensity level, the latter as previously determined.

QoL and fatigue assessments

An SLE-specific questionnaire [22] was used to assess patients' QoL, which has been translated into Persian, and its validity and reliability were confirmed [23, 24]. The questionnaire had 34 questions with 5 options based on the Likert scale. The purpose of the questions was to examine the effect of lupus disease on their life and the problems it caused in their life during the past month. A chronic fatigue syndrome (CFS)-specific questionnaire was used to assess subjective general fatigue levels [25], which has been translated into Persian, and its validity and reliability were confirmed as well [26]. The ques-

tionnaire had 10 questions with 4 options based on the Likert scale. The questionnaire was used to examine how the patients usually experience their complaints.

Statistical analysis

The quantitative and qualitative data are presented as Mean \pm SD and frequency (percentage), respectively. To compare variables between and within groups, independent and paired sample t-tests were used. The significance level was set at $P < 0.05$. All data were analyzed with SPSS software, version 19.

Results

As shown in Table 1, a comparison of baseline demographic variables demonstrated no significant differences between the control and the active exercise groups, and no differences were apparent regarding the drugs used by these groups (Table 2).

The results demonstrated that all of the tested cardiovascular variables were similar in the control, and active exercise patient groups before the active group undertook the 8-week combined exercise program. However, following this program, there were clear and significant improvements in all of these variables in the active exercise group, as summarized in Table 3.

Accordingly, there were significant improvements in functional capacity, resting HR, maximum HR during the Bruce protocol, and HRs at the end of stages 1, 2 and 3 of the protocol. There were also clear improvements in HRR and BP values at the end of stages 1-3 of the protocol. As a result, there were matched improvements in the RPP values at the end of Bruce stages 1-3 testing, as well as the maximum HR during stage 3 of the protocol.

The results of muscular endurance and flexibility assessments demonstrated no differences between the control and the active patients before the combined activity program, or ADL only, commenced. However, following the activity program, clear and significant differences became apparent, with significant improvements seen in muscle endurance (more sit-ups) and flexibility (greater measured improvements in the sit and reach test) in the active versus control groups, as summarized in Table 4.

Before the 8-week exercise program, or ADL only, there were no control/active group subjective fatigue differences detected by the use of a CFS-specific questionnaire, nor any QoL differences detected by a specific multi-domain questionnaire used for this purpose. Fol-

Table 1. Demographic details of participants in the intervention and control groups

Demographic Variables	Mean±SD		P
	Control (n=9)	Intervention (n=10)	
Age (y)	31.50±5.52	39.00±13.19	0.160
Height (m)	1.59±0.63	1.63±0.03	0.144
Weight (Kg)	60.33±9.06	67.70±14.82	0.215
BMI (m ² /kg)	23.71±3.31	25.51±5.95	0.435
Disease duration (y)	9.33±3.70	8.55±4.79	0.550
SLEDAI score	1.37±0.51	1.45±0.52	0.746

Iranian Rehabilitation Journal

Abbreviations: BMI: Body mass index; SLEDAI: Systemic lupus erythematosus disease activity index.

lowing the 8-week exercise program, or ADL only, there were clear improvements in both subjective fatigue and QoL in those patients who underwent the exercise program, as summarized in [Table 5](#) and [Table 6](#).

Discussion

The findings of this study indicated the combined aerobic endurance training and anaerobic Pilates resistance training used have produced apparent beneficial effects on reducing reported fatigue and enhancing cardiovascular fitness (functional capacity, RPP, HRR2, HRR3), muscular endurance, flexibility and endurance capacity, and on QoL of the SLE patients tested. There were no recorded detrimental effects in the active exercise group. Given the very limited previous use of resistance exercise training in SLE the current study assessed the effects of using weight to improve fatigue and muscle performance. The use of Pilates training and utilizing body

weight as the resistive load, in combination with aerobic endurance exercise, is the first time such activities have been employed to enhance cardiovascular and muscular performance in SLE patients. The results show that this combination has performed well in these respects, and if used over a prolonged period, would presumably improve cardiovascular health and potentially prolong the life span in SLE patients. The reason behind implementing a protocol consisting of both aerobic and anaerobic exercises is that it can provide a more comprehensive and effective approach to improving cardiovascular and muscular fitness in SLE patients. By combining both types of exercise, SLE patients may experience a more significant improvement in their overall fitness and QoL. Additionally, this type of exercise protocol can be tailored to the individual needs and limitations of each patient, making it a personalized and effective treatment option.

Table 2. Medications used by study patients

Drugs/Supplements	No. (%)	
	Control (n=9)	Intervention (n=10)
Prednisone ≥ 5 (mg/day)	8(88)	4(40)
Hydroxychloroquine ≥200 (mg/day)	6(66.7)	8(80)
Losartan	3(33.3)	2(20)
Atorvastatin	2(22.2)	1(10)
Folic acid/Fe	2(22.2)	5(50)
Calcium supplements	2(22.2)	3(30)

mg: Milligram

Iranian Rehabilitation Journal

Table 3. Comparison of cardiovascular parameters (functional capacity, HR, blood pressure, RPP) before, during and after exercise testing in the control group and the intervention exercise group

Variables	Time Point Before, During and After Bruce Exercise Testing	Mean±SD						P of Differences Between Groups
		Control Group		Intervention Exercise Group		Pre and Post-Program Difference		
		ADL Only	After	Before	After			
Functional capacity	In maximum of exercise testing by MET	10.55±1.97	10.54±1.07	-0.95±1.43	9.40±2.14	11.19±1.59	1.86±1.45	0.002*
	In maximum of exercise testing by VO _{2peak}	36.92±6.90	36.89±3.74	-3.32±5.00	32.9 ±7.49	39.16±5.56	6.51±5.07	
HR (beat/min)	Before Bruce testing	94.11±5.26	89.83±5.30	-0.87±3.83	100.50±8.14	88.55±6.69	-13.94±10.19	0.050
	End of stage 1 of Bruce testing	124.03±6.67	125.16±2.33	1.00±5.94	129.19±11.37	125.00±3.28	-6.39±9.71	0.087
	End of stage 2 of Bruce testing	146.63±10.10	144.68±7.20	-0.78±6.47	154.84±8.45	142.22±7.75	-13.04±9.12	0.007*
	End of stage 3 of Bruce testing	160.77±9.51	157.81±7.34	-1.40±5.23	165.08±13.20	152.14±8.81	-13.20±8.66	0.009*
	Maximum HR	162.55±16.16	152.73±7.08	-8.76±12.90	161.72±4.11	166.12±6.26	5.99 ±8.09	0.009*
	1 minute after cessation of Bruce testing ±HRR1	30.86±5.58	37.52±7.46	6.05±11.48	35.36±7.14	45.68±6.76	10.32±7.97	0.366
Systolic BP (mm Hg)	2 minutes after cessation of Bruce testing ±HRR2	48.11±7.84	48.54±9.54	1.42±10.06	47.60±10.17	64.48±5.78	16.88±12.37	0.012
	3 minutes after cessation of Bruce testing ±HRR3	52.88±9.26	51.75±6.25	0.62±7.24	55.68±8.29	68.89±5.61	13.20±8.66	0.005*
	Before Bruce testing	115.55±5.27	115.71±12.72	1.42±15.73	104.20±32.77	113.88±9.27	11.44±33.8	0.438
RPP (HR×BP)	End of stage 1 of Bruce testing	121.72±3.50	126.05±6.38	4.10±8.16	125.12±4.15	115.70±4.39	-9.42±4.28	<0.001*
	End of stage 2 of Bruce testing	130.00±5.00	128.35±5.43	-1.64±5.43	133.59±8.20	124.60±4.24	-8.99±7.66	0.036*
	End of stage 3 of Bruce testing	139.59±8.23	135.51±7.36	-3.92±13.56	140.36±5.51	128.33±7.90	-10.42±8.74	0.347
Maximum BP during Exercise testing	Maximum BP during Exercise testing	140.55±7.26	139.37±8.10	-1.25 ±12.39	146.84 ±8.39	154.50±4.04	7.65±7.99	0.083
	Before Bruce testing	10870.00 ±700.44	10478.33±1244.85	-128.57±1346.96	10497.20±3363.80	9890.62±1292.55	-1477.22±2119.68	0.016*
	End of stage 1 Bruce testing	15106.30±1082.38	15779.07±881.44	629.43±1475.23	16157.19±1409.45	11484.37±643.61	-1876.96±1446.11	<0.001*
	End of stage 2 Bruce testing	19084.16±1796.65	15106.30±1082.38	-3155.66±2326.20	20719.00±2077.37	16157.19±1409.45	-6318.12±2453.74	0.010*
	End of stage 3 Bruce testing	22455.06±2066.86	21379.07±1411.85	-838.79±1897.80	23167.55±2010.93	19541.77±1843.35	-3985.68±2510.51	0.030*
Maximum during Bruce testing	22926.11±3238.78	21553.03±1987.75	-1246.33±2863.62	23758.15±1636.86	25534.42±1211.23	1776.26±1879.25	0.010*	

Abbreviations: HR: Heart rate; HRR: Heart rate recovery; RPP: Rate pressure product; ADL: Activities of daily living.

*P<0.05, **Metabolic equivalence (1 met=3.5 mL/O₂/kg/ weight of body / min).

Table 4. Results of muscular endurance (sit-ups test) and flexibility (sit and reach test) in control and intervention exercise group

Variables	Mean±SD						P
	ADL Only			Intervention Exercise			
	Before	After	Pre and Post ADL Differences	Before	After	Pre and Post Exercise Differences	
Sit and reach (cm of improvement)	31.50±4.50	32.00±4.40	0.5±0.92	35.00±7.21	41.92±4.00	6.92±5.09	0.002
Sit-Ups (number achieved)	13.62±4.62	14.12±5.27	0.5±1.06	16.46±11.28	27.76±17.00	11.30±9.91	0.007

ADL: Activities of daily living; cm: Centimeter.

Iranian Rehabilitation Journal

Table 5. Results of chronic fatigue questionnaire scores in the intervention exercise and control groups

CFS Questionnaire Score	Mean±SD			P
	Program of Exercises, or ADL Only		Pre and Post Program/ADL Differences	
	Before	After		
Intervention exercise group	11.46±7.22	8.07±5.83	-3.38±5.59	0.021
Control group	11.55±3.97	13.62±3.62	1.75±1.48	

CFS: Chronic fatigue syndrome; ADL: Activities of daily living.

Iranian Rehabilitation Journal

Table 6. QoL subscale scores in the control and intervention exercise groups before and after activities of daily living only or the intervention exercise program

Variables	Mean±SD						P
	Control			Intervention			
	ADL		Before and After ADL Difference	Exercise Program		Before and After Exercise Difference	
Before	After	Before		After			
Physical health score	74.21±18.20	68.75±16.92	-2.5±4.63	79.29±9.13	86.16±8.23	3.75±1.39	0.020
Pain score	63.09±17.25	64.28±14.20	-1.38±6.27	73.80±18.27	86.90±16.56	3.33±4.56	0.196
Planning score	68.75±18.76	69.79±16.02	-1.19±5.75	82.29±22.46	94.79±14.73	12.5±15.43	0.046
Intimate relationship score	71.87±20.86	76.00±21.01	1.20±9.10	75.00±17.67	88.16±17.21	13.16±8.37	0.034
Burden score	51.38±26.57	52.77±24.53	1.38±6.27	69.79±21.79	86.45±15.39	16.66±10.54	0.012
Emotional score	40.10±24.59	42.12±23.61	2.02±4.35	67.70±22.24	81.77±23.77	14.06±13.16	0.028
Body image score	76.66±16.83	79.50±21.79	0.00±2.67	76.66±16.83	86.16±24.02	9.42±11.87	0.048
Fatigue score	70.31±16.95	71.09±19.17	0.78±4.00	83.03±18.29	91.96±8.62	13.54±12.12	0.016
Mean summed scores for all subscales	64.54±12.63	65.53±12.40	0.06±1.56	75.94±5.52	87.79±3.97	10.80±4.90	-

ADL: Activities of daily living.

Iranian Rehabilitation Journal

Decreased cardiovascular performance [8] reduced functional capacity [9] and delayed HR recovery are common problems in unfit SLE patients [10, 11, 19]. Also, myocardial weakness is a potential consequence of SLE and the associated increases in circulating pro-inflammatory factors [27]. According to the results (Table 4), endurance exercise in combination with sometimes anaerobic resistance training has had positive effects on cardiac function. Miossi et al. [11] reported that a 12-week exercise training program is capable of reversing the chronic incompetence of HR recovery in SLE patients. However, there is some debate as to whether myocardial incompetency is related solely to cardiac issues, or instead also related to weakness and incompetency of skeletal muscles causing increased peripheral fatigue.

Generalized and muscle-specific fatigue are important detrimental consequences of SLE [11]. The precise mechanisms by which fatigue occurs in SLE remain unclear, but an increase of some pro-inflammatory cytokines and their effects on the central nervous system may have a contributing role in the generation of SLE-related excess perceived fatigue [4]. Inflammation and abnormal IL-6, IL-1 β , and TNF- α levels could trigger a cascade to cause the occurrence of fatigue in the central nervous system [4]. On the other hand, fatigue may be an intelligent and protective mechanism for humans, and is used to prevent damage that could arise as a consequence of inflammation and or contusion after disease or exercise training. Increasing levels of cytokines could also have effects on the nervous system and thus contribute to the generation of central fatigue. Fatigue has central and peripheral components, and there may be differential central and peripheral fatigue mechanisms in some SLE patients. In SLE patients, there are also different phases of the disease, in the initial phase increased inflammatory markers may have central fatigue effects, but with disease progression, chronically decreased physical activity may contribute to physical unfitness (cardiovascular, muscle strength, and endurance) and thus to more involvement of peripheral mechanisms.

It was thought that more intense exercise training could have had a detrimental effect on the immune system [28]. We thus used low to moderate-intensity aerobic and resistance exercise training (about 50% to 60% of maximum capacity). Some research has shown that exercise training reduces immune system dysfunction in SLE patients. Perandini et al. showed that exercise training (with an intensity 10% lower than the anaerobic threshold) improves the inflammatory milieu in SLE women [29].

The results of the current study also showed improvements in the flexibility, strength, and endurance capacity of muscle, and these improvements appear to have had a positive effect by helping to reduce perceived fatigue, as assessed by a questionnaire. We recommend further research to investigate the efficacy of combinations of resistance and aerobic exercise training in comparison with aerobic or resistance protocols alone to optimize cardiovascular and muscle fitness to overcome fatigue in SLE patients.

Conclusion

Aerobic and sometimes anaerobic Pilates exercises are together able to enhance cardiovascular health and fitness, improve muscle strength and endurance, decrease perceived muscular and general fatigue, and enhance the QoL in SLE patients undertaking these activities. Selected exercise training could, if used regularly, help prevent the generation of a vicious cycle resulting in decreased physical activity and fitness in SLE patients. Since the patients with index SLEDAI scores >4 were excluded, further studies are needed to find the effects of combined aerobic and anaerobic exercises on them. The ACR currently recommends that SLE patients remain active, and exercise regularly, but rest when necessary. More specific guidelines regarding the utility of exercise programs could be provided as more research becomes available. The ACR can with more research add the combined exercise regimen for patients with SLE and other immune-mediated conditions.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Shiraz University of Medical Sciences (Code: IR.SUMS.REC.1395.138). Before registration, all participants read and signed the informed written consent form. The guidelines on research involving the use of human subjects were strictly adhered to according to the Helsinki Declaration.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

Conceptualization: AliAsghar Fallahi and Somayeh Hashemi; Supervision: AliAsghar Fallahi and Farhad Daryanoosh; Methodology: Somayeh Hashemi, Sahar Farahbakhsh; Investigation: Sahar Farahbakhsh, Narges

Jamshidian Tehrani and Somayeh Hashemi; Data collection: Somayeh Hashemi and Narges Jamshidian Tehrani; Data Analysis: Sahar Farahbakhsh and Mohammad Ali Babaei Beigi; Writing the original draft: Sahar Farahbakhsh and Somayeh Hashemi; Review and editing: AliAsghar Fallahi, Mohammad Ali Babaei Beigi and Farhad Dayanoosh; Funding administration: AliAsghar Fallahi.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgments

The authors are grateful to the patients who participated in this study. We are also grateful to the Vice-Chancellor for Research Affairs at Shiraz University of Medical Science for their support. Special thanks to Robert G. Cooper, MRC/ARUK Centre for Integrated Research into Musculoskeletal Ageing, University of Liverpool, UK, for his help in conducting this article.

References

- [1] Ramsey-Goldman R, Rothrock N. Fatigue in systemic lupus erythematosus and rheumatoid arthritis. *PM&R*. 2010; 2(5):384-92. [DOI:10.1016/j.pmrj.2010.03.026] [PMID]
- [2] Balsamo S, Santos-Neto LD. Fatigue in systemic lupus erythematosus: An association with reduced physical fitness. *Autoimmunity Reviews*. 2011; 10(9):514-8. [DOI:10.1016/j.autrev.2011.03.005] [PMID]
- [3] Andrews JS, Trupin L, Schmajuk G, Barton J, Margaretten M, Yazdany J, et al. Muscle strength, muscle mass, and physical disability in women with systemic lupus erythematosus. *Arthritis Care & Research*. 2015; 67(1):120-7. [DOI:10.1002/acr.22399] [PMID]
- [4] Ahn GE, Ramsey-Goldman R. Fatigue in systemic lupus erythematosus. *International Journal of Clinical Rheumatology*. 2012; 7(2):217-27. [DOI:10.2217/IJR.12.4] [PMID]
- [5] Norheim KB, Jonsson G, Omdal R. Biological mechanisms of chronic fatigue. *Rheumatology*. 2011; 50(6):1009-18. [DOI:10.1093/rheumatology/keq454] [PMID]
- [6] Späte U, Schulze PC. Proinflammatory cytokines and skeletal muscle. *Current Opinion in Clinical Nutrition & Metabolic Care*. 2004; 7(3):265-9. [DOI:10.1097/00075197-200405000-00005] [PMID]
- [7] Carvalho MR, Sato EI, Tebexreni AS, Heidecher RT, Schenkman S, Neto TL. Effects of supervised cardiovascular training program on exercise tolerance, aerobic capacity, and quality of life in patients with systemic lupus erythematosus. *Arthritis and Rheumatism*. 2005; 53(6):838-44. [DOI:10.1002/art.21605] [PMID]
- [8] Frieri M. Accelerated atherosclerosis in systemic lupus erythematosus: Role of proinflammatory cytokines and therapeutic approaches. *Current Allergy and Asthma Reports*. 2012; 12(1):25-32. [DOI:10.1007/s11882-011-0236-1] [PMID]
- [9] Sakauchi M, Matsumura T, Yamaoka T, Koami T, Shibata M, Nakamura M, et al. Reduced muscle uptake of oxygen during exercise in patients with systemic lupus erythematosus. *The Journal of Rheumatology*. 1995; 22 (8):1483-7. [PMID]
- [10] do Prado DL, Gualano B, Miossi R, Sá-Pinto A, Lima F, Roschel H, Borba E, et al. Abnormal chronotropic reserve and heart rate recovery in patients with SLE: A case-control study. *Lupus*. 2011; 20(7):717-20. [DOI:10.1177/0961203310397081] [PMID]
- [11] Dogdu O, Yarlioglu M, Kaya MG, Ardic I, Oguzhan N, Akpek M, et al. Deterioration of heart rate recovery index in patients with systemic lupus erythematosus. *The Journal of Rheumatology*. 2010; 37(12): 2511-5. [DOI:10.3899/jrheum.100163] [PMID]
- [12] Ramsey-Goldman R, Schilling EM, Dunlop D, Langman C, Greenland P, Thomas RJ, et al. A pilot study on the effects of exercise in patients with systemic lupus erythematosus. *Arthritis Care & Research*. 2000; 13(5):262-9. [PMID]
- [13] Miossi R, Benatti FB, Lúciade de Sá Pinto A, Lima FR, Borba EF, Prado DM, et al. Using exercise training to counterbalance chronotropic incompetence and delayed heart rate recovery in systemic lupus erythematosus: A randomized trial. *Arthritis Care & Research*. 2012; 64(8):1159-66. [DOI:10.1002/acr.21678] [PMID]
- [14] O'Dwyer T, Durcan L, Wilson F. Exercise and physical activity in systemic lupus erythematosus: A systematic review with meta-analyses. *Seminars in Arthritis and Rheumatism*. 2017; 47(2):204-15. [DOI:10.1016/j.semarthrit.2017.04.003] [PMID]
- [15] Bogdanovic G, Stojanovich L, Djokovic A, Stanisavljevic N. Physical activity program is helpful for improving quality of life in patients with systemic lupus erythematosus. *Tohoku Journal of Experimental Medicine*. 2015; 237(3):193-9. [DOI:10.1620/tjem.237.193] [PMID]
- [16] Fries JF. Methodology of validation of criteria for SLE. *Scandinavian Journal of Rheumatology. Supplement*. 1987; 65:25-30. [DOI:10.3109/03009748709102174] [PMID]
- [17] Petri M. Disease activity assessment in SLE: Do we have the right instruments?. *Annals of The Rheumatic Diseases*. 2007; 66 Suppl 3(Suppl 3):iii61-4. [DOI:10.1136/ard.2007.078477] [PMID]
- [18] Isacowitz R, Clippinger K. *Pilates anatomy*. Champaign, Illinois: Human Kinetics; 2019. [Link]
- [19] Bienias P, Czurzyński M, Chrzanowska A, Dudzik-Niewiadomska I, Irzyk K, Oleszek K, et al. Attenuated post-exercise heart rate recovery in patients with systemic lupus erythematosus: the role of disease severity and beta-blocker treatment. *Lupus*. 2018; 27(2):217-24. [DOI:10.1177/0961203317716318] [PMID]
- [20] Balsamo S, da Mota LM, de Carvalho JF, Nascimento Dda C, Tibana RA, de Santana FS, et al. Low dynamic muscle strength and its associations with fatigue, functional performance, and quality of life in premenopausal patients with systemic lupus erythematosus and low disease activity: A case-control study. *BMC Musculoskeletal Disorders*. 2013; 14:263. [DOI:10.1186/1471-2474-14-263] [PMID]

- [21] Shephard RJ, Berridge M, Montelpare W. On the generality of the "sit and reach" test: an analysis of flexibility data for an aging population. *Research Quarterly for Exercise and Sport*. 1990; 61(4):326-30. [DOI:10.1080/02701367.1990.10607495] [PMID]
- [22] McElhone K, Abbott J, Shelmerdine J, Bruce IN, Ahmad Y, Gordon C, et al. Development and validation of a disease-specific health-related quality of life measure, the LupusQoL, for adults with systemic lupus erythematosus. *Arthritis Care & Research*. 2007; 57(6):972-9. [DOI:10.1002/art.22881] [PMID]
- [23] Hosseini N, Bonakdar ZS, Gholamrezaei A, Mirbagher L. Linguistic validation of the LupusQoL for the assessment of quality of life in Iranian patients with systemic lupus erythematosus. *International Journal of Rheumatology*. 2014; 2014(1):151530. [DOI:10.1155/2014/151530]
- [24] Hosseini N, Bonakdar ZS, Gholamrezaei A, Fatemi A, Karimzadeh H. [Evaluating the validity and reliability of Persian Version of Lupus Quality of Life (LupusQoL) Questionnaire in Iranian Patients (Persian)]. *Journal of Isfahan Medical School*. 2013; 31(260):1836-47. [Link]
- [25] Tench CM, McCurdie I, White PD, D'Cruz DP. The prevalence and associations of fatigue in systemic lupus erythematosus. *Rheumatology*. 2000; 39(11):1249-54. [DOI:10.1093/rheumatology/39.11.1249] [PMID]
- [26] Haddadi M, Zakerian A, Mahmoodi M, Naslseraji J, Parsayekta Z, Aliyari A. Investigation of chronic fatigue syndrome questionnaire validity and reliability: CFS (DSQ revised). *Journal of School of Public Health & Institute of Public Health Research*. 2014; 12(1). [Link]
- [27] Doria A, Iaccarino L, Sarzi-Puttini P, Atzeni F, Turriel M, Petri M. Cardiac involvement in systemic lupus erythematosus. *Lupus*. 2005; 14(9):683-6. [DOI:10.1191/0961203305lu2200oa] [PMID]
- [28] Gleeson M. Immune function in sport and exercise. *Journal of Applied Physiology*. 2007; 103(2):693-9. [DOI:10.1152/jap-physiol.00008.2007] [PMID]
- [29] Perandini LA, Sales-de-Oliveira D, Mello SB, Camara NO, Benatti FB, Lima FR, et al. Exercise training can attenuate the inflammatory milieu in women with systemic lupus erythematosus. *Journal of Applied Physiology*. 2014; 117(6):639-47. [DOI:10.1152/jap-physiol.00486.2014] [PMID]