

Impact of aerobic versus resisted exercise training on systemic inflammation biomarkers and quality of Life among obese post-menopausal women

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Abstract

Background: Although post-menopausal obesity is an important public national health problem in Saudi Arabia, to date no study has evaluated the effects of weight reduction on biochemical & clinical parameters and quality of Life for obese Saudi post-menopausal women.

Objective: The aim of this study was examine the effects of aerobic versus resisted exercise training effects upon systemic inflammation biomarkers and quality of life for obese post-menopausal Saudi women.

Material and Methods: One hundred Saudi post-menopausal obese women participated in this study, their age ranged from 50-58 years and their body mass index (BMI) ranged from 30-35 kg/m². All participants were divided into two equal groups: The first group received aerobic exercise training on treadmill where, the second group received resisted exercise training. Health-related quality of life (SF-36 HRQL), tumor necrosis factor- α (TNF- α), Interleukin-2 (IL-2), Interleukin-4 (IL-4), Interleukin-6 (IL-6) and C-reactive protein (CRP) were measured before and after 3 months at the end of the study.

Results: The mean values of SF-36 HRQL subscale scores were significantly increased, while the mean value of TNF- α , IL-2, IL-4, IL-6, CRP and BMI were significantly decreased in both groups after treatments. There were significant differences between mean levels of the investigated parameters in group (A) and group (B) after treatment with more changes in patients received aerobic exercise training.

Conclusion: The current study provides evidence that aerobic exercise is more appropriate than resisted exercise training in modulating inflammatory cytokines and quality of life among obese post-menopausal women.

Keywords: Aerobic exercise; resisted exercises; inflammatory cytokine; quality of life; obesity; menopause.

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Introduction

Post-menopausal women, especially those with body mass index (BMI) greater than 30 kg/m², have lower health-related quality of life (HRQOL) in physical functioning, energy, and vitality compared with normal-weight women¹. Nearly two-thirds of American adults are overweight or obese². The current epidemic of overweight and obesity

is one of the major public health concerns worldwide³.

The prevalence of overweight and obesity has increased significantly over the past 30 years, with overweight and obesity now affecting 1.5 billion adults globally⁴. Worldwide, 2.8 million people die each year of obesity-related diseases, including type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and metabolic syndrome⁵.

Obesity may significantly reduce HRQOL. A review of 8 studies examining HROQL among women aged over 55 years old concluded that post-menopausal women, especially those with BMI greater than 30 kg/m², have lower HRQOL in physical functioning, energy, and vitality compared with normal-weight women¹. Obesity impacts a variety of dimensions of quality of life, including vitality, bodily pain, and even social functioning. Obese individuals report significantly lower HRQL than nor-

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mal-weight individuals⁶. General health problems, mobility/functional disability, depression and low self-esteem are commonly reported among obese subjects⁷.

Quality of life (QoL) in post-menopausal women may be compromised as a consequence of climacteric symptoms associated to psychosocial and cultural determinants⁸. There is a growing demand for health care proposals aimed at menopausal women and looking to promote a healthier female aging process and with a better QoL⁹. Hormone replacement therapy (HRT) has been indicated to minimize menopausal symptoms; however there are controversies as to whether its effects improve QoL. There are still some questions regarding the risks and benefits of HRT in post-menopausal women^{10,11}.

Aerobic exercise training is an effective and cost-efficient alternative therapy for disorders of anxiety and mood disorders¹². Also, exercise training slow down the progression of cognitive decline¹³, improves performance on tests of cognition and psychological wellbeing¹⁴ and enhances sleep quality¹⁵. However, the available previous studies involving the impact of exercise training upon the quality of life, psychological wellbeing along with systemic inflammation in post-menopausal women is limited in number¹⁶.

As the ideal exercise intensity that efficiently modulates the elevated inflammatory cytokines and abnormal HRQOL among obese post-menopausal women is inconclusive, this study was designed to compare the impact of aerobic versus resisted exercises on inflammatory cytokines and HRQOL in obese post-menopausal women.

Patients and methods

Subjects

One-hundred Saudi post-menopausal obese women participated in this study, their age ranged from 50-58 years and their BMI ranged from 30-35 kg/m². All volunteers were asked to read and sign an informed consent document prior to participation. Women who were smokers, having any endocrine, musculoskeletal, renal, liver, cardiac disorders, diabetes and chest diseases were excluded. Participants were assigned into 2 groups; group (A) received aerobic exercise training for 3 months and group (B) received resisted exercise training. The CONSORT diagram outlining the details of the screening, run-in and randomization phases of the study and reasons for participant exclusion can be found in figure (1). Informed consent was obtained from all participants. This study was approved by the Scientific Research Ethical Committee, Faculty of Applied Medical Sciences at King University.

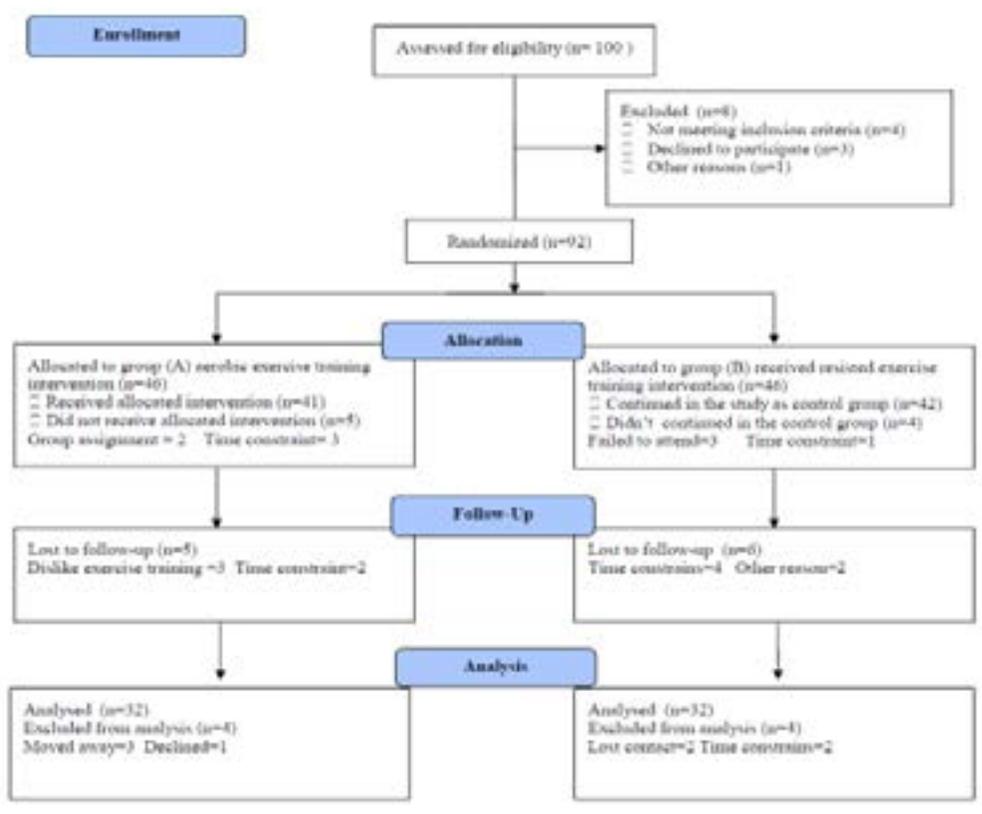


Figure (1): Subjects screening and recruitment CONSORT diagram.

Measurements

1. Health-related quality of life (SF-36 HRQL): The SF-36 included eight subscales: Vitality, Bodily Pain, General Health, Physical Functioning, Social Functioning, Physical Role Functioning, Emotional Role Functioning, and Mental Health. In addition to these subscales, the SF-36 also included a question asking participants to report the amount of change in their general health over the past year referred to as health transition¹⁷.

2. Biochemical analyses: Blood samples were drained from the antecubital vein after a 12-h fasting, the blood samples were centrifuged at + 4 °C (1000 = g for 10 min). Interleukin-2 (IL-2) Interleukin-4 (IL-4), Interleukin-6 (IL-6) levels were analyzed by “Immulite 2000” immunoassay analyzer (Siemens Healthcare Diagnostics, Deerfield, USA). However, tumor necrosis factor- alpha (TNF- α) and C-reactive protein (CRP) levels were measured by ELISA kits (ELX 50) in addition to ELISA microplate reader (ELX 808; BioTek Instruments, USA). Measurements of TNF- α , IL-2, IL-4, IL-6 and CRP were taken before starting of the study (pre-test) and after 12 weeks (post-test).

All measurements were taken before the starting of the study (pre-test) and after three months at the end of the study (post-test).

Procedures

Following the previous evaluation ,all participants were assigned into two groups:

1. Group (A) participated in a treadmill aerobic exercise (Enraf Nonium, Model display panel Standard,

NR 1475.801, Holand) which was conducted according to recommendation of aerobic exercise application approved by the American College of Sports Medicine¹⁸. Training program was included five minutes for warming –up in the form of range motion and stretching exercises , thirty minutes of aerobic exercise training (60-70% of maximum heart rate) and five minutes of cooling down (on treadmill with low speed and without inclination). Participants had three sessions /week for 3 months with close supervision of physical therapist.

2. Group (B) participated in the resistance exercises on some resistance gym machines (Nautilus Sports/Medical Industries, Independence, VA), three sessions of resistance exercise training /week for 3 months. Each session of resistance training program included five minutes for warming –up in the form of range motion and stretching exercises, 30 minutes of resistance exercise training and 5 minutes of cooling down¹⁹.

Statistical analysis

The mean values of the investigated parameters obtained before and after three months in both groups were compared using paired "t" test. Independent "t" test was used for the comparison between the two groups (P<0.05).

Results

Table 1 shows the baseline characteristics of the participants who entered the trial. There was no significant differences in baseline characteristics between the two groups were found.

Table 1: Baseline characteristics of study participants.

Characteristic	Group (A)	Group (B)	Significance
Age (years)	56.42 \pm 4.81	54.97 \pm 5.63	P>0.05
BMI (kg/m ²)	34.28 \pm 3.74	33.52 \pm 3.68	P>0.05
SBP (mmHg)	136.51 \pm 11.46	135.14 \pm 13.12	P>0.05
DBP (mmHg)	82.33 \pm 6.27	80.81 \pm 7.52	P>0.05
Glucose (mmol/L)	4.51 \pm 0.64	4.35 \pm 0.53	P>0.05
ALT (U/L)	40.16 \pm 7.23	38.62 \pm 6.11	P>0.05
AST (U/L)	28.45 \pm 6.18	27.71 \pm 5.39	P>0.05

BMI: Body mass index; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

The mean values of SF-36 HRQL subscale scores and 6MWT were significantly increased, while the mean value of TNF- α , IL-2, IL-4, IL-6, CRP and BMI were significantly decreased in both groups after treatments (Tables 2-5). There were significant differences between mean levels of the investigated parameters of group (A) and

group (B) after treatment with more changes in patients received aerobic exercise training (Tables 6 and 7). These results confirm that aerobic exercise is more appropriate than resisted exercise training in modulating inflammatory cytokines and quality of life among obese post-menopausal women.

Table 2: Mean value and significance of TNF- α , IL-2, IL-4, IL-6 and CRP of group (A) before and at the end of the study.

	Mean +SD		T- value	Significance
	Before	After		
TNF- α (pg/ml)	6.36 \pm 1.74*	4.38 \pm 1.86	7.11	P<0.05
IL-2 (pg/ml)	8.23 \pm 2.31*	4.75 \pm 1.97	6.58	P<0.05
IL-4(pg/ml)	5.72 \pm 1.44*	3.46 \pm 1.23	6.25	P<0.05
IL-6 (pg/ml)	7.85 \pm 2.13*	4.55 \pm 1.81	6.22	P<0.05
CRP(mg/dl)	14.93 \pm 3.82*	8.31 \pm 2.75	8.43	P<0.05

TNF- α : tumor necrosis factor – alpha; IL-2: Interleukin-2; IL-4: Interleukin-4; IL-6: Interleukin-6; CRP: C-reactive protein, (*) indicates a significant difference between the two groups, P < 0.05.

Table 3: Mean value and significance of SF-36 subscale scores of group (A) before and at the end of the study.

SF-36 subscale variables	Mean +SD		T- value	Significance
	Before	After		
SF-36: Health transition	2.75 \pm 0.83*	1.69 \pm 0.61	5.34	P<0.05
SF-36: Physical functioning	72.18 \pm 9.43*	80.32 \pm 10.12	6.76	P<0.05
SF-36: Role functioning: Physical	78.96 \pm 10.15*	87.13 \pm 12.37	6.81	P<0.05
SF-36: Bodily pain	75.11 \pm 7.63*	69.85 \pm 6.25	6.52	P<0.05
SF-36: General health	71.16 \pm 9.44*	77.38 \pm 10.19	7.35	P<0.05
SF-36: Vitality	57.27 \pm 6.32*	66.97 \pm 7.81	6.41	P<0.05
SF-36: Social functioning	85.18 \pm 11.17*	92.26 \pm 13.31	8.15	P<0.05
SF-36: Role functioning: Emotional	92.42 \pm 15.26*	84.51 \pm 14.13	7.86	P<0.05
SF-36: Mental health	84.71 \pm 10.14*	78.24 \pm 8.97	6.91	P<0.05

(*) indicates a significant difference between the two groups; P < 0.05.

Table 4: Mean value and significance of TNF- α , IL-6, IL-8 and CRP of group (B) before and after treatment.

	Mean +SD		T- value	Significance
	Before	After		
TNF- α (pg/ml)	5.93 \pm 1.82*	5.13 \pm 1.78	3.61	P<0.05
IL-2 (pg/ml)	8.15 \pm 2.49*	6.74 \pm 2.21	3.87	P<0.05
IL-4 (pg/ml)	5.63 \pm 1.61*	4.37 \pm 1.54	3.52	P<0.05
IL-6 (pg/ml)	7.65 \pm 2.38*	6.14 \pm 2.25	3.68	P<0.05
CRP (mg/dl)	14.67 \pm 3.91*	11.82 \pm 3.27	4.36	P<0.05

TNF- α : tumor necrosis factor – alpha; IL-2: Interleukin-2; IL-4: Interleukin-4; IL-6: Interleukin-6; CRP: C-reactive protein, (*) indicates a significant difference between the two groups, P < 0.05.

Table 5: Mean value and significance of SF-36 subscale scores of group (B) before and at the end of the study.

SF-36 subscale variables	Mean +SD		T- value	Significance
	Before	After		
SF-36: Health transition	2.61 \pm 0.92*	2.11 \pm 0.84	3.19	P<0.05
SF-36: Physical functioning	73.27 \pm 8.51*	77.68 \pm 8.96	3.23	P<0.05
SF-36: Role functioning: Physical	80.21 \pm 10.39*	84.34 \pm 10.75	3.42	P<0.05
SF-36: Bodily pain	73.92 \pm 7.48*	70.74 \pm 7.23	3.22	P<0.05
SF-36: General health	72.15 \pm 9.87*	75.22 \pm 10.12	3.15	P<0.05
SF-36: Vitality	57.81 \pm 6.42*	62.13 \pm 6.76	3.41	P<0.05
SF-36: Social functioning	86.24 \pm 11.26*	89.57 \pm 11.87	3.27	P<0.05
SF-36: Role functioning: Emotional	90.83 \pm 14.91*	87.14 \pm 13.22	3.31	P<0.05
SF-36: Mental health	84.16 \pm 10.38*	81.25 \pm 10.18	3.45	P<0.05

(*) indicates a significant difference between the two groups; P < 0.05.

Table 6: Mean value and significance of TNF- α , IL-6, IL-8 and CRP of group (A) and group (B) at the end of the study.

	Mean +SD		T- value	Significance
	Group (A)	Group (B)		
TNF- α (pg/ml)	4.38 \pm 1.86*	5.13 \pm 1.78	3.41	P<0.05
IL-2 (pg/ml)	4.75 \pm 1.97*	6.74 \pm 2.21	3.53	P<0.05
IL-4(pg/ml)	3.46 \pm 1.23*	4.37 \pm 1.54	3.68	P<0.05
IL-6 (pg/ml)	4.55 \pm 1.81*	6.14 \pm 2.25	3.47	P<0.05
CRP(mg/dl)	8.31 \pm 2.75*	11.82 \pm 3.27	4.15	P<0.05

TNF- α : tumor necrosis factor – alpha; IL-2: Interleukin-2; IL-4: Interleukin-4; IL-6: Interleukin-6; CRP: C-reactive protein, (*) indicates a significant difference between the two groups, P < 0.05.

Table 7: Mean value and significance of SF-36 subscale scores of group (A) and group (B) at the end of the study.

SF-36 subscale variables	Mean +SD		T- value	Significance
	Group (A)	Group (B)		
SF-36: Health transition	1.69 \pm 0.61*	2.11 \pm 0.84	3.27	P<0.05
SF-36: Physical functioning	80.32 \pm 10.12*	77.68 \pm 8.96	3.46	P<0.05
SF-36: Role functioning: Physical	87.13 \pm 12.37*	84.34 \pm 10.75	3.49	P<0.05
SF-36: Bodily pain	69.85 \pm 6.25*	70.74 \pm 7.23	3.35	P<0.05
SF-36: General health	77.38 \pm 10.19*	75.22 \pm 10.12	3.18	P<0.05
SF-36: Vitality	66.97 \pm 7.81*	62.13 \pm 6.76	3.52	P<0.05
SF-36: Social functioning	92.26 \pm 13.31*	89.57 \pm 11.87	3.32	P<0.05
SF-36: Role functioning: Emotional	84.51 \pm 14.13*	87.14 \pm 13.22	3.61	P<0.05
SF-36: Mental health	78.24 \pm 8.97*	81.25 \pm 10.18	3.54	P<0.05

(*) indicates a significant difference between the two groups; P < 0.05.

Discussion

Regular physical activity may attenuate post-menopausal symptoms related to physical and behavioral changes, positively influencing QOL^{9,11,20}. However, studies on the effects of aerobic exercises alone are found in literature^{11,21}. The fact that resisted exercise enhances muscle

strength²² and body composition²³ is well established, but the association of resisted exercise to QOL improvement has not been demonstrated. Therefore, the aim of this study was to examine the effects of aerobic versus resisted exercise training effects upon systemic inflammation biomarkers and quality of life among sedentary obese post-menopausal women.

The results of our study regarding the QOL proved that both aerobic and resisted exercise training group improved mean values of SF-36 subscale scores in obese post-menopausal women. In addition, there was a significant difference between both groups at the end of the study with more reduction of group (A) received aerobic exercise training. Our findings were consistent with several studies have shown that exercise intervention might enhance health-related quality of life and psychological well-being^{24,31} as Teomana et al. enrolled 81 volunteer post-menopausal women who have been taking hormone replacement treatment (HRT) were divided randomly into two groups: exercise group (which was composed of sub-maximal aerobic exercises for a 6-week period 3 times a week) and control group (received no training intervention). At the end of 6 weeks exercise period, they found statistically significant differences in quality of life, strength, endurance, flexibility and balance parameters in the exercise group²⁴. However, Kanemaru et al. randomly assigned sixty-three osteoporotic women over 60 years to 12 months of muscle exercise or to no intervention, they proved that QOL, grip strength and maximum walking speed increased significantly in the intervention group, while there were no improvements in any of the parameters in the control group²⁵.

While, de Souza Santos et al. conducted a longitudinal study that was quasi-experimental and correlational on 323 post-menopausal elderly women who practiced dancing or walking over a 10-month period, their results demonstrated significant differences for the post-test assessment of functional capacity (5.63%) and general QoL (9.19%)²⁶. In addition, Berin et al. conducted a randomized controlled study on sixty symptomatic and sedentary post-menopausal women with a mean of at least four moderate to severe hot flushes per day or 28 per week will be randomized to an exercise intervention or unchanged physical activity (control group). The intervention consists of 15 weeks of standardized resistance training performed three times a week under supervision of a physiotherapist. They proved that exercise training is an effective treatment for hot flushes among post-menopausal women²⁷. Moreover, Küçükçakır et al. enrolled seventy women with the diagnosis of post-menopausal osteoporosis in a supervised Pilates exercise program twice a week for one year, they concluded that Pilates exercises may be a safe and an effective treatment alternative for the quality of life in patients with post-menopausal

osteoporosis²⁸. In the other hand, Sattar et al. investigated the impact of aquatic-resistance training on Quality of life in twenty four post-menopausal women. The aquatic-resistance training was administered for a period of 8 weeks, 3 days a week; a session each day. Their results revealed aquatic-resistance training produced positive impacts on the quality of life in post-menopausal women²⁹. Also, Bonganha et al. assessed the body composition, muscle strength and quality of life (QoL) changes following 16 weeks of resistance training in 32 healthy, non-active women who were not under hormone replacement therapy (HRT), classified as control group (CG, n=16) and training group (TG, n=16), they concluded that the 16-week program of RT was not enough to influence the perception of QoL in post-menopausal women³⁰. While, Imayama et al. conducted a study one Middle-aged women (n=100) and men (n=102) were randomly assigned to either exercise (360 min/week of moderate-to-vigorous aerobic exercise) or control and HRQOL (SF-36) were assessed at baseline and 12 months and proved that this level of exercise may increase HRQOL among overweight women³¹.

Although the exact mechanism for the effect of exercises on mental health is still unknown, several physiological and psychological mechanisms have been proposed, including increased feelings of self-efficacy, self-perceptions of control, reduced emotional strain and physiological responses to stress, and beneficial effects on neurotransmitters³². In addition, physical activity appears to stimulate neurogenesis³³, enhance neuronal survival³⁴ and increase synaptic plasticity³⁵. Exercise promotes brain vascularization^{36,37}. Social contact may be an important mechanism, and subjects who take regular exercise may, as a result, get positive feedback from other people and an increased sense of self-worth³⁸.

In our study, the mean values of TNF- α , IL-2, IL-4, IL-6 and CRP were significantly decreased in both groups. In addition, there was a significant difference between both groups at the end of the study with more reduction of group (A) received aerobic exercise training. This means that in obese post-menopausal women aerobic exercise is more appropriate for modulating inflammatory cytokine levels than is resisted exercise training. These results are in line with many previous studies^{39,50} as Dekker et al. stated that a 12-week exercise intervention resulted in a significant decrease in circulating IL-6 in subjects with

type 2 diabetes mellitus who underwent an exercise program without weight loss³⁹. In addition, there is evidence of lowered IL-6 and TNF- α after prolonged exercise in obese women⁴⁰ and decreased TNF- α after 12 weeks of aerobic exercise in patients with heart disease⁴¹. Moreover, in obese post-menopausal women with type 2 diabetes, 14 weeks of aerobic exercise decreased CRP by 15% and marginally decreased IL-6 ($p=0.07$)⁴². Likewise, 12 week of exercise reduced IL-18 levels by 17.5% in patients with metabolic syndrome⁴³. On the other side, Rosety-Rodriguez and colleagues in their study on 24 young male adults with Down syndrome who were assigned to perform resistance circuit training with 6 stations, 3 days per week for 12 weeks. They proved that Resistance circuit training improved low-grade systemic inflammation⁴⁴. In addition, Brooks et al. stated that a 16-week resistance training intervention reduced CRP and increased adiponectin levels in older adults with type 2 diabetes⁴⁵. While, Neto et al. proved that high-intensity exercise training program induced an anti-inflammatory effect (a reduction of IL-6, TNF- α & leptin and an increase of IL-4 & IL-10)⁴⁶. In contrast to the previous studies Rall et al. reported that 12 week of high-intensity progressive resistance strength training does not affect TNF α , IL-6, or IL-2⁴⁷.

Also, Rodrigo and colleagues founded that weight-lifting exercises for 6 muscle groups in the upper and lower limbs (2 sets of 8 repetitions each), and the initial load was set at 80% of the 1-repetition maximum load for one month led to improvement in the six minute walking test, health related quality of life (HRQOL) and lower-limb muscle strength, without altering the levels of systemic inflammation⁴⁸. Also, Nikseresht et al. conducted a 12 week study on middle-aged obese men and proved that aerobic interval training consisted of running on a treadmill (4 sets of 4 minutes at 80-90% of maximal heart rate, with 3-minute recovery intervals) had better anti-inflammatory effects (as indicated by the IL-10: TNF- α ratio) than nonlinear resistance training consisted of 40-65 minutes of weight training at different intensities with flexible periodization⁴⁹. While, Kohut et al. proved that aerobic exercise intervention, but not flexibility/resistance exercise, reduces serum inflammatory cytokines including interleukin-18 (IL-18), CRP and IL-6 among older adults; this reduction would be mediated, in part, by improvements in psychosocial factors and/or by β -adrenergic receptor mechanisms⁵⁰.

The exact mechanisms by which physical activity may reduce inflammation are not entirely understood, there are some data pointing to factors that may contribute to an effect of repeated bouts of muscle contraction leading to improvements in inflammatory status over time as exercise training-induced improvements in inflammatory status may also result from the modulation of intracellular signaling pathways and cellular function that are mediated by nitric oxide (NO) and ROS⁵¹. Moreover, the potential mechanisms for the anti-inflammatory effect of exercise may include reduced percentage of body fat and macrophage accumulation in adipose tissue, muscle-released IL-6 inhibition of TNF- α and the cholinergic anti-inflammatory pathway⁵².

The current study has important strengths and limitations. The major strength is the supervised nature of the study. However, all exercise sessions were supervised. Moreover, the study was randomized; hence, we can extrapolate adherence to the general population. In the other hand, the major limitations is only post-menopausal women enrolled in the study, so the value of this study only related to women in this age group, also small sample size in both groups may limit the possibility of generalization of the findings in the present study. Finally, within the limit of this study, aerobic exercise training is recommended for modulation of low grade systemic inflammation and quality of life among obese post-menopausal women. Further researches are needed to explore the impact of weight reduction on quality of life and other biochemical parameters among post-menopausal women.

Conclusion

The current study provides evidence that weight reduction program improves biochemical & clinical parameters and quality of life among obese post-menopausal women. The strengths of this trial include its large sample size and randomized controlled design. There is no doubt that further studies are necessary to understand cellular and molecular mechanisms involved in relationships among weight reduction and changes of overall subscales of SF-36.

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Conflict of interest

None declared.

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