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ORIGINAL ARTICLE

Changes in inflammatory biomarkers following one-year of moderate resistance training in overweight women

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Background: Overweight individuals commonly demonstrate elevated levels of inflammatory and cell adhesion molecules. Elevated levels of inflammation and adhesion have been implicated in the pathogenesis of cardiovascular disease. Aerobic exercise has been shown to be effective in altering specific biomarkers of inflammation and cell adhesion; however, little is known regarding the effects of resistance training (RT) on these biomarkers. This study examined the effects of 1 year of moderate-intensity RT on biomarkers of inflammation and adhesion in healthy, overweight women.
Methods and Results: Participants included 28 (12 control, 16 RT) overweight (body mass index $\geqslant 25\,kg/m^2$) women, aged 25–44 years, studied before and after 1 year of RT. C-reactive protein (CRP), interleukin-6 (IL-6), adiponectin, intracellular adhesion molecule-1, vascular cell adhesion molecule-1 and E-selectin were measured by standard enzyme-linked immunosorbent assays. Body composition, blood pressure, fasting blood lipids, glucose and insulin also were assessed. There were no significant changes in blood pressure, fasting blood lipids, glucose or insulin levels in either group after 1 year. There was also no change in body mass or fat mass in either group; however, there was a significant increase in lean body mass ($P<0.05$) in the RT group. Both CRP ($P<0.01$) and adiponectin ($P<0.01$) demonstrated significant improvements in the RT group, with no change in IL-6. Conversely, there were no associated changes in the biomarkers of cell adhesion in either group.
Conclusions: This study demonstrates that moderate-intensity RT significantly results in modest improvements of inflammatory markers without affecting cell adhesion molecules in overweight women.
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Introduction

Obesity is recognized as a major risk factor for cardiovascular disease (CVD),[1] including coronary heart disease.[2] A number of mechanisms for this relationship have been suggested, including traditional risk factors such as hypertension, dyslipidemia, insulin resistance, type 2 diabetes and the metabolic syndrome.[3–5] Aerobic exercise training has been postulated to reduce the risk of CVD independently and through modification of these traditional risk factors.[6,7] Resistance training (RT) is also considered an integral component of a comprehensive physical activity program for healthy adults,[8] and has shown to be an effective component of a weight management program by means of increasing caloric expenditure, lean body mass and resting metabolic rate.[9]

Individuals who are obese commonly demonstrate elevated levels of blood markers suggesting chronic low-grade systemic inflammation.[10–13] The principle inflammatory molecule associated with obesity is C-reactive protein (CRP), which is primarily synthesized and secreted by the liver in response to adipocyte-derived interleukin-6 (IL-6).[14] Both CRP and IL-6 have been shown to play independent roles in the development of atherothrombosis[15,16] and thus may represent a mechanistic link between obesity and the development of coronary heart disease and overall CVD.

Elevated levels of inflammation also appear to directly mediate the expression of cell adhesion molecules, which have been linked to athroma formation.[17,18] Elevated blood levels of soluble intracellular adhesion molecule-1 (sICAM-1), soluble vascular cell adhesion molecule-1

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(sVCAM-1) and E-selectin are associated with increased severity of atherosclerosis and risk for myocardial infarction.[19–21] Conversely, the adipocyte-derived molecule adiponectin, which appears to have both anti-inflammatory and antiatherogenic properties, has been shown to be lower in obese participants compared to lean controls.[22] This obesity-mediated reduction in adiponectin levels is also inversely related with the upregulation of the adhesion molecules ICAM-1, VCAM-1 and E-selectin.[23]

Women typically demonstrate higher levels of total adiposity as compared to men,[24] which may result in a greater predisposition to chronic inflammation and conditions including atherothrombosis.[25] Although aerobic exercise training has demonstrated the ability to reduce chronic inflammation in a number of populations, the capacity of RT to alter markers of inflammation has not been examined. Because RT has been shown to improve body composition through reduction in body fat stores and increases in lean muscle tissue, it is hypothesized that an intervention utilizing RT will improve markers of inflammation and subsequently markers of cell adhesion. Therefore, the present study was designed to determine the effects of a 1-year RT intervention on biomarkers of inflammation and endothelial cell adhesion in overweight but otherwise healthy, eumenorrheic women. We hypothesized that RT would reduce levels of the inflammatory molecules CRP, IL-6, increase anti-inflammatory adiponectin and thereby reduce levels of the related cell adhesion molecules sICAM-1, sVCAM-1 and E-selectin.

Methods

Participant population and enrollment

Thirty-two overweight women (body mass index (BMI) $\geqslant 25\,kg/m^2$), aged 24–44 years, from the Minneapolis/St Paul Metropolitan area volunteered to participate in this study. Inclusion criteria included: sedentary (<3 sessions/week of physical activity of no greater intensity than brisk walking) with no history of RT for at least the past 6 months; not currently enrolled or plans to enroll in a formal weight loss program; stable body weight ($\leqslant$10% body weight change over the past year); no medical conditions or use of medications that could alter study results (including cholesterol-lowering medications, psychiatric medications at dosages known to alter weight, appetite suppressants, contraceptive or hormone replacement medications, and non-steroidal anti-inflammatory drugs); not currently or recently (past 6 months) pregnant; not currently or recently (past 2 months) lactating; no history of physician-diagnosed menstrual irregularities, significant gynecological conditions or peri/postmenopausal status; blood pressure less than 160/99 mm Hg and not currently or recently (past 6 months) taking hypertensive medications; non-smoker (past 2 years); non-hyperlipidemic (total cholesterol <200 and triglycerides (TG) <174 mg/dl) and normoglycemic (fasting glucose <100 mg/dl); and no history of cancer (past 5 years).

After enrollment, participants were randomly assigned to either a control or RT group. Randomization was stratified and balanced according to age (age 25–34 versus 35–44 years) and baseline body fat percentage (balanced within recruitment waves). Four participants dropped out of the study before the end of the intervention period for personal reasons (all from the control group). The results presented include the remaining 28 participants (12 in the control group and 16 in the RT group), who successfully completed the entire study. All participants were enrolled in this study after being provided a description of the protocol and obtaining written informed consent. The protocol was approved by the University of Minnesota Institutional Review Board for protection of human subject in research, and the study procedures followed were in accordance with institutional and HIPAA guidelines.

Body composition and blood pressure measures

Body composition and blood pressure measurements were performed between 0600 and 0900, after a 12-h overnight fast and at least 48 h after the last exercise session. Body composition was measured by dual energy X-ray absorptiometry (DXA) using a fast transverse speed mode (Prodigy, 3 M, Madison, WI, USA; software version 6.7). Height and weight were measured by a stadiometer and standard electronic scale, respectively (Model 5002, Scale-Tronix Inc., Wheaton, IL, USA). BMI was calculated as weight in kilograms divided by the square of height in meters. Systolic (SBP), diastolic (DBP), and mean arterial (MABP) blood pressure was measured by an automated blood pressure device (Press-Mate BP-8800, Colin Electronics Co. Ltd, San Antonio, TX, USA) in a seated position three times after 5 min of rest with 1 min between measurements and was reported as the mean of the last two measurements.

Blood chemistry measures

Venous blood was drawn from the anticubital vein into chilled tubes containing ethylenediaminetetraacetic acid between 0600 and 0900, after a 12-h overnight fast, at least 48 h after the last exercise session and at least 72 h before initiation or after completion of menstruation to avoid confounding by menstrual cycle hormonal fluctuations.[26] Plasma was separated by centrifugation for 20 min at 2500 r.p.m. and 4°C for the measurement of all inflammatory markers, cell adhesion molecules glucose and insulin, as well as TG, total cholesterol (total-C), low-density lipoproteins (LDL-C) and high-density lipoproteins (HDL-C) assessed by standard colorimetric reflectance spectrophotometry at the Fairview Diagnostics Laboratories, Fairview-University Medical Center (Minneapolis, MN, USA), a Center for Disease Control and Prevention certified laboratory. Fasting glucose and insulin concentrations were used to calculate the homeostasis model of assessment for insulin resistance (HOMA-IR).[27]

Circulating blood levels of CRP (American Laboratory Products Company, Windham, NH, USA), IL-6, adiponectin, E-selectin, sICAM-1 and sVCAM-1 (R&D Systems, Minneapolis, MN, USA) were measured in duplicate by commercially available standard plasma enzyme-linked immunosorbent assay by the Cytokine Laboratory at the University of Minnesota (Minneapolis, MN, USA). The Cytokine Laboratory assay sensitivity for CRP, IL-6 and adiponectin were 0.124 ng/ml, 0.7 pg/ml and 0.5 ng/ml, respectively. Assay sensitivity for sICAM-1, sVCAM-1 and E-selectin were 0.35, 2.0 and 0.1 ng/ml, respectively. With this, the inter-assay coefficients of variation for this laboratory were 5.5, 3.3, 5.8, 7.4, 8.5 and 5.7% for CRP, IL-6, adiponectin, sICAM-1, sVCAM-1 and E-selectin, respectively. Corresponding intra-assay coefficients of variation were 3.4, 13.6, 1.6, 4.8, 4.3 and 4.8%, respectively.

Strength assessments

At baseline, each subject underwent a maximal strength test for a bench and leg press to assess the maximum amount of weight that can be lifted one time (1 RM).[28] After a 4–8 min warm-up, consisting of treadmill walking and familiarization with the bench and leg press equipment and techniques, subjects rated the difficulty (on a scale of 1–10, 10 being the most difficult) of a warm-up set of 4–6 repetitions (reps) of 30 and 40 lbs, respectively. The difficulty rating was used to determine the first weight at which the 1 RM test was attempted and resistance was added until the rating reached 10. At least 48 h later and after a similar warm-up, the subjects performed single repetition lifts (separated by 90 s rest) beginning with the maximum weight achieved at the prior visit and continuing until a new maximum weight was achieved. This weight is recorded as the 1 RM. All measurements and strength assessments were completed at baseline and repeated after 1 year of intervention.

Intervention

Participants in both groups were asked not to alter their dietary habits for the purpose of weight change for the duration of the study period. Individuals who reported current participation in some regular conditioning physical activity at baseline were asked to continue their usual activities for the duration of the study period, regardless of group assignment. For ethical consideration, control participants were offered 'Walking for a Healthy Heart – Our Guide to Help you Start a Regular Walking Program' and 'Exercise and Your Heart – A Guide to Physical Activity' brochures from the American Heart Association, equivalent to current standard clinical practice recommendation but without further instruction.

The RT program consisted of at least two training sessions per week with at least 48 h between sessions for 1 year. Each training session began with a warm-up on a treadmill, cycle ergometer, elliptical trainer, stepper or by walking on a track for approximately 5 min, followed by deep abdominal and lower back exercises for core stability and injury prevention. Following the warm-up, three sets of 8–10 repetitions were performed using isotonic variable resistance machines and free weights targeting the following major muscle groups: quadriceps, hamstrings, gluteals, pectorals, latissimus dorsi, rhomboids, deltoids, biceps and triceps.

The protocol for progression of weight on each exercise was as follows: after two sessions in which a participant lifted the same weight for two sets of 10 reps and 12 reps on the third set, the weight was increased by the smallest increment. During the next training session, if the higher weight could be lifted at least eight times on the first set, and six times on the second set, an additional set was attempted. If at least eight and six repetitions were not accomplished on the first and second sets, respectively, the training weight was reduced to the amount lifted at the previous session. For the first 16 weeks, the RT sessions were supervised by a certified fitness trainer in small groups of five participants. Thereafter, participants completed the RT protocol on their own while meeting twice every 12 weeks with the fitness trainer. Participants were provided activity recording logs and were taught to record the exercise type, weight lifted, and number of repetitions and sets completed per session. Exercise logs were reviewed twice monthly by study staff to ensure participant compliance to the study protocol.

Statistical analysis

Statistical analysis and graphic presentation was accomplished using Graphpad Prism (v 4.0, San Diego, CA, USA). The number needed to treat for 95% power to detect statistical significance at an alpha level of 0.05 was calculated to be12 participants in the RT group. After identification of skewness by histogram analysis, the logarithmic transformation of CRP, IL-6 and adiponectin was used to obtain normal distributions. Analysis of variance (ANOVA) with repeated measures was used to compare both groups before and after the 1-year intervention. Bonferroni's *post hoc* analysis was applied when the ANOVA interaction term was significant. Statistical significance was set at an alpha level of 0.05 for all analyses. All data are presented as mean $\pm$ standard deviation (s.d.).

Results

There were no significant differences between the two groups at baseline for 1 RM bench press or 1 RM leg press. The RT group completed an average of 94 out of 104 (90%) training sessions during the 1-year intervention, which resulted in a significant difference for 1 RM bench press in the RT group compared to the control group ($P=0.04$). For the bench press, the RT group increased the weight lifted (37.2 ± 7.2 vs 40.5 ± 6.9 kg, $P=0.01$), whereas the control group showed no significant change (37.7 ± 10.4 vs

36.4±11.0 kg). Conversely, there was no significant difference in the weight lifted for the leg press following 1 year of RT between the two groups (RT group = 125.9±24.2 vs 136.1±27.9 kg; control group = 123.1±37.5 vs 128.0±40.1 kg, $P = 0.61$).

There were no significant differences between the two groups at baseline and following the intervention for changes in body mass, BMI, fat mass or percent body fat; however, there was a significant improvement in the intervention group in lean body mass as compared to the control group ($P = 0.05$) (Table 1). No significant differences were noted between the two groups in SBP, DBP or MABP at baseline or after 1 year of intervention (Table 1). The groups also demonstrated no significant differences at baseline or after 1 year of intervention for plasma levels of total-C, LDL-C, HDL-C, TG, glucose, insulin or HOMA-IR (Table 2).

At baseline there were no significant differences between the RT and control groups for circulating blood levels of the inflammatory markers CRP (RT group = 3.3±0.4 mg/dl; control group = 3.2±0.4 mg/dl), IL-6 (RT group = 2.8±1.8 pg/ml; control group = 2.4±0.9 pg/ml), adiponectin (RT group = 3.8±0.2 μg/ml; control group = 3.8±0.2 μg/ml). With this, there also were no significant differences between the adhesion molecules sICAM-1, sVCAM-1 or E-selectin at baseline (Table 3). After 1 year, there was a significant reduction in CRP (3.0±0.4 mg/dl, $P<0.01$) and increase in adiponectin (3.9±0.2 μg/ml, $P<0.01$) in the RT group and no significant change in the control group (3.4±0.4 mg/dl

Table 1 Physical characteristics at baseline and following 1 year of resistance training

	Resistance trained		*Control*		*Interaction*
	Baseline	*Follow-up*	*Baseline*	*Follow-up*	P-*value*
Anthropometric measures					
Age (years)	39±5	40±5	38±6	39±6	0.33
Height (m)	1.7±0.1	1.7±0.1	1.6±0.0	1.6±0.0	0.64
Weight (kg)	74.6±11.4	76.7±14.3	72.7±10	72.0±10.6	0.14
Body mass index (kg/m^2)	26.9±3.0	27.5±3.8	27.0±3.0	26.8±3.2	0.17
Lean body mass (kg)	42.2±5.9	44.4±5.5 *	40.0±5.2	40.8±5.1	0.05
Fat mass (kg)	32.8±7.0	32.3±9.5	32.7±6.3	31.2±7.1	0.58
Body fat (%)	43.4±3.7	41.5±4.7	44.8±4.4	43.0±4.9	0.92
Blood pressure measures					
Systolic (mm Hg)	118±9.5	105±25.8	121±10.4	114±12.6	0.45
Diastolic (mm Hg)	69±10.1	60±16.6	69±7.2	67±9.5	0.27
Mean arterial (mm Hg)	85±9.5	75±19.1	86±7.8	83±10.2	0.33

Data are presented as mean±s.d. *$P<0.01$ for within-group analysis.

Table 2 Fasting blood chemistry at baseline and following 1 year of resistance training

	Resistance trained		*Control*		*Interaction*
	Baseline	*Follow-up*	*Baseline*	*Follow-up*	P-*value*
Total-C (mmol/l)	4.5±0.7	4.5±0.9	4.3±0.6	4.4±0.7	0.22
LDL-C (mmol/l)	2.8±0.7	2.7±0.7	2.7±0.5	2.8±0.6	0.25
HDL-C (mmol/l)	1.3±0.3	1.3±0.3	1.2±0.2	1.2±0.2	0.24
Triglycerides (mmol/l)	1.1±0.5	1.0±0.6	1.0±0.5	1.1±0.5	0.46
Fasting glucose (mmol/l)	4.9±0.4	4.8±0.4	5.0±0.5	4.7±0.5	0.28
Fasting insulin (pmol/l)	6.7±4.1	6.3±3.8	6.4±4.3	5.9±2.8	0.94
HOMA-IR	1.5±0.9	1.3±1.0	1.5±0.9	1.3±0.7	0.82

Abbreviations: Total-C, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol. Data are presented as mean±s.d.

Table 3 Circulating adhesion molecules at baseline and following 1 year of resistance training

	Resistance trained		*Control*		*Interaction*
	Baseline	*Follow-up*	*Baseline*	*Follow-up*	P-*value*
sICAM-1 (ng/ml)	231.5±44.0	231.2±51.3	218.8±49.7	229.8±60.0	0.25
sVCAM-1 (ng/ml)	572.9±143.6	615.5±184.9	571.8±150.3	628.8±149.9	0.64
E-Selectin (ng/ml)	24.9±7.5	25.8±8.5	31.7±12.6	31.7±14.2	0.74

Abbreviations: sICAM-1, soluble intracellular adhesion molecule-1; sVCAM-1, soluble vascular cell adhesion molecule-1. Data are presented as mean±s.d.

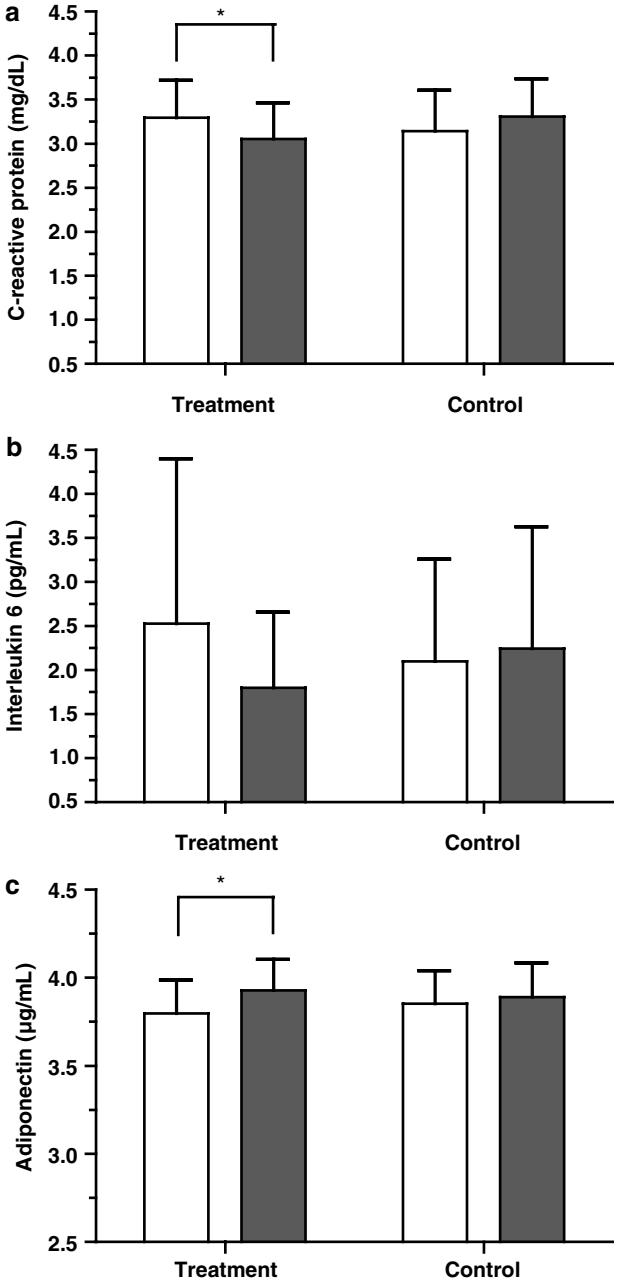

Figure 1 (**a**) CRP concentration in RT and control participants before and after 1 year. (**b**) IL-6 concentration in RT and control participants before and after 1 year. (**c**) Adiponectin concentration in RT and control participants before and after 1 year. For all graphs the open columns indicate baseline measures and closed columns indicate follow-up measures. Data are presented as mean $\pm$ s.d. *$P<0.05$ for within-group analysis.

and $3.8\pm0.2\,\mu$g/ml, respectively). Also, there was no significant change for IL-6 in either group (RT group $=2.0\pm0.7$ pg/ml; control group $=2.5\pm1.3$ pg/ml) (Figure 1a–c). After 1 year, there were no significant changes in either group for sICAM-1, sVCAM-1 or E-selectin (Table 3).

Discussion

To our knowledge, this is the first randomized, controlled trial examining the impact of a moderate intensity RT intervention on inflammatory and adhesion molecules in overweight or obese women. A close association between adipose tissue synthesis and secretion of inflammatory cytokines, and subsequent upregulation of adhesion molecules has previously been demonstrated.[18] These associations are postulated to contribute to the pathogenesis of atherothrombosis and subsequent development of CVD.[29] The results of the present study suggest that 1 year of moderate intensity RT contributes to improvements in the inflammatory profile in overweight but otherwise healthy women. However, this 1-year RT intervention did not alter cell adhesion molecules.

Previous investigations examining the ability of exercise to alter inflammatory markers have provided mixed results.[30–33] These disparities may be related to the acute and chronic phases of the inflammatory response to exercise training. Both CRP and IL-6 have been shown to increase in response to acute bouts of eccentric resistance exercise[30] and conventional RT as compared to running[33] in healthy participants. These results suggest that muscle injury resulting from repetitive loading and unloading of joints and muscle fibers may cause a significant elevation of inflammatory markers. In attempt to avoid potential confounding due to acute phase inflammation, all blood draws in the present study were conducted at least 48 h after the last exercise session.

In contrast to the acute phase inflammatory response, results from large cross-sectional and prospective epidemiological studies suggest not only significant inverse relationships between fitness levels and inflammation[34] but also that long-term engagement in dynamic physical activity results in reduced levels of inflammatory markers.[35,36] Although to date there are no data available on the effects of a structured long-term RT intervention on inflammatory markers, results of the present study coincide with the general theory that women who chronically engage in a structured exercise program demonstrate significant improvements in the inflammatory profile. The subtle changes in the inflammatory markers seen in the present study may be reflective of the relatively minor changes in body composition demonstrated between the groups. Specifically, the RT group demonstrated a reduction in body fat of approximately 4.4% with a concomitant increase in lean mass of approximately 5.2%. These changes are most certainly indicative of the moderate training intensity and limited number of exercise sessions per week indicated by the modest improvement in bench press (6.9%) and leg press (8.1%) in the RT group. However, it is important to note that although the bench and leg press exercises were used as markers of general strength gains and were incorporated in each training session, no greater focus was placed on these exercises as compared to other exercises in the program. With this, the primary goal of the present RT intervention was to mimic a

potentially feasible RT program for routine use in this population of overweight eumennorheic women and thus greater returns may be possible with elevated intensity, increased frequency, or greater focus on building lean muscle mass or reduction of fat mass during the RT program.

Aerobic exercise training intervention studies do support the hypothesized long-term training effect on the inflammatory process, resulting in reduced levels of inflammatory markers. Specifically, Tisi and Shearman[31] have demonstrated that chronic therapeutic exercise training in peripheral artery disease patients with claudication significantly reduced markers of inflammation. Also, Mattusch *et al*.[32] reported a significant reduction in CRP following a progressive 9-month aerobic training program in healthy adults and concluded that regular aerobic exercise training promotes a systemic anti-inflammatory balance. In contrast to traditional markers of elevated inflammation such as CRP or IL-6, the ability of physical activity to alter the anti-inflammatory molecule adiponectin remains unclear. For example, Hulver and *et al*.[37] demonstrated a nonsignificant increase in adiponectin levels in a group of men and women who engaged in 6 months of aerobic exercise training. Additionally, these authors demonstrated a significant increase in adiponectin levels in a group of morbidly obese subjects who underwent gastric bypass surgery. These authors concluded that for alterations in adiponectin levels to occur body mass must also altered.[37] Comparatively, Marcell *et al*.[38] reported no change in either CRP or adiponectin after 16 weeks of moderate intensity aerobic exercise training in obese men and women. The results of these studies are in contrast to the results of Esposito *et al*.,[39] who demonstrated a significant increase in adiponectin and reduction in CRP, IL-6 and IL-18 in obese premenopausal women after a 2-year multidisciplinary intervention aimed at reducing body mass by 10% and included dietary modification, exercise and behavioral/nutritional counseling. Interestingly, Brekke *et al*.[40] also demonstrated a significant increase in adiponectin levels in both men and women after 16 weeks of lifestyle intervention, including both dietary modification and exercise with no change in a diet only comparison group. With this, others have demonstrated significant increases in adiponectin levels after acute high-intensity exercise[41] and moderate intensity exercise training[42] without changes in body weight or composition. Thus, the hypothesis that significant weight loss or change in body composition is necessary to alter adiponectin concentrations has been proposed but not confirmed.[40,43,44] The results of the present study support the hypothesis that 1 year of regular moderate intensity RT in previously sedentary, overweight women results in a modest improvement of the adipose-related pro-inflammatory process. Specifically, we found that this program resulted in a significant reduction in CRP and a significant increase in the anti-inflammatory molecule adiponectin.

Previous investigations examining the effects of aerobic exercise training interventions on adhesion molecules have demonstrated favorable results in both animal[45] and human subjects.[46] For example, Wegge *et al*.[47] reported a significant reduction in both CRP and sICAM-1 after only 2 weeks of a combined low-fat/high fiber diet and daily aerobic exercise. However, with their intervention design, it is impossible to determine the independent effects of dietary changes and exercise training on CRP and sICAM-1. Adamopoulos *et al*.[48] found that 12 weeks of aerobic exercise training significantly reduced both sICAM-1 and sVCAM-1 in heart failure patients. Both of these investigators also reported significant correlations between increased exercise tolerance and reduction in cellular adhesion molecules.

In the present study, we failed to observe a significant improvement in the adhesion molecule profile with RT. This is in contrast to previous studies showing elevated levels of sICAM-1 and sVCAM-1 in the presence of elevated CRP.[18] It also has been suggested that adiponectin plays a significant role in the reduction of inflammation and inhibition of cell adhesion molecules.[23,49] Although there was a significant reduction in CRP and improvement in adiponectin levels in the present study, the magnitude and/or duration of these changes may have been insufficient to alter the levels of adhesion molecules. It should also be noted, however, that the women in this study did not have overt clinical manifestation of atherosclerosis and demonstrated relatively normal levels of adhesion molecules at baseline.

Conclusions

The results of this study suggest that regular, moderate intensity RT is an effective non-pharmacologic intervention to attenuate low-grade inflammation associated with overweight, in eumenorrheic women. These data support the rational for inclusion of RT to help reduce the inflammatory contribution to atherothrombosis in overweight women. Because of the narrow population and small sample size of this study, additional research is necessary to confirm our findings in a larger more representative population sample.

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Conflict of interest

The authors of this manuscript have no conflicts of interest.

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