Effects of Simultaneous or Sequential Weight Loss Diet and Aerobic Interval Training on Metabolic Syndrome

Abstract

Our purpose in this study was to investigate efficient and sustainable combinations of exercise and diet-induced weight loss (DIET), in order to combat obesity in metabolic syndrome (MetS) patients. We examined the impact of aerobic interval training (AIT), followed by or concurrent to a DIET on MetS components. 36 MetS patients (54±9 years old; 33±4 BMI; 27 males and 9 females) underwent 16 weeks of AIT followed by another 16 weeks without exercise from the fall of 2013 to the spring of 2014. Participants were randomized to AIT without DIET (E CON, n = 12), AIT followed by DIET (E-then-D, n = 12) or AIT concurrent with DIET (E + D, n = 12). Body weight decreased below E CON similarly in the E-then-D and E + D groups (~5%). Training improved blood pressure and cardiorespiratory fitness (VO$_2$peak) in all trials with no additional effect of concurrent weight loss. However, E + D improved insulin sensitivity (HOMA) and lowered plasma triglycerides and blood cholesterol below E CON and E-then-D (all P < 0.05). Weight loss in E-then-D in the 16 weeks without exercise lowered HOMA to the E + D levels and maintained blood pressure at trained levels. Our data suggest that a new lifestyle combination consisting of aerobic interval training followed by weight loss diet is similar, or even more effective on improving metabolic syndrome factors than concurrent exercise plus diet.

Introduction

Individuals with metabolic syndrome (MetS) are at higher risk of developing type 2 diabetes and cardiovascular disease than age-matched counterparts [1]. Obesity is the central feature in the pathogenesis of MetS [18]. Therefore, lifestyle interventions aimed at reducing body weight are the first clinical approach to treating patients with MetS [8]. Importantly, diet-induced weight loss (i.e., caloric restriction) can alleviate symptoms of MetS by reducing central obesity [21], blood pressure [4, 21, 25], insulin resistance [10] and improving blood lipids [21, 35]. Each kilogram of weight loss is associated with an 8% reduction in the probability of developing MetS [25]. Furthermore, 2-thirds of patients who lose at least 10% of their initial body weight no longer fulfill the criteria for MetS [21]. However, 8–10% body weight loss requires prolonged calorie restriction, which is difficult to achieve, contributing to high attrition rates and rebound weight recovery [34].

Exercise is the other lifestyle modification commonly prescribed to improve MetS. However, the caloric expenditure associated with health-oriented exercise programs (150–400 kcal/day, 3 days/wk) is unlikely to provoke a substantial body weight or fat loss following 3–5 months of training [9]. As a result, 3–4 months of exercise training yields small reductions in body weight (~1–2%) and moderate improvements in MetS components (i.e., blood pressure, waist circumference, HDL-c [20, 29, 32]). Significant exercise-induced reductions in body weight and fat mass requires longer exercise sessions (i.e., >60 min/day) and programs (>4 months), which may contribute to increased attrition rates [24]. Alternatively, aerobic interval training (AIT) is less time consuming than traditional continuous aerobic exercise, and evidence suggests that it may be more efficacious than continuous moderate-intensity training to reverse MetS factors [32]. Therefore, AIT combined with calorie restriction may have the most robust impact on MetS components. Although AIT and calorie restriction improve the metabolic disarrangements...
ments of MetS, its concomitant application may be burdensome for many patients. The main reason is that AIT results in large muscle glycogen depletion [23], and its restoration requires abundant carbohydrate ingestion [6], which is not provided when following a calorie restriction diet.

There is a compelling need for lifestyle interventions that treat obesity and metabolic syndrome and its associated health risks. Diet-induced weight loss in conjunction with exercise training effectively reverses metabolic syndrome factors. However, it is challenging to restrict calorie intake while undergoing demanding aerobic interval training. Alternatively, diet could be scheduled to follow AIT. To our knowledge, the efficacy of AIT and diet-induced weight loss, separately or combined, on MetS risk factors has not been addressed. The aim of this study was to determine the effects of simultaneous or sequential application of high intensity AIT and diet-induced weight loss on the reversal to the norm of MetS components (i.e., measured by MetS Z score [3, 15]). Our hypothesis is that the effects should be similar if the same weight reduction is achieved. Ultimately, results of this study may help to design lifestyle intervention programs aimed at improving health among MetS patients while reducing attrition rates [14].

Methods

Study population

Data were collected between September 2013 and May 2014. Primary care physicians in our metropolitan area (pop. 100,000) referred subjects to the study. 36 obese (n = 27 males and n = 9 females) adults (54±9 years old) completed this study. Females were equally distributed among the groups (3 per group). All participants were non-smokers, not pregnant and weight stable prior to the study. Participants were enrolled based on fulfilling ≥ 3 MetS criteria as per harmonized definition [1], using the population Euorpid waist circumference cut points. Exclusion criteria included the use of medications known to affect weight or appetite, history of type 2 diabetes, thyroid disease, cardiovascular, renal disease or any disease associated with exercise intolerance. Screening included physical examination comprising BMI, supine blood pressure and waist circumference, medical and dietary histories, blood biochemistry and 12-lead ECG at rest and during exercise stress test. Directions and magnitudes of time-normalized P, QRS and ST vectors, and other ECG parameters were analyzed by a physician to screen for myocardial diseases. All subjects provided written, witnessed, informed consent of the protocol approved by the Virgen de la Salud Hospital’s Ethics Committee, and the study thus meets the ethical standards of the journal [11].

Exercise training and dietary intervention

Participants were randomized to one of 3 groups: an exercise control group (“E CON”), exercise then diet (“E-then-D”) or exercise plus diet (“E+D”) [27]. All subjects underwent 16 weeks of supervised AIT, 3 sessions per week, followed by 16 weeks without exercise (Fig. 1). Training consisted of pedaling for 10 min as a warm-up at 70% HRmax, followed by 4 × 4-min intervals at 90% of HRmax interspersed with 3-min active recovery at 70% HRmax and a 5-min cool-down period for a total of 43 min. Exercise intensity was increased as training adaptations developed to maintain the target heart rate (Accurex coded, Polar, Finland). Participants were required to attend at least 85% of all the exercise sessions. Maximal heart rate was re-evaluated monthly and workloads adjusted accordingly. During the week prior to the study subjects kept daily, detailed food records that were analyzed using a computerized program (CESNID, Barcelona, Spain). The E+D group was asked to slightly reduce their habitual calorie intake by -150kcal/day during the 16 weeks of AIT. The reduction in calorie intake in conjunction with the energy expended during training (~400kcal/session) was intended to result in a loss of ~3.6kg of body fat. To maintain their reduced body mass during the following 16-wk period, calorie intake was reduced ~400kcal/day below the daily calorie intake recorded one week prior to the study. E-then-D group maintained their body weight during the 16-wk training by increasing calorie intake to match the exercise calorie expenditure (150–650kcal/session). This group reduced ~700kcal/day calorie intake during the following 16 weeks without exercise. Adherence to the protocol was determined by weekly body weight assessment and weekly 3-day dietary analysis (CESNID, Barcelona, Spain). Participants undergoing diet treatment attended a weekly seminar, at which a registered dietitian taught proper foodstuff combination and servings to ensure that macronutrient proportions were not altered. No vitamins or nutritional supplements were prescribed. Participants who failed to reach their target body weight for 3 consecutive weeks were withdrawn from data analysis.

Clinical investigation

Body composition, anthropometry (weight and waist circumference), resting blood pressure, blood metabolites, exercise maximal fat oxidation (FO_MAX) and peak oxygen consumption (VO2 peak) using a graded exercise test were measures before and after 16 weeks of AIT, and again after the following 16 weeks without exercise. All tests were scheduled at least 72 h after the last exercise training session to examine the chronic effects of the exercise training program, rather than the acute effects of their most recent exercise session. Blood was drawn in the morning after a 10 h overnight fast. Percent body fat and trunk body fat were determined by dual energy X-ray absorptiometry scans (Hologic Discovery DXA Series Wi QDR, Bedford, USA). Supine resting blood pressure was measured in triplicate using a blood pressure monitor (Tango, SunTech Medical, NC, USA).

Cardio-respiratory and metabolic fitness

Peak aerobic capacity (VO2 peak) was assessed on an electronically-braked cycle ergometer (Ergoselect 200, Ergoline, Germany) during graded exercise testing (GXT) using indirect calorimetry, (Quark b2, Cosmed, Italy) with 12-lead ECG monitoring (Quark T12, Cosmed, Italy). The highest heart rate value obtained during the test was considered HR_peak.

Blood analyses

Concentrations of plasma glucose (glucose oxidase-peroxidase assay), glycated hemoglobin (HbA1c; immune-turbidimetry assay), HDL-c (accelerator selective detergent assay), blood triacylglycerides (TG; glycerol-3-phosphate oxidase assay) and total serum cholesterol (T Cholesterol; enzymatic method) were run in an automated Mindray BS 400 Chemistry Analyzer (Mindray Medical Instrumentation, USA). Low-density lipoprotein-cholesterol (LDL-c) was calculated as proposed by Friedewald [7]. Insulin concentration was measured in duplicate using chemiluminescent micro particle immunoassay in an automated analyzer (Architect ci4100, Abbott Laboratories, USA). Insulin
sensitivity was calculated using the homeostasis model assessment (HOMA [19]).

Z scores calculation and MetS risk factor score
Z scores were calculated to assess the evolution to the norm of MetS risk factors and VO₂peak with the training program. The MetS Z score was a continuous score of the 5 metabolic syndrome variables [3, 15]. Gender-specific Z score equations were used to account for variations from the MetS harmonized definition [1] using population Europid waist circumference cut points. The equations used to calculate MetS Z score were:

Men’s MetS Z Score = [(40 − HDL)/SD] + [(TG − 150)/SD] + [(Glu-cose − 100)/SD] + [(Waist perimeter − 94)/SD] + [(Mean Arterial Pressure − 100)/SD]

Women’s MetS Z Score = [(50 − HDL)/SD] + [(TG − 150)/SD] + [(Glu-cose − 100)/SD] + [(Waist perimeter − 80)/SD] + [(Mean Arterial Pressure − 100)/SD]

The VO₂peak Z score was based on normative values [2] specific for participants’ age group and gender. A MetS risk factor score was also determined for each subject as a sum of the number of factors met before and after the interventions (● Table 1).

Statistical analyses
Data are presented as mean ±SEM and descriptive data as mean ±SD. Sample size was calculated based on 3 ±2.3 unit improvement in MetS Z Score observed in 3 pilot subjects during the E+D intervention [33]. MetS Z score power test revealed that at least 9 subjects were needed to reach significance for an statistical power at 80% (α=0.05). When the Shapiro-Wilk test revealed non-standard data distribution, differences were analyzed using Friedman’s non-parametric test. Normally, distributed data were analyzed using one-way ANOVA with repeated measures to test for time, group and interaction effects. Tukey’s post-hoc analysis was performed when a significant F value (Greenhouse-Geisser adjustment for sphericity) was obtained. Mann-Whitney U-test with correction for multiplicity was used as Post-hoc for non-normally distributed data. Effect size (ES [5]) was based on the following criteria; >0.70 large, 0.30–0.69 moderate and <0.30 small effect. 95% confidence intervals (CI) were also calculated. Statistical significance level was set at P<0.05. All test were performed with SPSS software v18 (IBM Software, Chicago IL, USA).

Results
Adherence to the exercise and diet programs
Participants were all Caucasians. There were no significant differences in response to training and/or diet between sexes (75% males and 25% females). Thus, group data was analyzed without sex distinctions. 9 subjects did not complete the experiment (● Fig. 1) due to injury, time commitments or lack of compliance with training or diet. Subjects that withdrew did not differ from

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![Fig. 1 Schematic diagram of study phases and participants.](image-url)
Table 1  Evolution of additional parameters related to the metabolic syndrome.

<table>
<thead>
<tr>
<th></th>
<th>CON</th>
<th>E-then-D</th>
<th>E + D</th>
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<tr>
<td><strong>Body composition</strong></td>
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<td>BMI (kg/m²)</td>
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<td>33.7 ± 1.1</td>
<td>31.5 ± 1.1</td>
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<td>32.1 ± 1.0 * †</td>
<td>31.3 ± 0.9 *</td>
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<td>Trunk fat (kg)</td>
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<td>20.3 ± 1.0</td>
<td>19.1 ± 1.2</td>
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<tr>
<td>Pre-training</td>
<td>18.5 ± 1.1 *</td>
<td>20.2 ± 1.0</td>
<td>16.7 ± 1.0 * §</td>
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<tr>
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<td>19.6 ± 1.1 †</td>
<td>18.1 ± 1.1 †</td>
<td>17.2 ± 1.1</td>
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<td><strong>Blood variables</strong></td>
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<td>HbA1c (%)</td>
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<tr>
<td>Pre-training</td>
<td>6.0 ± 0.22</td>
<td>5.80 ± 0.12</td>
<td>6.06 ± 0.27</td>
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<td>Post-training</td>
<td>5.91 ± 0.15</td>
<td>5.83 ± 0.22</td>
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<td>5.98 ± 0.19</td>
<td>5.87 ± 0.33</td>
<td>5.81 ± 0.11</td>
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<td>T Cholesterol (mmol/l)</td>
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<tr>
<td>Pre-training</td>
<td>5.05 ± 0.27</td>
<td>5.13 ± 0.34</td>
<td>5.02 ± 0.18</td>
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<td>4.88 ± 0.21</td>
<td>5.18 ± 0.34</td>
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<tr>
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<td>5.10 ± 0.19</td>
<td>4.87 ± 0.30</td>
<td>4.75 ± 0.20</td>
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<td>LDL-c (mmol/l)</td>
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<td>3.28 ± 0.20</td>
<td>3.39 ± 0.25</td>
<td>3.19 ± 0.17</td>
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<tr>
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<td>Follow-up</td>
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<td>3.22 ± 0.23</td>
<td>2.97 ± 0.20</td>
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<td><strong>Fitness parameters</strong></td>
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<td>VO2peak (l/min)</td>
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<tr>
<td>Pre-training</td>
<td>2.27 ± 0.21</td>
<td>2.31 ± 0.22</td>
<td>2.39 ± 0.15</td>
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<td>Post-training</td>
<td>2.52 ± 0.24 *</td>
<td>2.49 ± 0.25 *</td>
<td>2.85 ± 0.18 *</td>
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<td>2.39 ± 0.19</td>
<td>2.39 ± 0.23 †</td>
<td>2.49 ± 0.20 †</td>
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<td>Workload peak (W)</td>
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<tr>
<td>Pre-training</td>
<td>178 ± 19</td>
<td>187 ± 20</td>
<td>178 ± 12</td>
</tr>
<tr>
<td>Post-training</td>
<td>200 ± 22 *</td>
<td>198 ± 23 *</td>
<td>221 ± 15 *</td>
</tr>
<tr>
<td>Follow-up</td>
<td>182 ± 20 †</td>
<td>190 ± 22</td>
<td>195 ± 15 †</td>
</tr>
<tr>
<td><strong>MetS risk factors score</strong></td>
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<tr>
<td>Number of factors</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pre-training</td>
<td>4.1 ± 0.3</td>
<td>3.9 ± 0.3</td>
<td>3.6 ± 0.2</td>
</tr>
<tr>
<td>Post-training</td>
<td>3.9 ± 0.3</td>
<td>3.7 ± 0.3</td>
<td>2.9 ± 0.3 *</td>
</tr>
<tr>
<td>Follow-up</td>
<td>3.8 ± 0.3</td>
<td>3.3 ± 0.3 * †</td>
<td>3.6 ± 0.2</td>
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</table>

The other with regards to age, initial fitness or blood metabolites. Attendance to the exercise sessions averaged 95% (85–100%). Compared to the 1-week baseline period, in the E + D group daily caloric intake decreased by 152±25kcal/day during the 16-wk AIT period and by 410±53kcal/day during the following 16 weeks without exercise. E-then-D and E + D groups increased caloric intake by 150–450kcal/day during the 16-wk AIT period. E-then-D group reduced calorie intake by 152 ± 25 kcals/day during the period. E-then-D group reduced calorie intake by 691 ± 82 kcals/day during the 16-wk AIT period and by 410 ± 52 kcals/day during the following 16 weeks without exercise but diet-induced weight loss. Blood HDL-c did not change in any group. There was a transient reduction in blood glucose only in E + D after the 16-wk AIT period (95% CI 0 to −21.1mmol-L⁻¹; ES = −0.67; P = 0.04). Mean blood pressure (MBP) was reduced after training in all groups (avg 95% CI −2 to −11mmHg; ES = −0.78; P = 0.014). The 16 weeks without exercise returned MBP to pre-training values in E CON and E + D groups. However, the diet during the follow-up period in the E-then-D group maintained the reductions in MAP (95% CI −2.5 to −12.1mmHg; ES = −0.61; P = 0.013, Fig. 2). Z scores revealed that at pre-training, patients were 9.9 ± 3.2 (95% CI from 4.7 to 1.1) standard deviations above a healthy value for their respective gender. After 16 weeks of AIT, Z scores decreased in all groups but largely in the E + D group (95% CI −2 to −5 SD; ES = −1.32; P = 0.001) and it was further reduced during the 16 weeks without exercise but diet-induced weight loss in the E-then-D group (95% CI −3 to −4.2 SD; ES = −0.3; P = 0.001). In fact, there was a difference in the overall reduction after the 32-week program favoring the E-then-D group in comparison to E + D (Fig. 3). A similar response was observed for the MetS risk factor score, with a significant reduction when diet was present (Table 1).

Additional physiological parameters

Post-training body weight was reduced by 5.5±0.8% in the E + D group (95% CI −3.6 to −7.0kg; ES = −0.34; P = 0.0001). At follow-up, body weight was reduced by 4.9±0.8% in the E-then-D group (95% CI −2.7 to −5.6kg; ES = −0.36; P = 0.0003), and weight loss was maintained in the E-then-D group (all lower than E CON; P < 0.05, Fig. 3). Reductions in body weight were accompanied by reductions if whole body fat (Fig. 2) and trunk mass (Table 1, all P < 0.05). Insulin concentrations decreased with DIT during the first 16 weeks of E + D (95% CI −7.2 to −37.6pmol-L⁻¹; ES = −0.65; P = 0.016) and during the follow-up in the E-then-D group (95% CI −5.5 to −22.8kg; ES = −1.18; P = 0.008, Fig. 3). HOMA-IR was reduced when exercise was accompanied with diet in the E + D group (95% CI −0.4 to −2.7 Units; ES = −0.75; P = 0.024) and remained reduced during the 16-wk weight maintenance (95% CI −0.2 to −2.3 Units; ES = −0.10; P = 0.046). HOMA-IR decrease the 16-wk follow-up diet in the E-then-D group (95% CI −0.1 to −0.9 Units; ES = −0.04; P = 0.020, Fig. 3). However, HbA1c was not significantly affected by either exercise or diet (Table 1). Interestingly, T Cholesterol and LDL-c were only reduced when exercise training was combined with diet in the E + D group (Table 1, P < 0.05) and returned to pre-exercise values following the 16 weeks without exercise.

Exercise parameters

16 weeks of AIT significantly increased VO2peak in all groups (Table 1). Pre-training, VO2peak Z score was 1.7±0.2 (range 1.2–2.3) standard deviations below age adjusted normative values [2] on average for all groups. After AIT, Z score fell to 0.8±0.2 standard deviations, which represents a 50% improvement towards normative values. The increase in VO2peak in all groups was accompanied by enhanced maximal pedaling workload (WMAX: 13±4%, Table 1, P < 0.05). Conversely, 16 weeks without exercise resulted in reduced VO2peak and WMAX to pre-training values in all groups.
Discussion

We have recently reported that in previously sedentary metabolic syndrome (MetS) patients, 16 weeks of intense aerobic interval training (AIT; [12]) lowers MetS Z score by 40% [20]. This outcome was obtained despite calorie intake maintenance and thus a modest body weight loss (i.e., 2.1±0.4%). Seeking to further reduce MetS components, we complemented the 16-wk AIT program with diet-induced weight loss (~5%) either during training (E+D group) or after training (E-then-D group). In the
32 weeks of the experiment, MetS Z score (a continuous score of the 5 metabolic syndrome variables) was reduced after the diet in E-then-D group by 86%. This reduction was similar to that found by simultaneously applying exercise and diet (E + D group after the 16-wk training, Fig. 2). Reduction of MetS components accompanied improvements in trunk fat, blood lipid profile and insulin resistance. Our findings suggest that a combination of exercise followed by diet could be as effective as simultaneous exercise and diet to treat MetS. Therefore, lifestyle interventions including AIT and diet weight lost sequentially (considering they are equally tolerable) could be tailored to MetS patients. Furthermore, our data suggest that MetS Z score could be used by clinicians as a sensible measure of the effects of diet and exercise in reversing metabolic syndrome factors to healthy values.

Dieting while training (E + D group) did not improve VO$_2$ peak beyond the effect of exercise without weight loss (i.e., E CON and E-then-D, Table 2). In a similar cohort of MetS patients, we
reported that 16 weeks of an AIT program increased muscle mitochondria content despite minimal losses of body fat [20]. As a result, muscle adaptations to increase oxygen consumption are induced by AIT without the need for a concomitant weight loss. Some authors have found that obesity causes electron transport chain deficiency in human skeletal muscle mitochondria [16, 27], which could limit the aerobic adaptations to training in the obese population. However, our data in MetS patients with abdominal obesity suggest that an intense aerobic exercise training program could overcome this deficiency, if present. Therefore, our obese MetS patients experience the habitual cardiovascular adaptations that improve VO\(_2\)peak. The finding of gains in VO\(_2\)peak in MetS patient with AIT is clinically relevant, since other researchers have shown that an elevated VO\(_2\)peak reduces all-cause mortality despite adiposity (i.e., the ‘fat but fit’ paradigm [17]).

It is well established that diet-induced body weight loss reduces resting blood pressure in MetS patients [4, 21, 25]. On the other hand, we and others reported that exercise training has a significant blood pressure lowering effect despite minor body weight loss (1.3–2 kg [20, 32]). In this study we found a 5–9% reduction in systolic arterial pressure after 16 weeks of AIT. In turn, the diet-induced weight loss after exercise training (E-then-D) maintained the reductions in mean blood pressure (Fig. 3). Thus, exercise adaptations and diet weight loss seem to work in conjunction to lower blood pressure. Strazzincky and colleagues have shown that the combination of exercise training and weight loss (i.e., 9.3±0.8% reduction) results in larger reduction in systolic blood pressure than the same magnitude of weight loss without exercise (7.5 vs. 12% [30]). Therefore, their data and ours suggest that diet-induced body weight loss enhances the hypotensive effects of exercise training.

Exercising in the absence of weight loss has little or no effect on improving plasma lipid profile [9]. Conversely, fat loss through dieting or exercise produces comparable changes in lipoprotein concentrations [35]. Previous studies in MetS patients show that 12–16 weeks of aerobic intense training does not reduce blood triglycerides when body weight is not reduced [20, 32]. Accordingly, our 16 weeks of training without weight loss (E-then-D and E CON groups) did not lower the subject’s blood TG, LDL-c or total cholesterol. However, when combining exercise training with dieting (E+D group Post-training), blood TG, LDL-c and total cholesterol were reduced (Fig. 2 and Table 1). Diet after training (16-wk Follow-up in E-then-D group) tended to lower blood TG but not LDL-c or total cholesterol. As a result, our data indicate that rather than exercise training or body weight loss separately, their concurrent combination, seems to be needed to improve lipid profile in MetS patients.

Finally, insulin sensitivity (i.e., HOMA) was markedly improved when training was combined with diet-induced weight loss (i.e., E+D, Fig. 3). AIT results in large muscle glycogen depletion [23] and its restoration requires abundant carbohydrate ingestion in diet [6]. The mild calorie restriction during the 16 weeks of training in the E+D group likely prevented full replenishment of muscle glycogen stores. Carbohydrate deficit in diet is a potent stimulus to increase insulin sensitivity after a bout of exercise [22], which could explain the rapid HOMA improvements after only 16 weeks of training in E+D group. It has been found in MetS patients that 8 weeks of stationary cycle training without weight loss does not improve insulin sensitivity despite a 16% increase in VO\(_2\)max [31]. We also found that the 16-wk exercise period without weight loss had no effect in HOMA (i.e., E CON and E-then-D, Fig. 3).

Other authors maintain that a reduction in plasma fatty acid mobilization is the main cause of the improvements in insulin sensitivity [28]. Houmard and colleagues trained sedentary obese subjects for 6 months, and found the largest improvement in insulin sensitivity occurs with the training mode that elicited the largest lowering effect on blood triglycerides [13]. This association was also present in our data since HOMA improved when blood triglycerides and trunk fat [26] declined after training in the E+D group or upon 16 weeks of dieting in E-then-D group. Thus, our data add to the literature on suggesting that insulin sensitivity is only improved when body fat and circulating fat decreases due to dieting or dieting combined with exercise training.

Our study has some limitations that are worth mentioning. Due to the involving nature of the protocols that require completing at least 85% of the training sessions and adherence to the prescribed body weight, 9 subjects withdrew from the study (20% attrition rate). Likely, the final number of subjects per group limited reaching statistical significance in some variables. Despite being underpowered in some aspects, the main variable of interest that encompass the 5 metabolic syndrome factors (i.e., MetS Z score) showed significant changes with the treatments. In addition, insulin sensitivity was evaluated by a rather crude method based on fasting levels of glucose and insulin (HOMA-IR) rather than challenging the system with a glucose load (tolerance tests) or with an euglycemic-hyperinsulinemic clamp. The insulin sensitivity outcomes derived from our data should thus be confirmed in future studies using those more accurate measurement techniques.

In summary, the simultaneous combination of an intense 16-wk aerobic interval training program with diet-induced weight loss (i.e., 5%; E+D group) results in marked improvement in metabolic syndrome risk factors (i.e., Z score reductions, Fig. 2). Alternatively, weight loss of similar magnitude after the exercise program (E-then-D group) maintains some exercise adaptations (MAP) while improving Z score and insulin sensitivity to the levels found with E+D after the first 16 weeks of the program. Thus, the E-then-D strategy has a similar or higher potency than simultaneous exercise and diet, which could reduce attrition rates in lifestyle modification programs geared toward reversing metabolic syndrome.

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