Exercise-Induced Reduction in Obesity and Insulin Resistance in Women: a Randomized Controlled Trial

Robert Ross,† Ian Janssen,*‡ Jody Dawson,* Ann-Marie Kungl,* Jennifer L. Kuk,* Suzy L. Wong,* Thanh-Binh Nguyen-Duy,* SoJung Lee,* Katherine Kilpatrick,* and Robert Hudson†*

Abstract

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Objectives: To determine the effects of equivalent diet- or exercise-induced weight loss and exercise without weight loss on subcutaneous fat, visceral fat, and insulin sensitivity in obese women.

Research Methods and Procedures: Fifty-four premenopausal women with abdominal obesity [waist circumference 110.1 ± 5.8 cm (mean ± SD)] (BMI 31.3 ± 2.0 kg/m^2) were randomly assigned to one of four groups: diet weight loss ($n = 15$), exercise weight loss ($n = 17$), exercise without weight loss ($n = 12$), and a weight-stable control group ($n = 10$). All groups underwent a 14-week intervention.

Results: Body weight decreased by ~6.5% within both weight loss groups and was unchanged in the exercise without weight loss and control groups. In comparison with controls, cardiorespiratory fitness improved within the exercise groups only ($p < 0.01$). Reduction in total, abdominal, and abdominal subcutaneous fat within the exercise weight loss group was greater ($p < 0.001$) than within all other groups. The reduction in total and abdominal fat within the diet weight loss and exercise without weight loss groups was greater than within controls ($p < 0.001$) but not different from each other ($p > 0.05$). Visceral fat decreased within all treatment groups ($p < 0.008$), and these changes were not different from each other. In comparison with the control group, insulin sensitivity improved within the exercise weight loss group alone ($p < 0.001$).

Discussion: Daily exercise without caloric restriction was associated with substantial reductions in total fat, abdominal fat, visceral fat, and insulin resistance in women. Exercise without weight loss was also associated with a substantial reduction in total and abdominal obesity.

Key words: weight loss, exercise, visceral fat, abdominal fat, insulin resistance

Introduction

The escalation in the prevalence of obesity in both men and women (1,2) represents a major public health problem and reinforces the need to develop effective treatment strategies. Although caloric restriction remains the cornerstone of obesity reduction strategies (3,4), we have recently reported that exercise-induced weight loss is associated with a greater reduction in total body fat, a preservation of lean tissue mass, and an increase in cardiorespiratory fitness in comparison with equivalent diet-induced weight loss in men and that exercise without weight loss is associated with significant reductions in abdominal obesity (5). Little is known about the utility of exercise alone (e.g., no caloric restriction) as a strategy for obesity reduction in women. Although some exercise studies have included women, few prescribed an exercise program for which one would expect meaningful weight loss (6). A rationale that would support the exclusion of women in studies where exercise is performed for longer duration (e.g., 45 min/d) is not known. To the contrary, when performing moderate-intensity exercise,

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*School of Physical and Health Education and Departments of †Medicine, Division of Endocrinology and Metabolism and ‡Community Health and Epidemiology, Queen's University, Kingston, Ontario, Canada.
Address correspondence to Robert Ross, School of Physical and Health Education, Queen's University, Kingston, Ontario, Canada K7L 3N6.
E-mail: rossr@post.queensu.ca

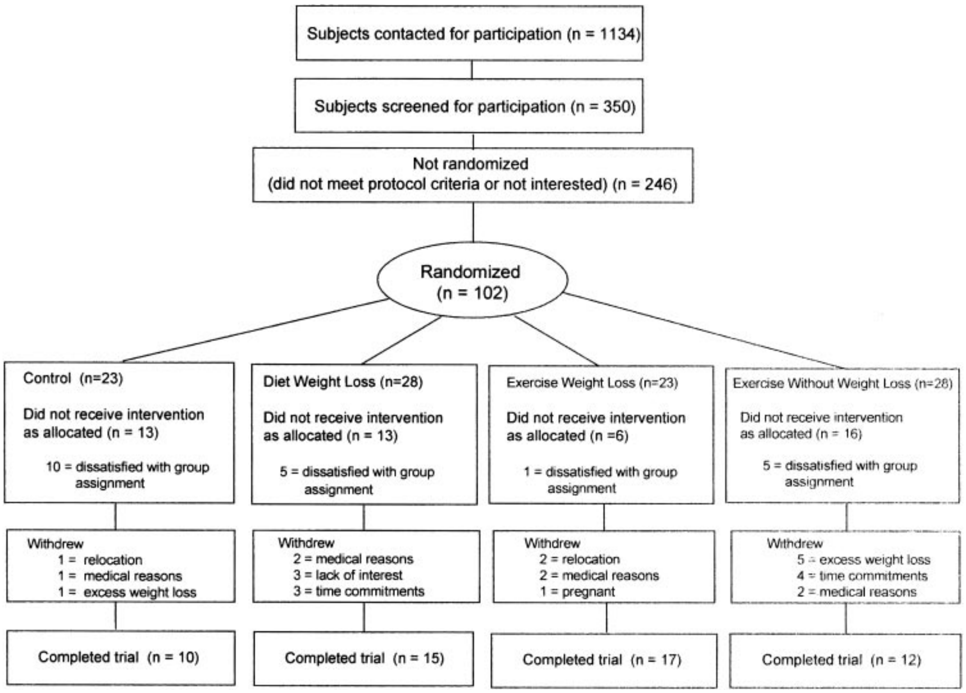

Figure 1: Flow of participants through the study.

women demonstrate a greater lipid and lower carbohydrate oxidation compared with men (7,8). Further, exercise in women is associated with a marked increase in lipolysis in abdominal subcutaneous adipose tissue in comparison with femoral adipose tissue (9), suggesting that exercise-induced weight loss would be associated with a preferential reduction in abdominal obesity. Were this true, it would have important public health implications because it is now established that abdominal obesity conveys a substantial health risk (3,10–13).

We performed a randomized controlled trial to determine the independent effect of diet- or exercise-induced weight loss on obesity and insulin resistance in moderately obese women. We also evaluated whether exercise without weight loss was associated with reductions in abdominal obesity and insulin resistance.

Research Methods and Procedures

Subjects

Subjects were recruited from Kingston, a typical suburban region, using the general media. Inclusion criteria required that the women were premenopausal, had a BMI (kilograms per meter squared) > 27, a waist circumference > 88 cm, were weight stable (± 2 kg) for 6 months before the beginning of the study, were nonsmokers, consumed on average <2 alcoholic beverages per day, led a sedentary lifestyle (no participation in structured physical activities during previous year), and were taking no medications, including oral contraceptives, known to affect the principal outcome measures. All subjects undertook a preparticipation medical exam including screening for normal glucose tolerance and plasma lipid profile. Menopausal status was confirmed by measurement of follicle-stimulating hormone and leuteinizing hormone values pretreatment.

Randomization Procedure

Before the initiation of the baseline (run-in) period, eligible women were randomly assigned using a computer program into one of the following four groups (Figure 1): control, diet weight loss, exercise weight loss, and exercise without weight loss. Of the 102 subjects randomized, 48 did not begin or complete the trial (Figure 1). Of the 48 who did not complete, 21 were dissatisfied with group assignment and, thus, chose not to begin the program. With a single exception, the "dissatisfied" volunteers indicated that they clandestinely sought exercise and/or weight loss and had been willing to chance randomization to a treatment group of their choice. A χ^2 analysis performed using the three treatment groups revealed that the dropout rate was lower in the exercise weight loss group in comparison with the diet weight loss and exercise without weight loss groups ($p < 0.05$).

For the anthropometric variables studied (Table 1), those who chose not to participate were similar to those who completed the trial ($p > 0.10$). Baseline characteristics were not different among groups ($p > 0.10$; Table 1).

Table 1. Baseline characteristics of subjects randomized who did not complete treatment compared with those who completed the study*

Variable and treatment	Control	Diet weight loss	Exercise weight loss	Exercise without weight loss
Number				
Subjects not completing treatment	13	14	7	16
Subjects completing treatment	10	15	17	12
Age (years)				
Subjects not completing treatment	40.4 ± 6.4	39.6 ± 6.8	36.3 ± 10.1	41.8 ± 5.4
Subjects completing treatment	43.7 ± 6.4	43.9 ± 4.9	43.2 ± 5.1	41.3 ± 7.2
Weight (kg)				
Subjects not completing treatment	89.3 ± 9.7	92.6 ± 8.2	91.2 ± 11.5	84.9 ± 11.3
Subjects completing treatment	88.1 ± 8.2	86.6 ± 10.8	86.9 ± 10.9	88.1 ± 10.9
BMI (kg/m^2)				
Subjects not completing treatment	32.8 ± 2.8	34.6 ± 2.8	32.7 ± 3.6	32.8 ± 3.1
Subjects completing treatment	32.4 ± 2.8	31.9 ± 2.8*	32.8 ± 3.9	32.9 ± 3.1
Waist circumference (cm)				
Subjects not completing treatment	103.2 ± 12.4	103.6 ± 10.1	102.7 ± 8.4	98.7 ± 12.6
Subjects completing treatment	98.1 ± 6.9	97.8 ± 8.0	100.5 ± 8.2	99.5 ± 8.0

Data are presented as means ± SD.
* With exception of BMI in the diet weight loss group, there were no differences between subjects completing vs. not completing treatment ($p > 0.05$).

All subjects gave their fully informed and written consent to participate in the study, which was conducted in accordance with the ethical guidelines as set by Queen's University. Financial incentives were not provided to the participants.

Diet and Exercise Regimen

During the baseline period, daily energy requirements for all subjects were determined by estimating resting energy expenditure and multiplying the obtained value by a factor of 1.5 (14). All subjects followed a weight maintenance diet (50% to 60% carbohydrate, 15% to 20% protein, and 20% to 30% fat) at this level for a 4- to 5-week baseline period. During this period, body weight was monitored to determine the accuracy of the prescribed energy requirement and adjusted accordingly so that body weight was maintained. Throughout the 14-week treatment period, the control group was asked to maintain body weight. The diet weight loss group was asked to reduce the isocaloric diet by 500 kcal/d for the duration of the treatment period. This was designed to achieve a weekly weight loss that approximated 1.0 lb (0.45 kg). The exercise weight loss group was asked to maintain the isocaloric diet for the duration of the treatment. This, combined with daily exercise wherein the energy expended was 500 kcal/d (see below), would also achieve a weight loss that approximated 1.0 lb (0.45 kg) per week. Participants within the exercise without weight loss group were asked to maintain body weight and, thus, consumed the calories required to compensate for the energy expended during the daily exercise sessions (~500 kcal). Adherence to this protocol was determined by examination of body weight on a weekly basis. If the participant was unable to maintain body weight within 1 kg of their baseline value for 3 consecutive weeks they were withdrawn from the program. At the end of the treatment period, isocaloric requirements were determined and prescribed for a 1-week weight stabilization period. All subjects were free living and consumed foods that were self-selected. No vitamins or other nutritional supplements were prescribed. Each subject participated in a series of weekly, 1-hour seminars wherein the dietitian taught proper food selection and preparation. Subjects were instructed that the composition of both the maintenance and energy reduced diets should provide energy as follows: ~55% to 60% carbohydrate, 20% protein, and 30% fat. For the duration of the study period (~20 weeks), subjects kept daily, detailed food records that were analyzed by the subjects and reviewed by the study dietitian. For 2 weeks (weeks 4 and 10), the subjects' diet records were analyzed using a computerized program (Food Processor; Esha Research, Salem, OR) to confirm that the fat, carbo-

Table 2. Self-reported food intake determined from daily diaries

	Self-reported dietary intake* (weeks 1 to 14)		Computerized analysis of diet records* (weeks 4 and 10)		
	Caloric intake (kcal/week)	Fat intake (% of total)	Protein (% of total)	Carbohydrate (% of total)	Fat (% of total)
C	1717 ± 238	27.5 ± 2.7	15.7 ± 1.3	55.1 ± 3.9	28.1 ± 3.1
DWL	1603 ± 323	24.8 ± 4.0	16.9 ± 1.6	57.9 ± 7.5	24.7 ± 4.2
EWL	1838 ± 256	27.2 ± 3.6	15.9 ± 2.1	56.8 ± 5.5	28.2 ± 3.5
EWW	2501 ± 410	28.0 ± 3.4	15.1 ± 1.4	56.9 ± 5.5	28.9 ± 4.6

C, control; DWL, diet weight loss; EWL, exercise weight loss; EWW, exercise without weight loss.
* No group differences ($p > 0.10$).

hydrate, and protein consumption was in line with that in the self-reported food diaries (Table 2).

Subjects within both exercise groups performed daily exercise (brisk walking or light jogging) on a motorized treadmill for the duration of the 14-week trial. The duration of each exercise session was determined by the time required to expend 500 kcal. Subjects were asked to exercise at ~80% of their maximal heart rate. Energy expenditure was determined using the heart rate and oxygen consumption data obtained from the pretreatment graded exercise test and adjusted from the results of two subsequent tests performed at weeks 4 and 8. Heart rate was monitored every 5 minutes during each session using an automated heart rate monitor (Polar Oy, Kempele, Finland). All exercise sessions were by appointment and were supervised. Maximal oxygen uptake was determined using a graded treadmill test and standard open-circuit spirometry techniques (SensorMedics, Yorba Linda, CA). Each subject was required to participate in a practice $V\text{O}_2$ treadmill test before initial baseline testing. Peak $V\text{O}_2$ was attained when at least two of the following three criteria were achieved: no increase in $V\text{O}_2$ despite further increases in treadmill grade, a heart rate at or above age-predicted maximum (220 − age), and/or a respiratory exchange ratio in excess of 1.0.

Magnetic Resonance Imaging (MRI)[1] and Anthropometric Measurements

Whole-body (~45 equidistant images) MRI data were obtained with a General Electric 1.5 Tesla magnet (Milwaukee, WI) using an established protocol described in detail elsewhere (15,16). Once acquired, the MRI data were transferred to computer work stations for analysis using specially designed computer software (Tomovision Inc., Montreal, QC, Canada), the procedures for which are described elsewhere (15,17). For adipose tissue (fat) and skeletal muscle, volume units (liters) were converted to mass units (kilograms) by multiplying the volumes by the assumed constant density for fat (0.92 kg/L) and fat-free skeletal muscle (1.04 kg/L) (18). Waist circumference measurements were obtained at the level of the last rib.

Insulin Sensitivity and Glucose Tolerance

Subjects consumed a weight maintenance diet consisting of at least 200 grams of carbohydrates for a minimum of 4 days before measurements of insulin sensitivity and were asked to avoid strenuous physical activity for 3 days preceding the studies. Exercise group posttreatment data were obtained 4 days after the last exercise session. Subjects stayed in the hospital the night before the measurement of insulin sensitivity. All studies were performed at 8 AM after a 12- to 14-hour overnight fast. An antecubital vein was catheterized for infusion of insulin and 20% glucose, and a hand vein was cannulated in a retrograde fashion and placed in a heating pad for sampling of arterialized blood. Insulin was infused at a rate of 40 mU/m^2 per minute for 3 hours. Plasma glucose was measured using an automated glucose analyzer (YSI 2300 Glucose Analyzer; YSI, Yellow Springs, OH) every 5 minutes in arterialized blood. Glucose disposal rate was calculated using the average exogenous glucose infusion rate during the final 30 minutes of euglycemia.

A 2-hour, 75-gram oral glucose tolerance test (OGTT) was administered the morning after an overnight fast pre- and ~6 days posttreatment. Blood samples were collected from an antecubital vein at −15, 0, 30, 60, 90, and 120 minutes. Glucose was measured using an automated glucose analyzer (YSI 2300 Glucose Analyzer, YSI) and insulin using a radioimmunoassay kit (Intermedico, Toronto, ON, Canada). Areas under the glucose and insulin curves were determined using a trapezoid model (19).

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[1] Nonstandard abbreviations: MRI, magnetic resonance imaging; OGTT, oral glucose tolerance test.

Determination of Sample Size and Power

The power calculations were based on our prior observations in obese men (5), wherein the within-group SDs for the relative changes in abdominal fat, visceral fat, and insulin sensitivity were 5%, 7%, and 10%, respectively. For a four-group comparison with 10 subjects or more per group and α set at 0.008 (to control for multiple comparisons), we had a power of >0.80 to detect a relative treatment difference of 8% for abdominal fat, 10% for visceral fat, and 16% for insulin sensitivity. Statistical power was calculated using Sample Power version 1.00 (SPSS Inc., Chicago, IL).

Statistical Analyses

Data are presented as group means ± SD unless otherwise indicated. Only the data from subjects who completed the study were analyzed. A one-way ANOVA was performed to examine differences among the treatments before intervention. A four- (group) by two- (time) way ANOVA with repeated measures was used to evaluate main treatment effects and interactions. A Bonferroni post hoc comparison test was used to locate significant treatment differences (interactions). Relationships between changes in fat depots and anthropometric variables were determined using Pearson correlation coefficients. Statistical procedures were performed using SPSS version 11.

Results

Adherence to the Diet and Exercise Programs

Attendance at the exercise sessions averaged 96% (range 76% to 100%) for both exercise groups. The average duration (exercise without weight loss vs. exercise weight loss, 63 vs. 64 minutes), intensity (82% vs. 80% of predicted maximum heart rate), and energy expenditure per exercise session (517 ± 58 vs. 524 ± 52 kcal) were not different among exercise groups ($p > 0.1$). Cardiorespiratory fitness improved within the exercise groups to a similar extent (23% vs. 24%) in comparison with controls ($p < 0.001$) but did not change within the diet weight loss group ($p > 0.2$) (Table 3).

Analysis of the daily dietary intake records indicated that the relative fat intake (percentage) was not different among groups ($p > 0.1$; Table 2). This observation was reinforced by a computer analysis of the diet records for weeks 4 and 10 (Table 2). In comparison with the baseline period, daily caloric intake decreased within the diet weight loss group (~400 kcal/d, $p < 0.05$), did not change within the exercise weight loss group ($p > 0.1$), and increased within the exercise without weight loss group (~400 kcal/d, $p < 0.05$).

Weight Loss and Anthropometric Variables

Body weight did not change within the control and exercise without weight loss groups (Table 3). The average weight loss in the diet weight loss and exercise weight loss groups was not different ($p > 0.05$; Table 4) and represented ~6.5% of initial body weight. The reduction in waist circumference within the weight loss groups was greater in comparison with controls ($p < 0.001$) but not different from each other ($p > 0.05$; Table 4). The reduction in waist circumference within the exercise weight stable group was greater in comparison with controls ($p < 0.001$), less than the exercise weight loss group, but not different from the diet weight loss group ($p > 0.1$; Table 3).

Total Fat and Skeletal Muscle

In comparison with controls, a significant reduction ($p < 0.001$) in total fat was observed within both weight loss groups; however, the average reduction in total fat was greater ($p < 0.001$) in the exercise weight loss [−2.6 kg (95% confidence interval, 1.4 to 3.9)] than the diet weight loss group (Figure 2; Table 4). The reduction in total fat within the exercise without weight loss group was greater in comparison with controls ($p < 0.001$), less than the exercise weight loss group, but not different from the diet weight loss group ($p > 0.1$; Figure 2). Reduction in total fat was related to weight loss in both the diet weight loss ($r = 0.59$, $p = 0.02$) and exercise weight loss ($r = 0.52$, $p = 0.03$) groups. However, these variables were not related in the exercise without weight loss group ($p > 0.9$).

In comparison with controls, skeletal muscle mass did not change within any of the treatment groups ($p > 0.05$). However, the increase in skeletal muscle within the exercise without weight loss group was different from the loss in the diet weight loss group ($p < 0.008$; Table 3).

Abdominal Fat

The average reduction in total abdominal fat (abdominal subcutaneous and visceral combined) and abdominal subcutaneous fat within the exercise weight loss group was greater ($p < 0.001$) than within all other groups (Figure 3). The reduction in total abdominal and abdominal subcutaneous fat within the diet weight loss and exercise without weight loss groups was different from controls ($p < 0.008$) but not different from each other ($p > 0.1$; Figure 3). In comparison with the controls, significant ($p < 0.001$) reductions were observed for visceral fat within all treatment groups, but these changes were not different from each other ($p > 0.1$; Figure 3). Collapsed across all groups ($n = 54$), changes in abdominal fat mass ($r = 0.57$) and visceral fat mass ($r = 0.47$) were significantly ($p < 0.001$) related to the corresponding change in waist circumference.

Insulin Sensitivity and Glucose Tolerance

Plasma glucose and insulin values during the last 30 minutes of the clamp studies pre- and posttreatment were not different within or among groups ($p > 0.05$; data not shown). Glucose disposal improved significantly within the

Table 3. Selected anthropometric, MRI, and metabolic variables pre- and posttreatment (14 weeks later)

	Control (n = 10)		**Diet weight loss (n = 15)**		**Exercise weight loss (n = 17)**		**Exercise without weight loss (n = 12)**	
	Pretreatment	**Posttreatment**	**Pretreatment**	**Posttreatment**	**Pretreatment**	**Posttreatment**	**Pretreatment**	**Posttreatment**
Anthropometric								
Age (years)	43.7 ± 6.4		43.9 ± 4.9		43.2 ± 5.1		41.3 ± 7.2	
Weight (kg)	88.1 ± 8.2	88.6 ± 7.4	86.6 ± 10.9	80.1 ± 11.2*	86.8 ± 10.9	80.9 ± 10.8*	88.1 ± 10.5	87.6 ± 10.6†‡
BMI (kg/m^2)	32.4 ± 2.8	32.7 ± 2.9	31.9 ± 2.8	30.2 ± 3.0*	32.8 ± 3.8	30.4 ± 3.7*	32.9 ± 3.2	32.4 ± 3.0†‡
Waist circumference (cm)	98.1 ± 6.9	99.2 ± 7.7	97.8 ± 8.0	94.0 ± 7.9*	100.5 ± 8.2	94.0 ± 8.3*	99.5 ± 8.0	96.4 ± 7.6*‡
MRI								
Total fat (kg)	40.4 ± 5.4	41.2 ± 5.2	39.2 ± 7.8	35.1 ± 7.1*	41.2 ± 7.6	34.5 ± 7.8*†	40.3 ± 6.8	37.6 ± 6.7*
Total subcutaneous fat (kg)	34.2 ± 4.3	35.2 ± 4.3	33.9 ± 6.9	30.3 ± 6.4*	35.2 ± 7.1	29.8 ± 7.3*†	34.3 ± 6.9	32.4 ± 6.5*‡
Abdominal fat (kg)	8.2 ± 1.6	8.2 ± 1.5	7.9 ± 1.7	7.0 ± 1.6*	8.7 ± 1.6	7.0 ± 1.5*†	8.4 ± 1.6	7.6 ± 1.6*‡
Subcutaneous fat (kg)	5.9 ± 1.1	6.0 ± 0.9	5.6 ± 1.5	5.1 ± 1.5*	6.5 ± 1.2	5.4 ± 1.2*†	6.1 ± 1.3	5.8 ± 1.4*
Visceral fat (kg)	2.3 ± 0.9	2.2 ± 0.9	2.4 ± 1.2	1.9 ± 1.0*	2.3 ± 0.8	1.6 ± 0.7*	2.2 ± 0.8	1.8 ± 0.6*
Skeletal muscle (kg)	22.7 ± 1.9	22.7 ± 2.1	22.5 ± 3.2	22.0 ± 2.7	22.2 ± 3.0	22.2 ± 2.6	22.8 ± 3.5	23.9 ± 2.8†
Metabolic								
Fasting glucose (mg/dL)	96.0 ± 8.3	91.5 ± 10.6	97.2 ± 12.4	92.6 ± 6.9	95.9 ± 9.8	90.1 ± 10.9	95.2 ± 10.5	93.7 ± 11.9
Fasting insulin (pM)	44.2 ± 20.8	38.7 ± 21.7	48.5 ± 33.7	41.5 ± 32.8	62.8 ± 50.6	34.9 ± 24.4	42.1 ± 23.4	36.3 ± 26.4
OGTT glucose (mM/2 hours)	25.8 ± 3.6	28.8 ± 6.2	30.2 ± 4.8	29.8 ± 4.7	28.7 ± 6.5	27.3 ± 4.9	30.7 ± 6.1	28.9 ± 5.3
OGTT insulin (pM/2 hours)	1095 ± 675	1156 ± 577	1573 ± 1064	1487 ± 1112	1757 ± 883	1327 ± 600*	1785 ± 808	1345 ± 474
Glucose disposal (mg/kg muscle per minute)	22.7 ± 5.6	22.9 ± 6.6	19.5 ± 7.4	22.8 ± 8.3	19.7 ± 9.5	26.0 ± 8.0*	18.8 ± 6.6	20.6 ± 5.9
Maximum oxygen uptake (L/min)	2.2 ± 0.2	2.2 ± 0.3	2.1 ± 0.3	2.0 ± 0.5	2.1 ± 0.5	2.6 ± 0.5*†	2.2 ± 0.3	2.7 ± 0.4*†

Data are presented as means ± SD.

* Significant treatment differences (pre vs. post) compared with control ($p < 0.05$).

† Significant treatment differences (pre vs. post) compared with diet weight loss ($p < 0.05$).

‡ Significant treatment differences (pre vs. post) compared with exercise weight loss ($p < 0.05$).

Table 4. Comparison of change scores between the diet and exercise weight loss groups

	Diet weight loss* ($n = 15$)	Exercise weight loss* ($n = 17$)	Difference	95% Confidence intervals
Anthropometric				
Weight (kg)	−5.2 ± 1.2	−6.1 ± 1.2	1.0	0.2 to 1.9
Waist circumference (cm)	−4.1 ± 2.4	−6.5 ± 2.6	2.3	0.5 to 4.1
MRI				
Total fat (kg)	−4.1 ± 1.5	−6.7 ± 1.9	2.6†	1.4 to 3.9
Total subcutaneous fat (kg)	−3.2 ± 1.3	−5.3 ± 1.9	2.1†	0.9 to 3.4
Abdominal fat (kg)	−0.9 ± 0.6	−1.7 ± 0.7	0.8†	0.3 to 1.3
Abdominal subcutaneous fat (kg)	−0.4 ± 0.5	1.1 ± 0.4	0.6†	0.3 to 1.0
Visceral fat (kg)	−0.5 ± 0.4	−0.7 ± 0.5	0.2	−0.1 to 0.5
Skeletal muscle (kg)	−0.5 ± 1.0	0.3 ± 1.3	−0.5	−1.4 to 0.4
Metabolic				
Fasting glucose (mg/dL)	−4.6 ± 14.4	−5.8 ± 13.2	1.2	−8.7 to 11.2
Fasting insulin (pM)	−10.5 ± 26.6	−27.8 ± 35.7	17.6	−5.9 to 41.2
OGTT glucose area (mM/2 hours)	−0.4 ± 2.9	−1.3 ± 5.2	0.8	−2.3 to 4.0
OGTT insulin area (pM/2 hours)	−85 ± 519	−501 ± 504	416	39 to 792
Glucose disposal (mg/kg muscle per minute)	3.2 ± 3.6	6.8 ± 6.7	−3.7	−7.8 to 0.5
Maximal oxygen uptake (L/min)	−0.6 ± 0.2	0.5 ± 0.3	−0.5†	−0.7 to −0.3

* Data are presented as means ± SD.

† Significant treatment differences (diet vs. exercise) for change scores ($p < 0.008$).

exercise weight loss group (7.2 mg/kg skeletal muscle per minute) in comparison with the controls ($p < 0.001$; Table 3). In comparison with controls, glucose disposal within the diet weight loss and exercise without weight loss groups did not change ($p > 0.05$).

In comparison with controls, no treatment effects ($p > 0.2$) were observed for either fasting glucose or OGTT values (Table 3). However, the change in OGTT-insulin area within the exercise weight loss group was greater ($p < 0.008$) in comparison with the control group. Insulin area did not change within the diet weight loss and exercise without weight loss groups ($p > 0.1$).

Discussion

Our findings demonstrated that in comparison with diet-induced weight loss, equivalent exercise-induced weight

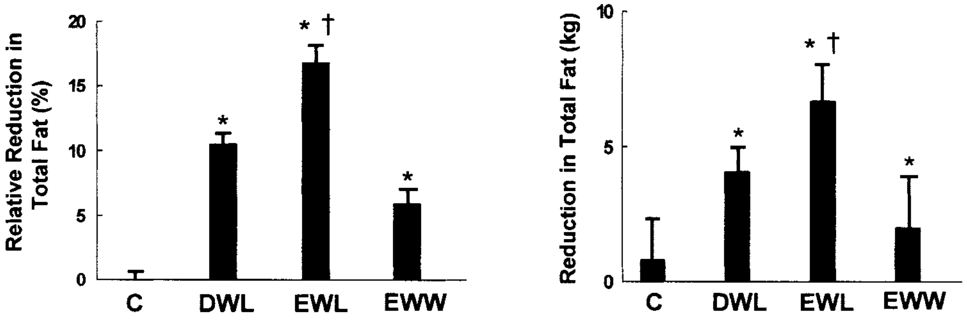

Figure 2: Reduction in total fat after a 14-week treatment period. The asterisks indicate a greater reduction in total fat in comparison with the control group. The daggers indicate a greater reduction in total fat in comparison with the diet weight loss and exercise without weight loss groups. Data are expressed as means ± SD. C, control group; DWL, diet weight loss group; EWL, exercise weight loss group; EWW, exercise without weight loss group.

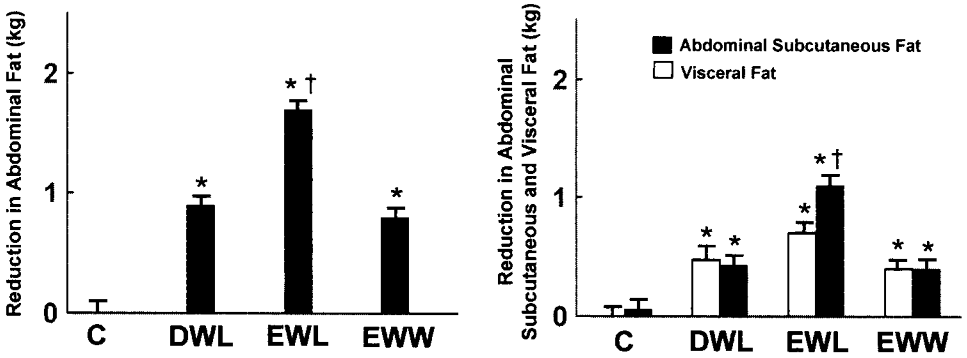

Figure 3: Reduction in total abdominal, subcutaneous, and visceral fat after a 14-week treatment period. The asterisks indicate a greater reduction in comparison with the control group. The daggers indicate a greater reduction in comparison with the diet weight loss and exercise without weight loss groups. Data are expressed as means ± SD. C, control group; DWL, diet weight loss group; EWL, exercise weight loss group; EWW, exercise without weight loss group.

loss was associated with a greater reduction in total fat, abdominal fat, and improvement in cardiorespiratory fitness. We also observed that exercise without weight loss was associated with substantial reductions in total and abdominal fat. These are novel observations and provide strong support for the recommendation that daily exercise with or without corresponding weight loss be recognized as effective strategies for obesity reduction in obese women. Furthermore, they highlight the importance of waist circumference as a tool to determine the benefits of obesity reduction and strongly suggest that BMI alone may mask the positive effects of exercise as a strategy for the treatment of obesity.

Absent from the literature are randomized, controlled studies that compare the efficacy of diet- and exercise-induced weight loss on obesity reduction in women. Although several nonrandomized exercise studies have included women, few prescribed an exercise program for which one would expect meaningful weight loss (6). Recently Irwin et al. (20) reported that a 12-month exercise program was associated with statistically significant reductions in total and abdominal obesity in comparison with controls in older women. In that study, an ~7% reduction in visceral (intra-abdominal) fat was observed as a consequence of an ~2-kg reduction in body weight. In comparison, we observed an ~30% reduction in visceral fat in response to an ~6-kg weight loss. Together, these observations are consistent with the finding here that within both weight loss groups, a dose-response relationship existed between weight loss and total fat.

Our finding that exercise is associated with a substantial reduction in total (18%; Figure 2) and abdominal (20%) fat in nondieting (e.g., no caloric restriction) women who exercise for ~60 min/d is consistent with Slentz et al. (21), who recently reported that in overweight and obese nondieting men and women, exercise performed for ~45 minutes, 4 d/wk was associated with a marked reduction in both total and abdominal (waist circumference) obesity. These findings confirm those previously reported from similar well-controlled trials (5,22) and suggest that daily exercise without caloric restriction for 45 to 60 minutes at ~65% to 80% of maximal heart rate is associated with substantial reductions in obesity independent of gender. However, these findings are countered by Donnelly et al. (23), who performed a well-designed, rigorously controlled investigation and reported that overweight and obese women were resistant to weight loss in response to exercise performed 5 d/wk wherein the women expended ~440 kcal/session. In that study, doubly labeled water measurements performed on one-half the women ($N = 7$) suggested that they were in a negative energy balance of ~200 kcal/d. The resistance to weight loss is, thus, a perplexing finding for which we have no explanation. Clearly, there is a need for further studies that will shed light on the contradictory findings.

A novel finding in this study was that exercise without weight loss was associated with substantial reductions in total (7%), abdominal (10%), and visceral (18%) fat. In fact, these values were not different from those observed in the diet weight loss group in response to a 6% (5.2 kg) reduction in body weight. The pronounced reduction in abdominal adiposity in response to exercise is consistent with previous studies wherein moderate-intensity exercise in women is associated with a significant increase in lipolysis in abdominal subcutaneous adipose tissue in comparison with femoral adipose tissue (9,24). Combined with the observation that abdominal obesity conveys the greatest health risk (3,10–13) and that increased cardiovascular fitness is associated with a reduction in morbidity and mortality independent of BMI (25,26), our findings provide compelling evidence that exercise without weight loss should be recognized as a useful strategy for reducing obesity and related comorbidity. Furthermore, the finding that waist circumference decreased in the exercise without weight loss group without a corresponding reduction in BMI underscores the importance of waist circumference as a tool to determine the benefits of obesity reduction and strongly suggests that BMI alone may mask the positive effects of exercise as a strategy for reducing obesity. The challenge to practitioners will be to educate participants regarding the benefits of exercise without weight loss as a strategy for obesity reduction. Indeed, it is likely that many now consider a program of obesity reduction without weight loss to be a failure and, thus, discontinue participation.

Given that weight loss reverses the insulin resistance that is characteristic of obesity (27–29), we were surprised that insulin sensitivity did not improve within the diet weight loss group. In comparison, a 32% reduction in insulin resistance was observed within the exercise weight loss group. A reduction of this magnitude is particularly impressive given that insulin sensitivity was measured 4 days after the last exercise session. Accordingly, it is likely that the improvement in insulin sensitivity within the exercise weight loss group could be explained in large measure by the greater reduction in both total and abdominal adiposity and not by the residual effects of the last exercise session (30,31). This notion is consistent with our finding that insulin sensitivity did not improve within the exercise without weight loss group.

Limitations of this study warrant mention. Because many of the volunteers chose not to participate after group assignment, we were unable to perform an intent-to-treat analysis and, thus, cannot make unequivocal statements regarding causation. However, because those who did not participate were not different (age, BMI, waist circumference) in comparison with those who completed the study, and given that the mechanism by which diet or exercise induces weight loss is understood, it seems reasonable to infer an etiologic relation. In addition, the small number of participants may have underpowered the study, and we may have been unable to detect true differences among groups. Additional studies with larger cohorts are required to confirm our findings.

In summary, the findings of this study indicated that in comparison with diet-induced weight loss, equivalent exercise-induced weight loss was associated with a greater reduction in total fat, abdominal fat, and improvement in cardiorespiratory fitness. These observations paralleled those previously observed in response to a similar study with obese men (5). Together, they support the recommendation that exercise with or without weight loss be recognized as a useful strategy for reducing total and abdominal obesity, preserving skeletal muscle mass, and improving cardiorespiratory fitness in obese men and women. This recommendation is reinforced by the knowledge that 60 minutes of daily exercise is associated with improvements in the maintenance of weight loss long term (32). These observations provide the basis for an improved therapeutic strategy for the treatment of obesity, the reduction in health risk, and the management of cardiovascular disease, findings that are directly relevant for the one in three American women who are obese (2). Although the recommendation to progress to 60 minutes of continuous exercise may present a challenge to some obese individuals who perceive continuous exercise as a barrier to participation, evidence suggesting that shorter, intermittent bouts of exercise result in weight loss that is not different from longer exercise sessions is encouraging (33) and should be considered when prescribing exercise to adults seeking weight loss.

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References

1. **Mokdad AH, Bowman BA, Ford ES, Vinicor F, Marks JS, Koplan JP.** The continuing epidemics of obesity and diabetes in the United States. *JAMA*. 2001;286:1195–200.
2. **Flegal KM, Carroll MD, Ogden CL, Johnson CL.** Prevalence and trends in obesity among US adults, 1999-2000. *JAMA*. 2002;288:1723–7.
3. **National Institutes of Health National Heart Lung and Blood Institute.** Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. *Obes Res*. 1998;6:S51–210.
4. **Levy AS, Heaton AW.** Weight control practices of U.S. adults trying to lose weight. *Ann Intern Med*. 1993;119:661–6.
5. **Ross R, Dagnone D, Jones PJ, et al.** Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men: a randomized, controlled trial. *Ann Intern Med*. 2000;133:92–103.
6. **Ross R, Janssen I.** Physical activity, total and regional obesity: dose-response considerations. *Med Sci Sports Exerc*. 2001;33:S521–7; discussion S528–9.
7. **Davis SN, Shavers C, Costa F.** Gender-related differences in counterregulatory responses to antecedent hypoglycemia in normal humans. *J Clin Endocrinol Metab*. 2000;85:2148–57.
8. **Tarnopolsky LJ, MacDougall JD, Atkinson SA, Tarnopolsky MA, Sutton JR.** Gender differences in substrate for endurance exercise. *J Appl Physiol*. 1990;68:302–8.
9. **Horowitz JF, Leone TC, Feng W, Kelly DP, Klein S.** Effect of endurance training on lipid metabolism in women: a potential role for PPARalpha in the metabolic response to training. *Am J Physiol Endocrinol Metab*. 2000;279:E348–55.

10. **World Health Organization.** *Obesity: Preventing and Managing the Global Epidemic*. Geneva, Switzerland: World Health Organization; 1998.
11. **Janssen I, Katzmarzyk PT, Ross R.** Body mass index, waist circumference, and health risk: evidence in support of current National Institutes of Health guidelines. *Arch Intern Med*. 2002;162:2074–9.
12. **Ross R, Freeman J, Hudson R, Janssen I.** Abdominal obesity, muscle composition, and insulin resistance in premenopausal women. *J Clin Endocrinol Metab*. 2002;87:5044–51.
13. **Ross R, Aru J, Freeman J, Hudson R, Janssen I.** Abdominal adiposity and insulin resistance in obese men. *Am J Physiol Endocrinol Metab*. 2002;282:E657–63.
14. **Harris JA, Benedict FF.** *A Biometric Study of Basal Metabolism in Man*. Washington, DC: Carnegie Institution of Washington; 1919.
15. **Ross R, Rissanen J, Pedwell H, Clifford J, Shragge P.** Influence of diet and exercise on skeletal muscle and visceral adipose tissue in men. *J Appl Physiol*. 1996;81:2445–55.
16. **Ross R, Leger L, Guardo R, De Guise J, Pike BG.** Adipose tissue volume measured by magnetic resonance imaging and computerized tomography in rats. *J Appl Physiol*. 1991;70: 2164–72.
17. **Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D, Ross R.** Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. *J Appl Physiol*. 1998;85:115–22.
18. **Snyder WS, Cooke MJ, Manssett ES, Larhansen LT, Howells GP, Tipton IH.** *Report of the Task Group on Reference Man* Oxford, United Kingdom: Pergamon; 1975.
19. **Allison DB, Paultre F, Maggio C, Mezzitis N, Pi-Sunyer FX.** The use of areas under curves in diabetes research. *Diabetes Care*. 1995;18:245–50.
20. **Irwin ML, Yasui Y, Ulrich CM, et al.** Effect of exercise on total and intra-abdominal body fat in postmenopausal women: a randomized controlled trial. *JAMA*. 2003;289:323–30.
21. **Slentz CA, Duscha BD, Johnson JL, et al.** Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE: a randomized controlled study. *Arch Intern Med*. 2004;164:31–9.
22. **Sopko G, Leon AS, Jacobs DR, Jr., et al.** The effects of exercise and weight loss on plasma lipids in young obese men. *Metabolism*. 1985;34:227–36.
23. **Donnelly JE, Hill JO, Jacobsen DJ, et al.** Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: the Midwest Exercise Trial. *Arch Intern Med*. 2003;163:1343–50.
24. **Arner P, Kriegholm E, Engfeldt P, Bolinder J.** Adrenergic regulation of lipolysis in situ at rest and during exercise. *J Clin Invest*. 1990;85:893–8.
25. **Blair SN, Kohl HW 3rd, Paffenbarger RS Jr, Clark DG, Cooper KH, Gibbons LW.** Physical fitness and all-cause mortality: a prospective study of healthy men and women. *JAMA*. 1989;262:2395–401.
26. **Lee CD, Blair SN, Jackson AS.** Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr*. 1999;69:373–80.
27. **Goodpaster BH, Kelley DE, Wing RR, Meier A, Thaete FL.** Effects of weight loss on regional fat distribution and insulin sensitivity in obesity. *Diabetes*. 1999;48:839–47.
28. **Dengel DR, Pratley RE, Hagberg JM, Rogus EM, Goldberg AP.** Distinct effects of aerobic exercise training and weight loss on glucose homeostasis in obese sedentary men. *J Appl Physiol*. 1996;81:318–25.
29. **Niskanen L, Uusitupa M, Sarlund H, Siitonen O, Paljarvi L, Laakso M.** The effects of weight loss on insulin sensitivity, skeletal muscle composition and capillary density in obese non-diabetic subjects. *Int J Obes Relat Metab Disord*. 1996; 20:154–60.
30. **Henriksson J.** Effects of physical training on the metabolism of skeletal muscle. *Diabetes Care*. 1992;15:1701–11.
31. **King DS, Baldus PJ, Sharp RL, Kesl LD, Feltmeyer TL, Riddle MS.** Time course for exercise-induced alterations in insulin action and glucose tolerance in middle-aged people. *J Appl Physiol*. 1995;78:17–22.
32. **Schoeller DA, Shay K, Kushner RF.** How much physical activity is needed to minimize weight gain in previously obese women? *Am J Clin Nutr*. 1997;66:551–6.
33. **Jakicic JM, Winters C, Lang W, Wing RR.** Effects of intermittent exercise and use of home exercise equipment on adherence, weight loss, and fitness in overweight women: a randomized trial. *JAMA*. 1999;282:1554–60.