Detraining-induced alterations in adipokines and cardiometabolic risk factors after nonlinear periodized resistance and aerobic interval training in obese men

Mahmoud Nikseresht, Mohammad Reza Hafezi Ahmadi, and Mehdi Hedayati

Abstract: This study compared the effects of nonlinear resistance training (NRT), aerobic interval training (AIT), and detraining on adipokines and cardiometabolic risk factors in middle-aged obese men. Thirty-three obese men were randomly allocated to NRT (n = 12), AIT (n = 10), and control (CON, n = 11) groups. Subjects in experimental groups performed exercise protocols 3 days per week for 12 weeks followed by a 4-week detraining period. The NRT involved 55 min of weight training with flexible periodization. The AIT consisted of running on a treadmill (4 × 4-min intervals at 90% of maximal heart rate, with each interval separated by 3 min at 65%). Peak oxygen consumption increased significantly after training compared with CON (P < 0.01), but it increased more in the AIT group than in the NRT group (P = 0.004). After detraining, peak oxygen consumption decreased significantly in both training groups (P < 0.001); however, the value in the AIT group was still higher than that in the CON group (P = 0.003). No significant changes were observed in serum levels of omentin-1 and interleukin (IL)-18 after training (P > 0.05), but omentin-1 decreased significantly in both training groups and IL-18 increased significantly in the NRT group after detraining (P < 0.05). High-density lipoprotein cholesterol (HDL-C) increased significantly after training in the AIT group compared with the CON group (P < 0.05) and returned to the pre-training level after detraining. Conversely, apelin-13 increased significantly in response to training, compared with baseline (P < 0.05), and remained unchanged after detraining. Both training regimens had similar effects on most markers; however, AIT seems to have stronger anti-coronary disease effects (as indicated by HDL-C and peak oxygen consumption) than NRT.

Key words: strength training, inflammation, lipid metabolism, obesity.

Introduction

White adipose tissue has been recognized as a secretory organ that can produce bioactive polypeptides known as adipokines. Adipokines could play a major role in the development of diseases associated with obesity, such as cardiovascular disease, type 2 diabetes, and metabolic disorders (Leal and Mafra 2013). In obese individuals, the expression, synthesis, and release of proinflammatory adipokines such as retinol-binding protein-4 (RBP-4) and interleukin (IL)-18 are enhanced, but anti-inflammatory adipokines including adiponectin and omentin-1 are decreased (Trayhurn

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Apelin is a fairly novel adipokine with a favorable influence on metabolism owing to its positive effects on blood pressure and cardiac contractility (Kleinz and Davenport 2005). It is also upregulated by insulin and is involved in glucose homeostasis (Soriguer et al. 2009). Apelin expression is induced by exercise; thus, apelin may be a novel exercise-regulated myokine with autocrine/paracrine action (Besse-Patin et al. 2014).

Recent evidence supports the hypothesis that exercise training reduces chronic inflammation, especially in obese individuals with high levels of inflammatory markers and after long-term training (Beavers et al. 2010). Furthermore, it has been suggested that training-induced changes in cardiometabolic risk factors might be partially mediated by changes in adipokines (Stefanyk and Dyck 2010). Studies have shown a decrease in IL-18 after aerobic training in patients with type 2 diabetes (Kadoglou et al. 2007), elderly adults (Kohut et al. 2006), people with metabolic syndrome (Troseid et al. 2009), and obese women (Esposito et al. 2003). In contrast, no significant change in IL-18 was observed after 12 weeks of strength training in obese individuals with metabolic syndrome (Stensvold et al. 2012). It was also reported that serum omentin-1 levels increased significantly after 12 weeks of aerobic training in overweight and obese men (Saremi et al. 2010). Furthermore, 4 weeks of exercise training was associated with a reduction in serum RBP-4 levels, but only in subjects in whom insulin resistance improved (Graham et al. 2006). However, other studies demonstrated that RBP-4 was significantly reduced after 3 months of a combined exercise program in obese women (Choi et al. 2013) and after 12 weeks of aerobic exercise training in obese men (Numao et al. 2012). Kadoglou et al. (2013) showed that circulating apelin levels increased significantly after 6 months of aerobic training in patients with type 2 diabetes, whereas resistance training did not change apelin levels. In addition, it was reported that 8 weeks of endurance training did not alter resting plasma levels of apelin in obese nondiabetic men (Besse-Patin et al. 2014).

Physiological responses to aerobic training, including inflammatory responses, differ from responses to resistance training (Knuttgen 2007). These responses may vary according to exercise intensity and duration, recovery time between exercise bouts, and training status (Miles 2008). In addition, differences in load and training mode have an influence on these responses during and after exercise resistance (Buirrago et al. 2012). Nonlinear resistance training (NRT) is a type of training that produces greater daily variation in training stimuli and may induce less muscle damage (Kraemer and Fleck 2007). This is important because the inflammatory response to damaging exercise is greater than that to non-damaging exercise. This sort of training is at least as effective or possibly more effective than linear periodization for producing maximal strength gains (Fleck 2011). As far as we know, no previous study has investigated the effects of this type of training on adipokine responses and lipid profiles. We also used high-intensity aerobic interval training (AIT) because moderate-intensity aerobic training seems to have no effect on adipokine gene expression (Polak et al. 2006).

It has been demonstrated that increased physical activity and positive lifestyle interventions reduce chronic inflammation (Beavers et al. 2010). Furthermore, it has been shown that weight loss leads to reductions in inflammatory markers in overweight subjects following a very low-carbohydrate and low-fat diet (Sharman and Volek 2004). Because training programs lead to an increase in energy expenditure, they could improve inflammatory markers. Thus, it is hypothesized that an intervention utilizing NRT (with energy expenditure similar to that of AIT) will improve concentrations of selected adipokines similarly to AIT in obese men with a normal diet.

It is evident that exercise training reduces cardiometabolic risk factors, especially in obese men, but there is limited research directly comparing different types of training. Moreover, there is little information available on adaptations caused by detraining. Therefore, the present study was designed to determine and compare the effects of 12 weeks of NRT and AIT (with similar energy expenditure) and a subsequent 4-week detraining period on serum IL-18, apelin-13 (AP-13), RBP-4, and omentin-1 levels, glucose concentrations, and lipid profiles in middle-aged obese men. An additional aim was to compare adipokines and lipid profiles between obese and age-matched lean men at baseline.

**Materials and methods**

**Subjects**

This study was approved by the regional ethics committee. Before data collection, subjects were informed of the procedures. They signed a consent form and completed a medical history questionnaire in accordance with the human subjects guidelines of the Research Institute for Endocrine Sciences of Shahid Beheshti University of Medical Sciences. Forty-four subjects (33 obese and 11 lean men) between 34 and 46 years old completed the study (Fig. 1). Obese men were first matched by age, body fat percentage, and aerobic fitness. Then, they were randomly allocated to NRT (age = 40.4 ± 5.2 years, n = 12), AIT (age = 39.6 ± 3.7 years, n = 10), and control (CON, age = 38.9 ± 4.1 years, n = 11) groups. A control group of lean men (age = 39 ± 5.9 years, n = 11) matched for age and aerobic fitness was recruited for baseline comparisons. The inclusion criteria were as follows: nonsmoker, sedentary (less than 60 min physical activity per week), no regular exercise training for at least the past 6 months, no regular use of medication, no history of diabetes (determined by history, use of medication, and fasting glucose <126 mg·dl⁻¹), no special diet, and no history of...
any medical condition that would prevent participation in the exercise intervention. Body fat percentages for obese and lean men were 28%–32% and 14%–18%, respectively. The subjects in experimental groups performed at least 90% of the training sessions. This study was performed between October 2012 and February 2013.

**Procedures**

All subjects were asked to complete a lifestyle evaluation and personal health and medical history questionnaires, which served as screening tools. Before the start of testing, subjects were familiarized with all procedures. After completion of the training programs, subjects in the NRT and AIT groups were instructed to resume their normal lifestyles and avoid any type of regular exercise for 4 weeks. Subjects in the CON group maintained a sedentary lifestyle throughout the study. The volume of training was matched between training groups by estimating energy expenditure using a heart rate monitor (Polar RCX5 sd Run; Electro Inc., N.Y., USA) (Nikseresht et al. 2014a, 2014b). The algorithm used in the heart rate monitor software for energy expenditure estimation is based on physical activity level, type of exercise, maximal oxygen consumption, age, sex, and body mass index. Energy expenditure for aerobic and resistance exercise was estimated using the heart rate monitor in a small group (n = 8), and the training programs were designed to ensure the same energy expenditure between training groups. Energy expenditure was estimated in both training groups during the 12 weeks of the intervention period, and no significant difference was observed between the 2 groups (AIT: 623.4 ± 52.3 kcal; NRT: 604.9 ± 41.3 kcal; P = 0.347). Peak oxygen consumption (VO₂peak), maximal strength, and anthropometric assessments were measured before interventions, after the 12 weeks of training, and after the 4 weeks of detraining. Blood samples were collected to determine serum omentin-1, AP-13, RBP-4, and IL-18 levels, lipid profiles, and glucose concentrations at baseline and at the end of the training and detraining periods. All measurements were performed at the same time of day for each subject.

**Maximal strength and VO₂peak assessments**

After familiarization, subjects were asked to report to the laboratory to determine their 1-repetition maximum (1-RM) for the bench press and knee extension. After a warm-up, subjects performed the 1-RM test using the Brzycki method (Kraemer and Fleck 2007). Measures of 1-RM were obtained within 3 to 4 consecutive attempts, with 3–5 min of rest between lifts. Accepted 1-RM was the greatest load the subject could lift through a full range of motion using proper technique. The warm-up consisted of riding a stationary bicycle for 10 min, 2 sets of progressive resistance training similar to the exercises used in the main experiment, and 3 min of rest accompanied by some light stretching. VO₂peak was estimated using a modified version of the Bruce treadmill protocol (Bruce et al. 1973) 48 h after the maximum strength tests. These tests were repeated after 4 days to eliminate the effects of learning and fatigue.

**Anthropometry**

Each subject’s body weight was measured after a 10-h fast with minimum clothing on a Seca 700 mechanical column scale (Seca, Birmingham, UK) calibrated to the nearest 0.1 kg. Waist circumference was measured midway between the lowest rib and the iliac crest. The hip circumference was measured at the widest part of the gluteal region. Subcutaneous skinfold thickness was measured sequentially, in triplicate, at the chest, abdomen, and thigh using a Lange skinfold caliper (Country Technology, Gays Mills, Wis., USA) and standard technique. The average of 3 measurements for each skinfold was used. Body fat percentage was estimated using the equation of Jackson and Pollock (2004). The same researcher performed all skinfold and girth measurements during the interventions.

**Estimated dietary energy intakes**

All subjects were asked to record their dietary intake over a 48-h period so that the composition of their diet could be determined. Subjects were instructed to consume a normal diet (10%–15% protein, 20%–30% fat, and 50%–60% carbohydrate) and to maintain their normal energy intake throughout the study.

**Blood sampling**

On the day of blood sampling, each subject reported to the laboratory in the morning (0700–0800) after a 10-h overnight fast and 8 h of sleep. Subjects rested in a supine position for 20 min. Blood samples (−10 mL) were obtained from the antecubital vein at baseline and at the end of the training and detraining periods. Subjects were asked to avoid physical exercise for at least 4 days before blood sampling. Subjects were also asked whether they had experienced any symptoms of illness or taken any medication in the 4 days prior to sampling. If a subject indicated that this was the case, a new appointment was scheduled for 4 days later. Subjects were asked to consume similar diets for at least 48 h before blood sampling at baseline, after training, and after detraining. Post-training blood samples from subjects in the training groups were obtained 4 days after their last exercise session. Blood samples were allowed to clot for 60 min and were then centrifuged at 1000g for 15 min (4 °C), and the serum was removed and stored at −20 °C until subsequent analysis.

**Biochemical analysis**

Serum samples were used to measure IL-18, omentin-1, RBP-4, and AP-13 concentrations at baseline, at the end of the 12 weeks of training, and following the 4 weeks of detraining. The concentrations were measured in duplicate by enzyme-linked immunosorbent assay according to the specifications of the manufacturers (Boster Biological Technology Ltd., Pleasanton, Calif., USA, for both IL-18 and RBP-4; Hangzhou Eastbiopharm Co., Ltd., USA, for both omentin-1 and AP-13). The intra- and inter-assay coefficients of variation were less than 12% for these variables. The minimum detectable concentrations were less than 15.6, 100, 2, and 0.5 pg·mL⁻¹ for IL-18, RBP-4, omentin-1, and AP-13, respectively. The assay sensitivity was less than 1, 10, 1.04, and 0.3 pg·mL⁻¹ for IL-18, RBP-4, omentin-1, and AP-13, respectively. Serum samples were also used to measure triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and glucose before training and after the training and detraining periods. Fastings TC, TG, HDL-C, and glucose were measured by an enzymatic colorimetric method using an AutoChemistry Analyzer (CS240; DURIL, China). LDL-C was calculated using the Friedwald formula: LDL-C = TC − HDL-C − (TG/5). Intra- and interassay coefficients of variation were less than 1.9% for these variables.

**Training programs**

The NRT program involved different intensities with flexible periodization and consisted of 55 min of weight training per session and 3 sessions per week for 12 weeks. The details of this training program are shown in Tables 1 and 2.

NRT included running on a treadmill (4 × 4-min intervals at 80%–90% of maximal heart rate, with each interval separated by 3 min at 65%). The intensity of the training program was controlled by using a heart rate monitor (Polar RCX5 sd Run; Electro Inc., N.Y., USA). All training sessions were performed at the University laboratory and were supervised by the researchers.

**Statistical analysis**

All data analysis was performed using SPSS 18.0 (SPSS, Inc., Chicago, Ill., USA). Normality of distribution was tested using the Shapiro–Wilk test. Independent t tests were used to determine...
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For the variance was performed to detect differences between interventions and time points. When F ratios indicated significant interactions among means (intervention x time), a post hoc Bonferroni analysis was performed to identify where the differences occurred. The effect sizes were calculated for the intervention x time interactions to determine the meaningfulness of the intervention effects. Intraclass correlation coefficients (ICCs) were determined to assess within-group reliability of the dependent variables for each group at the 3 measurement points. ICCs ranged between 0.58 and 0.98 for all variables except IL-18 (0.12 and 0.32) with NRT group, the training groups had significantly lower waist circumference compared with the CON group (P < 0.02), but this difference was not maintained after detraining. There were significant increases in VO_{2peak} in the AIT and NRT groups compared with the CON group after training (P < 0.01), but the increase in the AIT group was greater than that in the NRT group (P = 0.004). After 4 weeks of detraining, VO_{2peak} decreased significantly in both training groups (P < 0.001); however, while VO_{2peak} returned to baseline in the NRT group (P = 0.7), it was still higher than the control value in the AIT group (P = 0.003). The maximum strength (1-RM) for knee extension and bench press increased significantly in the NRT group compared with the other groups (P < 0.001); however, a significant increase was also found for knee extension in the AIT group compared with the CON group (P = 0.001). Interestingly, these improvements persisted in the training groups after the detraining period.

Serum biochemistry

There were significant differences between obese and lean subjects at baseline for omentin-1, RBP-4, glucose, TC, LDL-C, HDL-C, and TG (P < 0.05) but not for IL-18 and AP-13 (Table 3). Biochemical variables of the subjects in the NRT, AIT, and CON groups at baseline and after the training and detraining periods are shown in Table 5. Omentin-1 increased slightly in response to training but decreased significantly after detraining (P < 0.05). While neither exercise program caused significant changes in IL-18, the cytokine level increased significantly in the NRT group after detraining (P = 0.04). Glucose concentration decreased significantly after AIT and NRT (P < 0.05), and these improvements persisted in both groups after detraining. AP-13 increased significantly after 12 weeks of AIT or NRT, compared with the pre-training level, and remained unchanged after detraining.

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## Results

### Anthropometry and functional capacity

Physical characteristics of obese and lean subjects are reported in Table 3. There were significant differences between obese and lean subjects at baseline for body fat percentage, body weight, waist circumference, and waist-to-hip ratio (WHR) (P < 0.05) but not for VO_{2peak} (P = 0.23). Anthropometric variables and VO_{2peak} of obese subjects in all groups (AIT, NRT, and CON) at baseline and after the training and detraining periods are reported in Table 4. After training, significant reductions were observed in body weight in the AIT group compared with the other groups (3.3%, P < 0.05) and in body fat percentage in the AIT (7.8%) and NRT (7.4%) groups compared with the CON group (P < 0.05). After the 4-week detraining period, body weight and body fat percentage remained lower than baseline values. Compared with the CON group, the training groups had significantly lower waist circumference at the end of training (P < 0.05), and this difference was maintained in the AIT group but not in the NRT group after detraining. AIT resulted in a significant reduction in WHR at the end of training compared with CON (P = 0.02), but this difference was not significant in VO_{2peak}, IL-18, or AP-13.

### Discussion

The present study was designed to investigate the effects of different exercise programs (NRT and AIT) and detraining on selected adipokines and lipid profiles in middle-aged obese men. At baseline, obese men showed significantly lower HDL-C and higher omentin-1, RBP-4, TG, LDL-C, TC, and glucose than lean controls, but there was no significant difference in VO_{2peak}. IL-18, or AP-13.
tumor necrosis factor-α (TNF-α), which is associated with downregulated inflammatory markers such as IL-18, AP-13, and RBP-4 in endothelial cells via NF-κB and other confounding factors in men (Oda et al. 2013). Thus, it seems that the lack of a significant difference in IL-18 or AP-13 between obese and lean subjects might be due to a similar status of inflammatory markers in obese subjects (Saremi et al. 2010; Auguet et al. 2011). The bidirectional relationship between obesity and inflammation due to obesity.

Recent studies have suggested that regular exercise training is most effective in improving insulin resistance and diabetes (Graham et al., 2006), considered. In the present study, the initial mean level of IL-18 was 71 ± 41 pg·mL⁻¹, which was lower than the values reported by Stensvold et al. In addition, factors such as the degree of obesity, age, physical inactivity, and most importantly metabolic syndrome and diabetes may increase levels of IL-18. Thus, it is possible that regular exercise training is most effective in improving this marker in subjects with elevated levels.

In the present study, a slight increase was observed in omentin-1 in response to training, but there was no change in RBP-4. However, others (Saremi et al. 2010) showed that omentin-1 levels increased significantly after 12 weeks of aerobic training, compared with baseline, in overweight and obese men. A possible explanation for these different findings is that the increase in omentin-1 is not required when the baseline level is higher than that in lean controls. It was reported that 4 weeks of exercise training decreased omentin-1 levels increased significantly after 12 weeks of aerobic training, compared with baseline, in overweight and obese men. A possible explanation for this discrepancy, we suggest that baseline IL-18 levels should be considered. In the present study, the initial mean level of IL-18 was 71 ± 41 pg·mL⁻¹, which was lower than the values reported by Stensvold et al. In addition, factors such as the degree of obesity, age, physical inactivity, and most importantly metabolic syndrome and diabetes may increase levels of IL-18. Thus, it is possible that regular exercise training is most effective in improving this marker in subjects with elevated levels.

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training did not alter resting plasma levels of apelin in obese
flammatory markers in obese subjects (Madsen et al. 2008). Thus, a
the initial body weight was necessary for improvement in inflam-
Another study showed that a net weight loss greater than 10% of
these variables can change over time.
However, a major limitation of these studies is the lack of a con-
within- and between-group comparisons of biochemical variables of groups at baseline, after training, and after detraining.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
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<tbody>
<tr>
<td></td>
<td>NRT (n = 12)</td>
<td>AIT (n = 10)</td>
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<tr>
<td>Total cholesterol (mg·dL⁻¹)</td>
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<tr>
<td>Baseline</td>
<td>219.6±22.8</td>
<td>224.5±28.9</td>
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<tr>
<td>After training</td>
<td>194.9±21.6</td>
<td>192.1±23.7</td>
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<tr>
<td>After detraining</td>
<td>214.2±20.9</td>
<td>205.1±33.9</td>
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<td>Triglycerides (mg·dL⁻¹)</td>
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<td>Baseline</td>
<td>210.2±75.9</td>
<td>182.0±47.0</td>
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<tr>
<td>After training</td>
<td>208.1±73.6</td>
<td>160.4±27.4</td>
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<td>After detraining</td>
<td>190.3±94.8</td>
<td>156.6±36.7</td>
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<tr>
<td>HDL-C (mg·dL⁻¹)</td>
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<tr>
<td>Baseline</td>
<td>34.6±55.8</td>
<td>33.8±13.9</td>
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<tr>
<td>After training</td>
<td>38.4±93.3</td>
<td>43.6±80.0*</td>
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<tr>
<td>After detraining</td>
<td>37.3±27.4</td>
<td>39.3±39.7</td>
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<td>LDL-C (mg·dL⁻¹)</td>
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<td>Baseline</td>
<td>128.3±26.6</td>
<td>132.2±26.2</td>
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<tr>
<td>After training</td>
<td>105.3±19.6</td>
<td>106.4±29.7</td>
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<tr>
<td>After detraining</td>
<td>107.8±17.7</td>
<td>108.7±13.1</td>
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<td>Glucose (mg·dL⁻¹)</td>
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<tr>
<td>Baseline</td>
<td>111.8±81.1</td>
<td>101.7±27.6</td>
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<tr>
<td>After training</td>
<td>99.3±55.9</td>
<td>96.6±26.6*</td>
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<td>After detraining</td>
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<td>Omentin-1 (pg·mL⁻¹)</td>
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</tr>
<tr>
<td>Baseline</td>
<td>99.0±26.7</td>
<td>116.8±43.3</td>
</tr>
<tr>
<td>After training</td>
<td>108.7±27.1</td>
<td>128.1±50.1</td>
</tr>
<tr>
<td>After detraining</td>
<td>87.8±23.8</td>
<td>63.5±12.8*</td>
</tr>
<tr>
<td>Apelin-13 (pg·mL⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>26.7±59.4</td>
<td>36.4±29.5</td>
</tr>
<tr>
<td>After training</td>
<td>37.5±19.4</td>
<td>46.1±14.9*</td>
</tr>
<tr>
<td>After detraining</td>
<td>37.5±3.3</td>
<td>43.5±8.3*</td>
</tr>
<tr>
<td>Interleukin-18 (pg·mL⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>76.5±47.4</td>
<td>56.6±24.6</td>
</tr>
<tr>
<td>After training</td>
<td>66.4±35.4</td>
<td>62.3±38.2</td>
</tr>
<tr>
<td>After detraining</td>
<td>119.1±55.5</td>
<td>74.6±40.9</td>
</tr>
<tr>
<td>RBP-4 (pg·mL⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>3137.62±766.43</td>
<td>2607.50±655.60</td>
</tr>
<tr>
<td>After training</td>
<td>2670.25±506.95</td>
<td>2597.62±556.28</td>
</tr>
<tr>
<td>After detraining</td>
<td>2438.50±516.95</td>
<td>2612.50±556.28</td>
</tr>
</tbody>
</table>

Note: Data are presented as means ± SD. AIT, aerobic interval training; CON, control; ES, effect size; i, intervention; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NRT, nonlinear resistance training; RBP-4, retinol-binding protein-4; SP, statistical power; t, time.

*Significant difference from CON group (P < 0.05).
|Significant difference within group compared with baseline (P < 0.05).
|Significant difference within group compared with after training (P < 0.05).
|Significant difference within group compared with baseline (P < 0.05).

Table 5. Within- and between-group comparisons of biochemical variables of groups at baseline, after training, and after detraining.

cantly reduced after 3 months of combined exercise (45 min of aerobic training and 20 min of strength training) in obese women (Choi et al. 2013) and after 12 weeks of exercise training (45–60 min of aerobic exercise) in obese men (Numao et al. 2012). However, a major limitation of these studies is the lack of a control group. Therefore, there is no precision in the results because these variables can change over time.

In this study, fat mass decreased by less than 5% after training. Another study showed that a net weight loss greater than 10% of the initial body weight was necessary for improvement in inflammatory markers in obese subjects (Madsen et al. 2008). Thus, a further reduction in fat mass may lead to a significant improvement in adipokines.

AP-13 increased significantly after NRT and AIT compared with baseline. This result corresponds to the findings of Fujie et al. (2014), who reported a significant increase in AP-12 (which has cross-reactivity with AP-13) after 8 weeks of moderate aerobic exercise training in healthy middle-aged and older adults. Also, it was reported that apelin was increased by 6 months of aerobic training (but not resistance training) in patients with type 2 diabetes (Kadoglou et al. 2013). In contrast, 8 weeks of endurance training did not alter resting plasma levels of apelin in obese nondiabetic men (Besse-Patin et al. 2014). This discrepancy may be partly explained by the obesity or health status of the subjects, their age, and differences in the intensity, volume, or duration of exercise training. Recently, a significant increase in apelin mRNA was found in muscles but not in adipose tissue after 8 weeks of endurance training in obese nondiabetic men (Besse-Patin et al. 2014). Furthermore, apelin may be secreted by skeletal muscles, but it has a very short half-life (less than 5 min) (Barnes et al. 2010). According to these findings, there is the possibility that apelin secretion increases in other tissues such as the heart and pancreas. However, the present study did not examine apelin concentrations in these tissues. Thus, considering the physiological actions of apelin, such as improving heart function and glucose homeostasis, it seems that increased apelin after training has a potential therapeutic impact in diabetes and cardiovascular disease. After 4 weeks of detraining, subjects in the training groups maintained their average increase in AP-13 concentration. In addition, body fat percentage and waist circumference did not return to baseline after detraining. It seems that if body fat percentage or waist circumference is not restored after short-term detraining, some of the key training adaptations are preserved (i.e., AP-13).
In this study, serum levels of omentin-1 decreased significantly in the training groups after detraining. A recent study from our laboratory showed that insulin and adiponectin concentrations worsened significantly in the same training groups after 4 weeks of detraining (Nikseresht et al. 2014b). Thus, this study suggests that the decrease in omentin-1 after detraining is probably due to an increase in insulin levels. Furthermore, similar to adiponectin, omentin-1 decreases in visceral adipose tissue due to obesity. Omentin-1 is negatively correlated with body mass index, leptin, insulin resistance, and waist circumference but positively correlated with HDL-C and adiponectin (de Souza Batista et al. 2007; Tan et al. 2008). It seems that this pattern of results for omentin-1 is similar to that of adiponectin. Also, the inverse relationship between obesity indices and both omentin-1 and adiponectin suggests that these 2 adipokines have similar regulatory roles. Thus, omentin-1 could play a role in reducing risk factors associated with type 2 diabetes and cardiovascular disease, and the reduction in omentin-1 after detraining is associated with a reduction in these improvements.

Serum levels of IL-18 increased significantly in the NRT group but not in the AIT group after 4 weeks of detraining. This finding could indicate that the mechanisms that regulate IL-18 after detraining differ between training programs. In human muscle, IL-18 is solely expressed and regulated by type II fibers (Plomgaard et al. 2005). Because of the negative effects of detraining on muscle fibers (mostly type II fibers), it is likely that the increased IL-18 in the NRT group after detraining was caused by a decrease in type II muscle fibers. In addition, cortisol concentration decreased by 21% after 6 weeks of detraining in strength-trained men (Kraemer et al. 2002). Cortisol inhibits the production of proinflammatory cytokines, so a decrease in serum cortisol levels after detraining may lead to an increase in IL-18. However, the exact mechanisms underlying the detraining-induced increases in serum IL-18 in this study remain unknown.

In this study, HDL-C improved significantly in the AIT group and then returned to the pre-training level after 4 weeks of detraining. In accordance with our results, HDL-C improved significantly after 4 months of aerobic interval training in patients with metabolic syndrome and returned to I–2 month training values after 1 month of detraining (Mora-Rodriguez et al. 2014). A meta-analysis showed that a 1% decrease in HDL-C would be associated with a 2%–3% increase in the risk of coronary disease (Kelley et al. 2005). In addition, it has been suggested that the sort of training that results in a large increase in VO2max is associated with the removal of more metabolic syndrome factors (Franks et al. 2004). Moreover, in a prospective study, it was observed that an increase of 1 standard deviation in VO2max increased the likelihood of resolving metabolic syndrome factors 1.8 times (Hassinen et al. 2010). Thus, AIT has positive effects on HDL-C, and perhaps a greater increase in aerobic fitness in individuals following an NRT program (similar to that in the AIT group) could lead to similar effects. Moreover, VO2peak was found to be the single best predictor of both cardiac and all-cause deaths in patients with established cardiovascular disease (Kavangh et al. 2002). Therefore, AIT may be employed to optimize rehabilitation programs for patients with stable cardiovascular disease.

In summary, the current study showed that 12 weeks of NRT or AIT (with similar energy expenditure) was equally effective in improving waist circumference, body fat percentage, TC, LDL-C, glucose, and AP-13, but TC in both training groups returned to pre-training levels after 4 weeks of detraining. HDL-C increased significantly in response to AIT but returned to the pre-training level after detraining. Omentin-1 increased slightly in response to training but was significantly reduced in both training groups after detraining. The training programs did not cause significant changes in IL-18, but the cytokine level increased significantly in the NRT group after detraining. Thus, it seems that both exercise programs are beneficial overall, but AIT was the only program that had positive effects on HDL-C, which can reduce the risk of coronary disease. Therefore, obese men can use either training program to reduce some metabolic syndrome factors, although AIT may have stronger biochemical effects. A 4-week detraining period had comparable results after AIT and NRT (except for IL-18). Thus, it is suggested that to prevent future cardiovascular events, training programs should not be discontinued.

Conflicts of interest statement
The authors declare that there is no conflict of interest that would prejudice their impartiality.

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