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Weight Loss, Exercise, or Both and Cardiometabolic Risk Factors in Obese Older Adults: Results of a Randomized Controlled Trial

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Abstract

Background—Obesity exacerbates the age-related decline in insulin sensitivity and is associated with risk for cardiometabolic syndrome in older adults; however, the appropriate treatment for obese older adults is controversial.

Objective—To determine the independent and combined effects of weight loss and exercise on cardiometabolic risk factors in obese older adults.

Design—One-hundred-seven obese (BMI≥30 kg/m^2) older (≥65 yrs) adults with physical frailty were randomized to control group, diet group, exercise group, and diet-exercise group for 1 year.

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Conflict of interest
The authors declare no conflict of interests.

Outcomes for this study included change in insulin sensitivity index (ISI), glucose tolerance, central obesity, adipocytokines, and cardiometabolic syndrome.

Results—Although similar increases in ISI occurred in the diet-exercise and diet groups at 6 months, the ISI improved more in the diet-exercise than in the diet group at 12 months (2.4 vs. 1.2; between-group difference, 1.2; 95% CI, 0.2-2.1); no changes in ISI occurred in both exercise and control groups. The diet-exercise and diet groups had similar improvements in insulin area under the curve (AUC) (−2.9 and −2.9 $\times 10^3$mg.min/dl), glucose AUC (−1.4 and −2.2$\times 10^3$mg.min/dl), visceral fat (−787 and −561 cm^3), tumor-necrosis factor (−17.0 and −12.8 pg/mL), adiponectin (5.0 and 4.0 ng/mL), waist circumference (−8.2 and −8.4 cm), triglyceride (−30.7 and −24.3 g/dL), and systolic/diastolic BP (−15.9 and −13.1/−4.9 and −6.7 mmHg), while no changes in these parameters occurred in both exercise and control groups. The cardiometabolic syndrome prevalence decreased by 40% in the diet-exercise and by 15% in the diet group. Body weight decreased similarly in the diet-exercise and diet groups (−8.6 and −9.7kg) but not in the exercise and control groups.

Conclusions—In frail, obese older adults, lifestyle interventions associated with weight loss improve insulin sensitivity and other cardiometabolic risk factors, but continued improvement in insulin sensitivity is only achieved when exercise training is added to weight loss.

Keywords

Aging; Obesity; Cardiometabolic Risks

Introduction

Obesity is increasingly prevalent and is expected to become an even greater public health concern in coming years (1;2). Current trends in the US suggest that older adults, defined as age ≥65 years, will represent 20% of the population by 2030, half of whom will be obese (3). This expanding population is particularly vulnerable as obesity in older adults is associated with loss of functional independence and diminished quality of life (1). Moreover, obese older adults are at increased risk for the cardiometabolic syndrome, a cluster of metabolic abnormalities predictive of cardiovascular disease and mortality (1;4). However, the clinical approach to obesity in older adults is controversial because of the reduction in relative health risks associated with increasing body mass index (BMI) in this group (5), and the concerns regarding the difficulty of behavioral change with advancing age, exacerbation of age-related loss of lean tissues, and feasibility of long-term weight loss and associated health consequences (1;6;7). Accordingly, the combination of weight loss and exercise is recommended as part of standard care for obese patients in general, but this recommendation is not universally accepted by geriatricians in elderly subjects. It is the prevailing concept that an extra weight may be protective against health risks (8;9). However, the absolute risk of death attributed to obesity in older adults increases with age up to 75 years (5). Moreover, lifestyle interventions directed at weight loss in obese adults are associated with reduced mortality in all age groups, regardless of successful weight loss (10). The mechanism for this observation has not been determined. Further, it is unclear from existing studies whether the beneficial effects of diet and regular exercise are distinct from one another or whether they have additive effects.

We recently reported that the combination of weight loss and exercise provides greater improvement in physical function than either intervention alone (11). We now report the results of the independent and combined effects of weight loss and exercise on insulin sensitivity and other cardiometabolic risk factors in this population of frail, obese older adults.

Methods

The principal aim of the parent randomized controlled trial (RCT) was to determine the independent and combined effects of weight loss and exercise on physical performance in obese older adults. The primary results showed that weight loss alone or exercise alone improves physical function and ameliorates frailty; however, a combination of weight loss and exercise provide greater improvement in physical function and amelioration of frailty than either intervention alone (11). The current study reports the secondary analyses of the RCT examining changes in insulin sensitivity and other cardiometabolic risk factors, which was pre-specified in the protocol.

Study Population

This monocentric RCT was followed in accordance with the ethical standards of the Washington University School of Medicine (WUSM) and was approved by the WUSM institutional review board. The study was conducted from April 2005 through August 2009 and was monitored by an independent data and safety monitoring board.

The participants of this trial have been described previously (11). Volunteers were recruited from the community through advertisements and provided written informed consent for participation. Eligible subjects were age ≥ 65 year with BMI ≥3 0 kg/m^2, stability of body weight within 2 kilograms over the preceding year, sedentary lifestyle (regular exercise of < 1hour/week), and on a stable medications for at least 6 months prior to enrollment. Additionally, all participants were required to have mild-to-moderate frailty determined by meeting at least two operational criteria: modified physical performance test score of 18-32, VO_{2peak} of 11-18 ml/kg/min, or difficulty in performing two instrumental activities of daily living (ADL) or one basic ADL (11). Exclusion criteria included severe cardiopulmonary disease, musculoskeletal/neuromuscular impairments that precluded exercise training, significant cognitive impairment, a history of malignancy, and current smoking. Candidates were also excluded if they had a history of diabetes or fasting glucose of ≥126 mg/dl.

Study Design

In this 1-year RCT, 107 participants were randomly assigned to one of four groups stratified for sex: 1) control group, 2) 10% diet-induced weight loss group (diet group), 3) exercise training without weight loss (exercise group) and 4) 10% diet-induced weight loss and exercise training (diet-exercise group). The randomization algorithm was generated by the WUSM Biostatistics Division and maintained by a member of the research team who did not interact with the participants.

As previously described (11), participants in the control group received general information regarding a healthy diet at monthly visits with the staff, and prohibited from participating in diet or exercise programs.

Participants in the diet group were prescribed a balanced diet that provided a deficit of 500-750 kcal/day from daily energy requirement and consisted of 1 g/kg body weight of high-quality protein (1). Dietary compliance was reinforced during weekly visits with a dietitian. Standard behavioral strategies were used to modify eating habits. Goals for weight loss included a reduction of 10% from baseline at 6 months, followed by maintenance of this weight for the remaining 6 months of the study.

Participants in the exercise group were counseled on maintaining a weight-stable diet. The multicomponent exercise sessions were of ~90 minutes duration (~15- min flexibility exercise, 30-min aerobic exercise, 30-min progressive resistance training, and 15-min balance exercises) conducted three times weekly at our exercise facility. All sessions were led by a physical therapist. Aerobic exercises consisted of treadmill, stationary cycling, and stair climbing. An initial goal of 65% of peak heart rate was achieved, followed by an increase in intensity to 70-85% of peak heart rate. Resistance training was performed using weight-lifting machines and consisted of nine upper and lower extremity exercises. Participants initially performed 1-2 sets of 8-12 repetitions at 65% of one-repetition maximum. The number of repetitions was then decreased to 6-8 repetitions/set and resistance was increased to approximately 70-85% of the one-repetition maximum (11).

Participants in the diet-exercise group participated in both weight management and exercise programs described above.

Additional details about the interventions including compliance data and exercise adaptations (e.g. improvements in strength, VO_{2peak}) have been reported (11).

Outcome Measures

The outcome in this secondary analyses was change in insulin sensitivity index (ISI) (12) at 12 months. Other outcomes included oral glucose tolerance test (OGTT) variables, abdominal adiposity, blood pressure (BP), lipids, adipocytokines, and cardiometabolic syndrome. Outcomes were assessed at baseline, 6 months, and 12 months, except MRI which was repeated only at 12-months. Personnel who conducted the assessments were not aware of group assignments.

Oral glucose tolerance test

A standard 75-g oral glucose tolerance test (OGTT) was performed after an overnight fast. Venous blood samples were obtained in fasted state, 30, 60, 90, and 120 min after glucose ingestion for the measurement of glucose and insulin using glucose oxidase method (YSI Inc., Yellow Springs) and radioimmunoassay. Areas under the curve (AUC) were calculated using the trapezoid method (13). ISI (12) was calculated using the formula: ISI=10000/ square root of [(fasting glucose × fasting insulin) × (mean glucose × mean insulin during OGTT)]. This index correlated (r=0.73) with the rate of whole-body glucose disposal during

a euglycemic insulin clamp study (12). HOMA-IR was also calculated (14). OGTT was performed ~72 hours after the last exercise to minimize acute effects on insulin sensitivity.

Waist circumference

Waist circumference was measured horizontally at the midpoint between the highest point of the iliac crest and the lowest portion of the 12th rib in the standing position (15;16).

Blood pressure

Blood pressure was measured with a sphygmomanometer cuff of the appropriate size after participants remained in the supine position for 15 min.

Fasting blood analyses

Lipoprotein levels were measured using automated enzymatic/colorimetric assays (Roche/Hitachi System). High-sensitive C-reactive protein (hs-CRP) was measured by immunoturbidimetric assay (Hitachi 917). Soluble tumor necrosis factor receptor 1 (sTNF R1) (R&D, Minneapolis) and adiponectin (Linco., St Louis) were measured using ELISA.

Body composition

Body fat mass, percent fat, and trunk fat were measured by dual X-ray absorptiometry (Hologic, Waltham MA) as described previously (17). Visceral and subcutaneous abdominal adipose tissue volumes were measured by MRI (Siemens), as described previously (18).

Cardiometabolic syndrome

Subjects who met ≥3 of the following criteria (19) were defined as having the cardiometabolic syndrome: waist circumference ≥102 cm in men and ≥88 cm in women, fasting glucose ≥100 mg/dL, triglyceride ≥150 mg/dL or drug treatment for elevated triglycerides, HDL-cholesterol <40 mg/dL in men and <50 mg/dL in women or drug treatment for low HDL-cholesterol, and systolic BP ≥130 or diastolic BP ≥85 mm Hg or on antihypertensive treatment with a history of hypertension.

Statistical Analysis

The sample size calculated for the main outcome of this study was sufficient to detect a clinically meaningful difference of 1.2±1.6 in the change in ISI among the groups, at an alpha level of 5%. Intention-to-treat analyses were performed using SAS version 9.2 (SAS Cary, NC). Baseline characteristics were compared using analyses of variance (ANOVAs) or chi-square tests. Longitudinal changes between groups were tested with the use of mixed-model repeated-measures ANOVA, adjusting for baseline values and sex. The primary focus of the analyses was the 12-month change in outcome in the four groups. In the mixed model, when the group-visit p value was <0.05, prespecified contrast statements were used to test three hypotheses: changes in the diet group were different from those in the control group; changes in the exercise group were different from those in the control group; and changes in the diet-exercise group were different from those in the diet group and exercise group. Analyses for within-group changes were performed using mixed-model repeated-measures ANOVA. Subjects were classified as having 3, 4, or 5 components of the cardiometabolic

syndrome; chi-square test was used to compare proportions with the cardiometabolic syndrome before and after treatment. Pearson's correlation was used to examine relationships among changes in variables and ISI, followed by stepwise multiple linear regression analyses to identify which variables were independent contributors to the changes in ISI. Data are presented as mean±SD unless otherwise stated. Statistical tests were two-tailed, and $p<0.05$ was considered significant.

Results

Study population

The results of recruitment, randomization, and follow up have been reported.[11] Briefly, 107 volunteers were randomized and 93 (87%) completed the study. Fourteen participants (4 in the control group, 3 in the diet group, 4 in the exercise group, and 3 in the diet-exercise group) discontinued the intervention due to personal or medical reasons but were included in the intention-to-treat analyses. Baseline characteristics were not significantly different (**Table 1**).

Attendance at group diet-behavioral therapy sessions was 82±8% in the diet-exercise group and 83±9% in the diet group. Attendance at exercise sessions was 82±10% (2.5±0.3 d/wk) in the diet-exercise group and 88±16% (2.5±0.3 d/wk) in the exercise group. Body weight decreased similarly in the diet-exercise (−8.6±3.8 kg [9% decrease]) and diet (−9.7±5.4 kg [10% decrease]) groups, while weight was constant in the exercise and control groups (**Figure 1 A, Table 2**) (11). VO_{2peak} relative to body weight (ml/kg/min) improved more ($p<.001$) in the diet-exercise group (3.2±2.4 ml/kg/min) than in the exercise group (1.4±1.0 ml/kg/min) or diet group (1.7±2.3 ml/kg/min) as previously reported (11). Absolute VO_{2peak} (L/min) improved similarly ($p=.92$) in the diet-exercise group (0.15±0.12 L/min) and exercise group (0.14±0.15 L/min) and did not change in the diet group (−0.03±0.19 L/min) or control group (−0.09±0.15 L/min).

Insulin sensitivity index

Although similar increases in ISI occurred in the diet-exercise group and diet group at 6 months, the ISI increased more ($p<.001$) in the diet-exercise group than in the diet group at 12 months: an increase of 2.4±2.3 points in the diet-exercise group (71% increase), compared with an increase of 1.2±1.6 points in the diet group (44% increase) (**Figure 1B, Table 2**). No significant changes in ISI occurred in both exercise and control groups.

Other OGTT variables

Insulin AUC (−2.9±3.9 and −2.9±6.1 × 10^3 mg.min/dL), glucose AUC (−1.4±2.8 and −2.2±2.7 × 10^3 mg.min/dL), fasting insulin (−6.2±7.1 vs. −4.5±7.3 μU/mL), and HOMA-IR (−1.7±1.9 vs. −1.4±1.8) decreased similarly in the diet-exercise group and diet group, respectively (**Table 2**). No significant changes occurred in these variables in both exercise and control groups.

Central obesity

Trunk fat (−3.3±1.9 and −3.4±2.4 kg), visceral fat (−787±896 and −561±454 cm^3) and subcutaneous fat (−464±475 and −457±326 cm^3) decreased similarly in the diet-exercise group and diet group, respectively (**Table 2**). Trunk fat (−0.8±1.3 kg) and visceral fat (−115±244 cm^3) decreased modestly in the exercise group.

Lean body mass

Lean body mass decreased less in the diet-exercise group (−1.8±1.7 kg) than in the diet group (−3.2±2.0 kg), while it increased in the exercise group (1.3±1.6 kg) as previously reported (11).

Adipocytokines

Serum hsCRP (−1.8±3.4 and −1.1±1.4 mg/L) and sTNF R1 (−17.0±29.2 and −12.8±21.7 pg/mL) decreased in the diet-exercise group and diet group, respectively, while sTNF R1 1 (12.3±20.6 pg/mL) increased in the control group (**Table 2**). Serum adiponectin (5.0±8.4 ng/mL and 4.0±5.5 ng/mL) increased in the diet-exercise group and diet group, respectively, but not in the exercise group and control group.

Cardiometabolic syndrome components

Fasting glucose (−5.4±9.0 and −3.7±11.5 mg/dL), waist (−8.2±10.3 and −8.4±8.6 cm), triglyceride (−30.7±40.0 and −24.3±33.1 mg/dl), systolic (−15.9±18.9 and −13.1±15.1 mmHg), and diastolic (−4.9±9.5 and −6.7±10.3 mmHg) BP decreased similarly in the diet-exercise group and diet group, respectively (**Table 2**). Waist (−4.0±9.1 cm) decreased modestly in the exercise group but otherwise no changes occurred in both exercise and control groups.

Prevalence of the cardiometabolic syndrome

The prevalence of the cardiometabolic syndrome (from 22/28 to 11/28 [−40% from baseline] and from 19/26 to 15/26 [−15% from baseline]) decreased in the diet-exercise group and diet group, respectively (**Table 3**). No changes in the prevalence occurred in the exercise and control groups.

Variables associated with ISI

Changes in body weight (r=−0.44; p<.001), trunk fat (r=−0.37; p<.001), visceral fat (r=−0.35; p<.01), sTNF R1 (r=−0.32; p<.01), and absolute VO_{2peak} (r=.27; p=.02) correlated with changes in ISI. In the stepwise multiple regression analyses, only changes in body weight (β=−0.42) remained significant in the final model, explaining 18% of the variance in ISI changes (r=−0.42; P<.001).

Discussion

In this one-year RCT, diet-induced weight loss alone but not exercise training alone improved insulin sensitivity and other cardiometabolic risk factors in obese older adults. Importantly, the combination of these two interventions resulted in an even greater

improvement in insulin sensitivity **at 12 months**, a novel finding in this population, suggesting a distinct complementary effect of exercise training added to weight loss.

The cardiometabolic syndrome is a cluster of metabolic derangements predictive of cardiovascular disease (19) which increases with age (20) Likewise, increased intraabdominal fat typical of aging (21) is independently associated with cardiometabolic syndrome (22). Notably, the risk of cardiovascular disease is 3-fold higher in adults with cardiometabolic syndrome (23;24). The observation of improved insulin sensitivity in the current study is of particular significance as insulin resistance has been implicated as the principal mediator of cardiometabolic syndrome (25). Indeed, insulin resistance, as estimated by the ISI, has been associated with an increased risk of death in older adults (26). Accordingly, an intervention directed at improving insulin sensitivity may reduce the incidence of cardiometabolic syndrome and perhaps improve mortality in this population.

Existing data pertaining to the effects of weight loss and exercise training on insulin sensitivity have been conflicting. While it is widely accepted that weight loss is associated with improvements in insulin sensitivity, the independent effects of exercise are less clear. Several studies support the notion that exercise training *per se* is not associated with chronic effects on insulin sensitivity (27-29). Conversely, other studies showing positive effects of exercise were confounded by lack of control for weight loss (30-35) or assessment of insulin sensitivity in proximity to the exercise (36-39), introducing acute effects which are transient in nature (40). Similarly, previous data on the effect of lifestyle interventions on inflammation have been inconsistent. Studies associating inflammation with inactivity have suggested a role for exercise (41); however, while exercise and weight loss have been shown to reduce subclinical inflammation, the role of exercise in the absence of weight loss has been less apparent (42). Studies have demonstrated that diet-induced weight loss, but not exercise alone, is associated with increased adiponectin levels (43) and decreased markers of inflammation (44).

The design of the current study allowed for the effects of diet-induced weight loss and exercise training on cardiometabolic risk factors to be investigated independently and in combination. Weight loss of ~10 percent was achieved at 6 months, followed by a 6-month weight-maintenance in both, the weight loss (diet group) and the weight loss and exercise (diet-exercise group) interventions. In contrast, weight remained unchanged in the exercise intervention (exercise group) and control group. Lifestyle interventions associated with weight loss, but not exercise training alone, resulted in favorable changes in cardiometabolic risk factors including waist, BP, triglycerides, and glucose metabolism, which translated into reduced prevalence of cardiometabolic syndrome. Additionally, visceral adiposity and adipocytokines were positively affected by weight-loss interventions, but not by exercise training alone. These findings highlight the importance of weight loss-based lifestyle interventions for reducing multiple cardiometabolic risk factors in obese older adults.

A novel finding in this obese older cohort with frailty syndrome was that of improved insulin sensitivity at 12 months in the diet-exercise group beyond which was observed in the diet group achieving similar weight loss without exercise. Our findings suggest a beneficial effect of exercise on insulin sensitivity which is not apparent without a significant

prerequisite weight loss. At 6 months, we found no differences in improvement in insulin sensitivity between the diet group and diet-exercise group, suggesting that the changes in insulin sensitivity were entirely due to weight loss. However, while there were no differences in insulin sensitivity initially between the diet group and diet-exercise group , there was continued improvement in insulin sensitivity during the weight-stable half of the trial observed only in the diet-exercise group. No further improvement in insulin sensitivity occurred in the diet group during this phase of the trial. Because weight was stable during the second half of the trial, the continued improvement in insulin sensitivity in the diet-exercise group could only be attributed to the exercise. Conversely, exercise without prerequisite weight loss (and similar fitness improvement) was not associated with improvement in insulin sensitivity, ruling out an effect of exercise that might have been overshadowed by weight loss during the first 6 months in the diet-exercise group. Rather, this novel finding suggest a threshold effect by which the deleterious effect of excess adiposity on insulin sensitivity precluded any benefit of exercise until a significant amount of weight loss was achieved. Interestingly, variables which correlated with improved insulin sensitivity consisted mainly of weight- and fat-associated changes (e.g. trunk fat, visceral fat, S-TNF R1), which did not differ between the diet and the diet-exercise groups, suggesting a distinct complementary mechanism by which exercise potentiated insulin sensitivity. It is possible that the beneficial effect of exercise following a prerequisite weight loss may be related to improvement in peripheral insulin sensitivity, as exercise training has been shown to enhance responsiveness of muscles to insulin with increased activity of proteins involved in insulin signaling (45;46). Further, there is a growing literature describing beneficial effect of exercise but not weight loss on the muscle fatty acid oxidation capacity of obese individuals (47;48). The present study provides the first evidence that this independent effect of exercise may be contingent upon preceding weight loss in this older population.

The strengths of our study include the degree of adherence to the 1-year interventions which allowed for assessment of the distinct effects of weight loss versus exercise without weight loss on multiple cardiometabolic risk factors. The similar degree of weight loss in the diet and diet-exercise groups allowed for unbiased comparison of the two interventions. The 6-month weight loss followed by 6-month weight maintenance phase±exercise training allowed for examination of the temporal pattern of changes over time. Our study was designed to examine the chronic rather than acute effects of exercise; therefore, we performed the metabolic tests several hours (~72 hours) after the last bout of exercise. Potential limitations include that we assessed insulin sensitivity using OGTT rather than the gold standard of glucose clamp technique. However, the ISI has been validated against the clamp (12) and found to be similar in its relationship with cardiovascular risk factors (49). We did not have muscle biopsy samples to directly assess metabolic outcomes within skeletal muscles in response to lifestyle interventions, which should be considered in future investigations in this population. We selected participants who volunteered for the study so our results may not necessarily apply to the general obese older population. Another potential limitation is that many statistical tests have been performed without rigorous correction for the multiplicity of tests. Our approach to minimize the risk for type 1 error included: 1) using pre-specified contrast statements to test three specific hypotheses and 2)

performing these focused tests only after achieving a significant omnibus F test ($p<0.05$) (see *Statistical Analysis*).

In conclusion, lifestyle interventions associated with weight loss result in clinically important improvements in insulin sensitivity and multiple other cardiometabolic risk factors in obese older adults. Importantly, exercise training in combination with diet-induced weight loss results in an even greater improvement in insulin sensitivity when continued for a prolonged period. Therefore, a lifestyle intervention strategy incorporating weight loss and regular exercise may best reduce the risk for cardiometabolic syndrome in obese older adults. Moreover, optimal treatment strategy in obese older adults should consider the positive effects of exercise on lean tissues and its additive effect on improving physical function when combined with weight loss (11).

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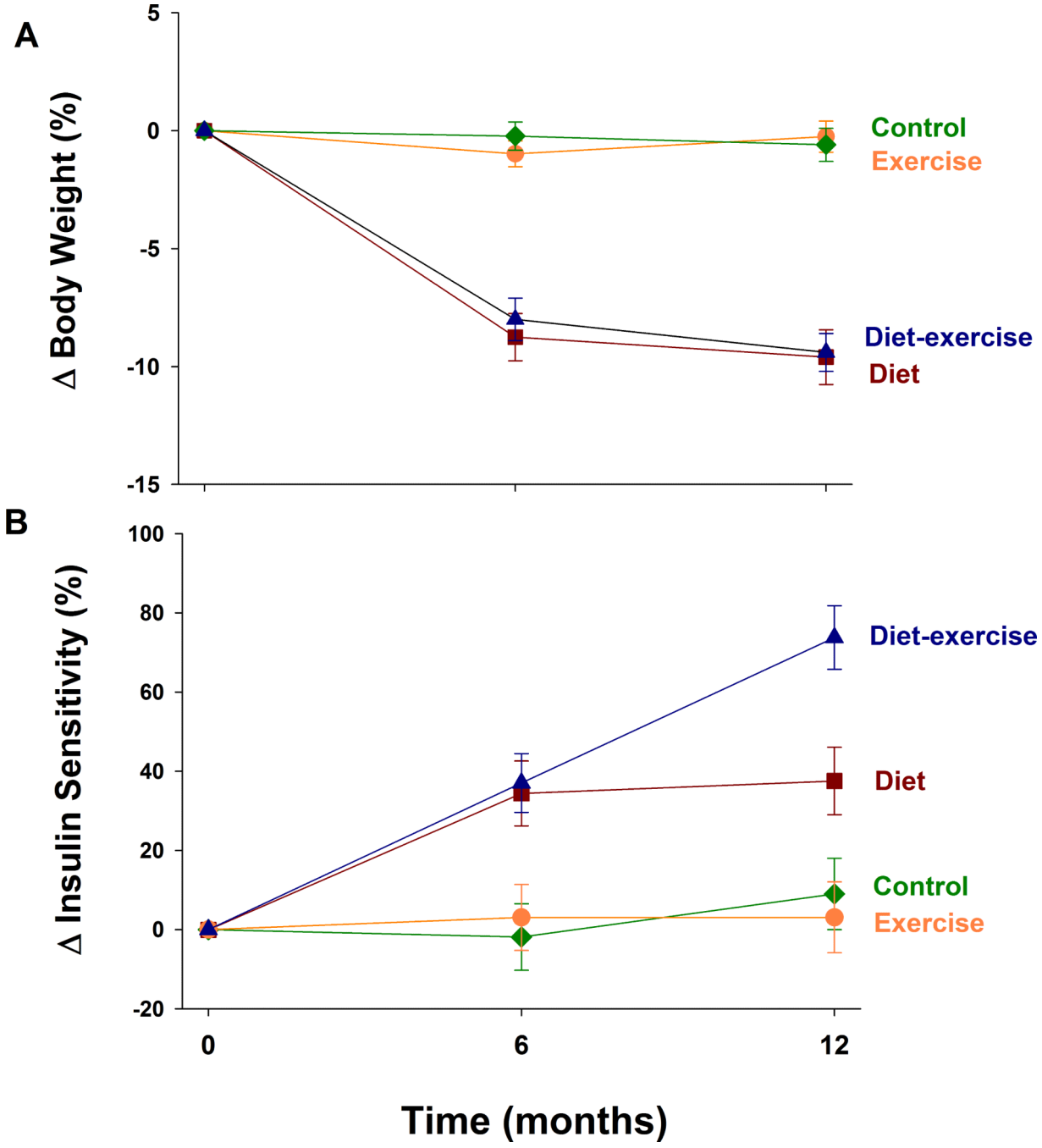

Figure 1.

Mean percent changes in body weight (Panel A) and insulin sensitivity (Panel B) during the 1-year interventions. In Panel A, the changes in body weight in the diet-exercise group and the diet group differed significantly from the changes in body weight in the exercise group and control group. In Panel B, the change in insulin sensitivity in the diet-exercise group differed significantly from the changes in insulin sensitivity in the diet group, exercise group, and control group. Values are mean ± standard error.

Table 1

Baseline Characteristics of Participants

	Control (n = 27)	Diet (n = 26)	Exercise (n = 26)	Diet-Exercise (n = 28)	*P* Value *
Age, mean (SD), y	69 (4)	70 (4)	70 (4)	70 (4)	0.85
Female, n (%)	18 (67)	17 (65)	16 (61)	16 (57)	0.89
White, n (%)	22 (81)	23 (88)	21 (81)	25 (89)	0.78
Height, mean (SD), cm	165.8 (9.7)	169.2 (9.5)	168.1 (1.1)	165.4 (8.7)	0.38
Weight, mean (SD), kg	101.0 (16.3)	104.1 (15.3)	99.2 (17.4)	99.1 (16.8)	0.66
Body mass index, mean (SD), kg/m^2	37.3 (4.7)	37.2 (4.5)	36.9 (5.4)	37.2 (5.4)	0.93
Total fat mass (kg)	43.8 (9.9)	42.8 (6.6)	41.6 (9.4)	41.9 (11.5)	0.67
Body fat percent, mean (SD)	43.4 (6.7)	41.6 (5.8)	40.2 (10.5)	42.1 (7.1)	0.53
Modified Physical Performance Test, mean (SD)	26.8 (4.5)	28.6 (1.9)	27.1 (3.1)	28.0 (2.9)	0.17
VO_{2peak} relative to body weight, mean (SD), ml/kg/min	16.3 (3.8)	17.6 (2.2)	17.4 (3.5)	17.3 (3.5)	0.55
Absolute $VO_{2peak,}$ mean (SD), L/min	1.69 (0.49)	1.84 (0.41)	1.76 (0.51)	1.73 (0.38)	0.66
History of cardiovascular disease, n (%)	8 (30)	8 (31)	7 (27)	9 (31)	0.98
Previous cigarette use, n (%)	9 (33)	7 (26)	9 (34)	11 (39)	0.82
Medication use, n (%)					
Antihypertensive	16 (59)	15 (57)	18 (69)	18 (64)	0.82
Antidyslipidemic	8 (29)	8 (30)	10 (26)	8 (25)	0.86

* *P* values, as calculated with the use of analyses of variance for quantitative data and chi-square tests for counts.

Table 2

Effect of Diet, Exercise, or Combined on Outcome Variables in Obese Older Adults

	Mean (SD) Value			Difference in Change from Baseline to 12 mo (95% CI)	*P* Value*
	Baseline	Change at 6 mo	Change at 12 mo		
Insulin sensitivity index					
Control group	3.3 (2.0)	−0.1 (0.8)	0.2 (1.4)	-	-
Diet group	2.7 (1.6)	1.1 (1.2)†	1.2 (1.6)†	-	-
Exercise group	3.5 (2.6)	0.1 (1.4)	0.1 (1.9)	-	-
Diet-exercise group	3.4 (2.4)	1.2 (1.6)†	2.4 (2.3)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	1.0 (0.0 to 1.8)	0.05
Exercise vs. control	-	-	-	−0.1 (−1.2 to 0.8)	0.66
Diet-exercise vs. diet	-	-	-	1.2 (0.2 to 2.1)	0.02
Diet-exercise vs. exercise	-	-	-	2.3 (1.4 to 3.4)	<0.001
Other OGTT variables					
Insulin AUC (× 10^3 mg.min/dL)					
Control group	9.1 (5.1)	0.9 (3.3)	0.6 (4.0)	-	-
Diet group	12.9 (7.5)	−3.1 (−5.9)†	−2.9 (6.1)†	-	-
Exercise group	10.7 (6.8)	0.1 (3.6)	−0.1 (3.6)	-	-
Diet-exercise group	10.8 (5.5)	−2.9 (4.1)†	−2.9 (3.9)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−3.5 (−6.3 to −1.4)	<0.01
Exercise vs. control	-	-	-	−0.5 (−3.0 to 1.9)	0.78
Diet-exercise vs. diet	-	-	-	0.0 (−1.8 to 2.9)	0.67
Diet-exercise vs. exercise	-	-	-	−3.0 (−5.2 to 0.4)	0.02
Glucose AUC (× 10^3 mg.min/dL)					
Control group	19.0 (2.8)	0.2 (3.2)	−0.3 (1.9)	-	-
Diet group	18.6 (3.5)	−1.8 (2.3)†	−2.2 (2.7)†	-	-
Exercise group	18.1 (2.8)	0.3 (2.2)	−0.3 (2.7)	-	-
Diet-exercise group	18.1 (3.6)	−0.9 (2.9)†	−1.4 (2.8)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−2.5 (−3.8 to −0.8)	<0.01
Exercise vs. control	-	-	-	0.0 (−1.8 to 1.4)	0.80
Diet-exercise vs. diet	-	-	-	0.8 (−0.8 to 2.2)	0.35
Diet-exercise vs. exercise	-	-	-	−1.7 (−2.9 to 0.2)	0.08
Fasting insulin (μU/mL)					
Control group	16.0 (9.9)	0.1 (7.1)	−2.0 (9.5)	-	-
Diet group	17.5 (9.9)	−5.0 (6.8)†	−4.5 (7.3)†	-	-
Exercise group	16.0 (10.2)	−1.1 (6.3)	−2.1 (6.4)	-	-

	Mean (SD) Value			Difference in Change from Baseline to 12 mo (95% CI)	*P* Value*
	Baseline	Change at 6 mo	Change at 12 mo		
Diet-exercise group	17.0 (12.0)	−3.3 (6.3)†	−6.2 (7.1)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−2.5 (−6.7 to 1.2)	0.12
Exercise vs. control	-	-	-	0.1 (−4.4 to 3.3)	0.88
Diet-exercise vs. diet	-	-	-	−1.7 (−5.4 to 2.4)	0.45
Diet-exercise vs. exercise	-	-	-	−4.1 (−8.4 to −0.6)	0.02
HOMA-IR					
Control group	4.1 (2.9)	0.3 (2.6)	−0.3 (2.9)	-	-
Diet group	4.2 (2.8)	−1.3 (1.7)†	−1.4 (1.8)†	-	-
Exercise group	4.0 (2.7)	−0.3 (1.7)	−0.7 (1.8)	-	-
Diet-exercise group	4.4 (3.6)	−1.1 (1.4)†	−1.7 (1.9)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−1.1 (−2.0 to 0.2)	0.12
Exercise vs. control	-	-	-	−0.4 (−1.3 to 1.0)	0.78
Diet-exercise vs. diet	-	-	-	−0.3 (−1.5 to 0.6)	0.43
Diet-exercise vs. exercise	-	-	-	−1.0 (−2.3 to −0.1)	0.04
Body weight and central obesity					
Body weight (kg)					
Control group	101.0 (16.3)	0.9 (2.8)	−0.1 (3.5)	-	-
Diet group	104.1 (15.3)	−9.0 (5.4)†	−9.7 (5.4)†	-	-
Exercise group	99.2 (17.4)	−0.3 (2.3)	−0.5 (3.6)	-	-
Diet-exercise group	99.1 (16.8)	−7.7 (4.2)†	−8.6 (3.8)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−9.0 (−1.1 to −6.7)	<0.001
Exercise vs. control	-	-	-	−0.4 (−2.7 to 1.8)	0.72
Diet-exercise vs. diet	-	-	-	0.3 (−1.9 to 2.6)	0.78
Trunk fat (kg)					
Control group	22.4 (5.6)	−0.3 (1.4)	0.5 (2.9)	-	-
Diet group	21.8 (4.1)	−3.2 (2.7)†	−3.4 (2.4)†	-	-
Exercise group	21.2 (4.1)	−0.6 (1.1)†	−0.8 (1.3)†	-	-
Diet-exercise group	20.9 (4.8)	−3.4 (1.8)†	−3.3 (1.9)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−3.9 (−5.2 to −2.9)	<0.001
Exercise vs. control	-	-	-	−1.3 (−2.4 to −0.8)	0.04
Diet-exercise vs. diet	-	-	-	0.1 (−0.9 to 1.3)	0.74
Diet-exercise vs. exercise	-	-	-	−2.5 (−3.8 to −1.5)	<.001
Visceral fat (cm^3)					
Control group	2591 (1539)	-	15 (589)	-	-

	Mean (SD) Value			Difference in Change from Baseline to 12 mo (95% CI)	*P* Value*
	Baseline	Change at 6 mo	Change at 12 mo		
Diet group	2175 (1087)	-	−561 (454)†	-	-
Exercise group	2231 (1183)	-	−115 (244)†	-	-
Diet-exercise group	2086 (1337)	-	−787 (896)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−576 (−866 to −285)	<0.001
Exercise vs. control	-	-	-	−130 (−380 to 120)	0.39
Diet-exercise vs. diet	-	-	-	−226 (−615 to 163)	0.19
Diet-exercise vs. exercise	-	-	-	−672 (−1031 to −312)	<0.001
Subcutaneous fat (cm^3)					
Control group	3805 (1036)	-	305 (889)	-	-
Diet group	3558 (958)	-	−457 (326)†	-	-
Exercise group	3256 (978)	-	−83 (326)	-	-
Diet-exercise group	3600 (1389)	-	−464 (475)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−762 (−1134 to −389)	<0.001
Exercise vs. control	-	-	-	−388 (−760 to −16)	0.02
Diet-exercise vs. diet	-	-	-	−7 (−231 to 217)	0.96
Diet-exercise vs. exercise	-	-	-	−381 (−605 to −156)	0.03
Lean body mass (kg)					
Control group	57.3 (11.5)	−0.7 (2.3)	−0.8 (2.5)		
Diet group	61.4 (13.0)	−3.5 (2.7)†	−3.2 (2.0)†		
Exercise group	57.6 (13.7)	1.1 (2.1)†	1.3 (1.6)†		
Diet-exercise group	57.2 (10.3)	−1.7 (1.6)†	−1.8 (1.7)†		
Intergroup comparisons					
Diet vs. control	-	-	-	−2.4 (−3.6 to 1.2)	<0.001
Exercise vs. control	-	-	-	2.1 (0.9 to 3.3)	<0.001
Diet-exercise vs. diet	-	-	-	1.2 (0.3 to 2.3)	0.04
Diet-exercise vs. exercise	-	-	-	−3.1 (−4 to −2.2)	<0.001
hs-CRP and adipocytokines					
hs-CRP (mg/L)					
Control group	3.8 (3.9)	0.7 (3.2)	2.2 (5.0)	-	-
Diet group	3.5 (3.0)	−1.0 (1.4)†	−1.1 (1.4)†	-	-
Exercise group	4.0 (4.0)	−0.2 (1.7)	0.7 (2.8)	-	-
Diet-exercise group	4.8 (6.3)	−1.8 (3.7)†	−1.8 (3.4)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−3.3 (−5.2 to −1.6)	<0.001
Exercise vs. control	-	-	-	−2.9 (−4.7 to −1.1)	<0.01

	Mean (SD) Value			Difference in Change from Baseline to 12 mo (95% CI)	*P* Value*
	Baseline	Change at 6 mo	Change at 12 mo		
Diet-exercise vs. diet	-	-	-	−0.7 (−2.2 to 1.2)	0.56
Diet-exercise vs. exercise	-	-	-	−1.1 (−2.7 to 0.7)	0.23
sTNF R1 (pg/mL)					
Control group	167.2 (34.7)	−2.2 (24.7)	12.3 (20.6)†	-	-
Diet group	155.8 (34.7	−11.9 (−19.7)†	−12.8 (21.7)†	-	-
Exercise group	166.6 (51.2)	−0.6 (22.4)	9.6 (20.4)	-	-
Diet-exercise group	177.5 (49.1)	−21.6 (26.1)†	−17.0 (29.2)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−25.1 (−36.7 to −8.7)	<0.01
Exercise vs. control	-	-	-	−2.7 (−15.2 to 12.9)	0.87
Diet-exercise vs. diet	-	-	-	−4.2 (−18.7 to 8.1)	0.44
Diet-exercise vs. exercise	-	-	-	−26.6 (−40.3 to −13.5)	<0.001
Adiponectin (ng/mL)					
Control group	31.9 (23.3)	−3.2 (10.8)	−4.9 (20.6)	-	-
Diet group	23.3 (12.1)	2.8 (4.7)†	4.0 (5.5)†	-	-
Exercise group	20.8 (7.4)	1.0 (5.9)	1.6 (5.1)	-	-
Diet-exercise group	24.4 (13.0)	2.5 (5.7)†	5.0 (8.4)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	8.9 (3.5 to 14.8)	<0.01
Exercise vs. control	-	-	-	6.5 (0.8 12.3)	0.02
Diet-exercise vs. diet	-	-	-	1.0 (−4.5 to 6.2)	0.74
Diet-exercise vs. exercise	-	-	-	3.4 (−1.9 to 9.0)	0.21
Metabolic syndrome components					
Fasting glucose (mg/dL)					
Control group	101.7 (10.1)	2.4 (9.4)	−0.6 (11.8)	-	-
Diet group	96.2 (12.2)	−3.5 (8.7)†	−3.7 (11.5)†	-	-
Exercise group	99.7 (8.4)	0.9 (8.9)	−1.3 (8.3)	-	-
Diet-exercise group	99.3 (11.3)	−2.4 (7.0)†	−5.4 (9.0)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−3.1 (−8.3 to 2.3)	0.27
Exercise vs. control	-	-	-	−0.7 (−5.5 to 5.3)	0.96
Diet-exercise vs. diet	-	-	-	−1.7 (−6.6 to 3.7)	0.58
Diet-exercise vs. exercise	-	-	-	−4.1 (−9.5 to 0.9)	0.11
Waist circumference (cm)					
Control group	117.5 (12.8)	−1.2 (7.2)	1.0 (6.1)	-	-
Diet group	118.2 (11.5)	−8.5 (10.5)†	−8.4 (8.6)†	-	-
Exercise group	114.9 (12.7)	−0.1 (8.0)	−4.0 (9.1)†	-	-

	Mean (SD) Value			Difference in Change from Baseline to 12 mo (95% CI)	*P* Value*
	Baseline	Change at 6 mo	Change at 12 mo		
Diet-exercise group	116.0 (14.8)	−7.9 (10.0)†	−8.2 (10.3)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−7.4 (−12.3 to −1.3)	0.02
Exercise vs. control	-	-	-	−3.0 (−8.4 to 2.8)	0.15
Diet-exercise vs. diet	-	-	-	0.2 (−5.3 to 5.1)	0.97
Diet-exercise vs. exercise	-	-	-	4.2 (−9.4 to 1.3)	0.13
HDL cholesterol (mg/dL)					
Control group	51.7 (13.4)	0.0 (4.9)	1.3 (5.5)	-	-
Diet group	53.3 (12.9)	1.0 (6.1)	1.6 (5.8)	-	-
Exercise group	53.7 (13.9)	−1.6 (3.1)	−1.5 (3.4)	-	-
Diet-exercise group	55.2 (15.4)	−1.3 (7.9)	1.1 (8.7)	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	2.9 (−1.2 to 6.5)	0.17
Exercise vs. control	-	-	-	−0.2 (−4.3 to 3.4)	0.82
Diet-exercise vs. diet	-	-	-	−0.5 (−4.1 to 3.1)	0.79
Diet-exercise vs. exercise	-	-	-	2.6 (−1.1 to 6.3)	0.17
Triglyceride (mg/dL)					
Control group	123.2 (50.4)	0.3 (33.2)	7.1 (29.3)	-	-
Diet group	144.6 (60.1)	−26.2 (39.2)†	−24.3 (33.1)†	-	-
Exercise group	158.4 (73.8)	−4.2 (65.9)	−18.9 (45.6)	-	-
Diet-exercise group	134.7 (65.1)	−18.9 (45.6)†	−30.7 (40.0)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−31.4 (−60.9 to −3.1)	0.03
Exercise vs. control	-	-	-	−16.1 (−46.7 to 11.9)	0.24
Diet-exercise vs. diet	-	-	-	−6.7 (−34.0 to 20.8)	0.63
Diet-exercise vs. exercise	-	-	-	−21.7 (−49.1 to 6.7)	0.14
Systolic blood pressure (mm Hg)					
Control group	133.3 (18.6)	−4.8 (19.8)	−5.9 (23.0)	-	-
Diet group	135.3 (19.1)	−15.9 (13.6)†	−13.1 (15.1)†	-	-
Exercise group	131.2 (11.7)	−0.4 (15.3)	−1.2 (15.5)	-	-
Diet-exercise group	138.6 (23.6)	−13.4 (24.5)†	−15.9 (18.9)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−7.2 (−18.5 to 4.1)	0.23
Exercise vs. control	-	-	-	4.7 (−7.4 to 15.5)	0.49
Diet-exercise vs. diet	-	-	-	−2.8 (−14.1 to 7.8)	0.49
Diet-exercise vs. exercise	-	-	-	−14.7 (−25.5 to −3.3)	<0.01
Diastolic blood pressure (mm Hg)					
Control group	71.5 (10.7)	0.7 (12.1)	−1.1 (11.2)	-	-

	Mean (SD) Value			Difference in Change from Baseline to 12 mo (95% CI)	*P* Value*
	Baseline	Change at 6 mo	Change at 12 mo		
Diet group	75.7 (11.0)	−6.0 (9.6)†	−6.7 (10.3)†	-	-
Exercise group	70.9 (8.3)	−1.4 (11.1)	−2.1 (6.1)	-	-
Diet-exercise group	74.0 (10.1)	−4.5 (10.6)†	−4.9 (9.5)†	-	-
Intergroup comparisons					
Diet vs. control	-	-	-	−5.5 (−11.1 to 0.8)	0.09
Exercise vs. control	-	-	-	−1.0 (−7.6 to 4.4)	0.60
Diet-exercise vs. diet	-	-	-	−1.8 (−5.0 to 6.6)	0.77
Diet-exercise vs. exercise	-	-	-	−2.8 (−8.6 to 3.2)	0.36

Abbreviations: CI, confidence interval; OGTT, oral glucose tolerance test; AUC, area under the curve, HOMA-IR, homeostasis model assessment of insulin resistance, hs-CRP, high sensitivity C-reactive protein; sTNF R1, soluble tumor necrosis factor receptor 1

*P values, as calculated with the use of mixed-model repeated-measures analyses of variance contrasts

†$P<.0.05$ for the comparison of the value from baseline, as calculated with the use of mixed-model repeated-measures analyses of variance

Table 3

Effect of Diet, Exercise, or Combined on the Prevalence of the Cardiometabolic Syndrome in Obese Older Adults

Participants with cardiometabolic syndrome, no. (%)	**Control (n=27)**	**Diet (n=26)**	**Exercise (n=26)**	**Diet-Exercise (n=28)**	***P* Value***
Baseline					
3 criteria	9 (33)	8 (31)	7 (27)	11 (39)	
4 criteria	8 (30)	7 (27)	12 (46)	9 (32)	
5 criteria	3 (11)	4 (15)	2 (8)	2 (7)	
Total	20 (74)	19 (73)	21 (81)	22 (79)	0.90
Six months					
3 criteria	8 (30)	7 (27)	6 (23)	6 (21)	
4 criteria	13 (48)	4 (15)	11 (42)	8 (29)	
5 criteria	1 (4)	2 (8)	3 (12)	2 (7)	
Total	22 (82)	13 (50)	20 (77)	16 (57)	0.04
1 year					
3 criteria	7 (26)	10 (39)	9 (35)	4 (14)	
4 criteria	9 (33)	4 (15)	9 (35)	5 (18)	
5 criteria	4 (15)	1 (4)	2 (8)	2 (7)	
Total	20 (74)	15 (58)	20 (77)	11 (39)	0.02

*Between-group difference in the proportions of participants with the cardiometabolic syndrome at baseline, six months, and 1 year, as calculated with the use of Chi-square test