Effects of an Energy-Restrictive Diet With or Without Exercise on Abdominal Fat, Intermuscular Fat, and Metabolic Risk Factors in Obese Women

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OBJECTIVE — The primary objective was to examine whether the combination of diet and aerobic exercise (DA) or diet and resistance exercise (DR) is associated with greater improvements in metabolic risk factors by comparison to diet only (DO) in obese women. A second objective considered whether reductions in metabolic risk factors are related to concurrent changes in abdominal and/or intermuscular fat distribution.

RESEARCH DESIGN AND METHODS — A total of 38 premenopausal obese women were randomly assigned to one of three 16-week treatments: DO ($n = 13$), DA ($n = 11$), or DR ($n = 14$). Plasma glucose, insulin, and lipid levels were measured in a fasting state and after a 75-g oral glucose challenge (oral glucose tolerance test [OGTT]). Total, abdominal subcutaneous, visceral, and intermuscular fat were measured by magnetic resonance imaging.

RESULTS — Significant reductions ($P < 0.02$) in body weight (~10 kg or 10%) and in total, abdominal subcutaneous, visceral, and intermuscular fat were observed within each group. Fasting and OGTT insulin, total cholesterol, LDL cholesterol, and apolipoprotein B also decreased within each group ($P \leq 0.02$). The changes in the body fat and metabolic variables were not different across treatment ($P > 0.05$). Visceral fat alone was related to the metabolic risk factors both before and after the treatment.

CONCLUSIONS — Weight loss was associated with reductions in metabolic risk factors in obese women. The improvement in the metabolic profile was not enhanced by the addition of aerobic or resistance exercise. The findings reinforce the importance of diminished visceral fat in the treatment of insulin resistance.

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The prevalence of obesity and associated comorbidities is increasing (1,2), which underscores the importance of developing effective strategies for reducing obesity and the risk of metabolic disease in women. Diet-induced weight loss (3–5) as well as aerobic exercise (6–8) and resistance exercise (7–9) are effective treatments for reducing metabolic risk factors in women. Although these observations suggest that the combination of diet and exercise would have a greater effect on metabolic risk factors than weight loss alone, the influence of diet and exercise combined in women is unclear. Whereas some studies report greater improvements in the plasma lipid profile in response to the combination of diet and exercise than diet alone (10–12), others report no treatment differences (13–15). It is also reported that the addition of aerobic (16,17) or resistance (16) exercise does not enhance the reductions in plasma insulin and glucose levels in comparison to diet alone in obese women. These observations do not reflect those in a recent report in obese men wherein a twofold greater improvement in insulin action was observed in response to diet combined with aerobic or resistance exercise than diet alone (18). A rationale that explains the equivocal findings is unknown; however, taken together, these observations suggest that the utility of exercise to enhance the effects of diet-induced weight loss on the metabolic profile may be sex-dependent. Given the importance of clearly establishing an independent role for exercise in the treatment of obesity and related comorbidities, the primary objective of this study was to examine whether the combination of diet and aerobic or resistance exercise is associated with greater improvements in metabolic risk factors by comparison to diet alone in obese women.

The second objective of this study was to clarify whether the reductions in metabolic risk factors with weight loss are related to concurrent changes in whole-body and regional adiposity. Recent studies have also shown that an increased muscle lipid content is a strong marker of insulin resistance (19–22). Furthermore, although it is clear that the changes in abdominal obesity are more closely related to changes in metabolic variables than the degree of obesity per se (18,23–25), controversy exists as to whether abdominal subcutaneous or visceral fat is responsible for these relationships (26).

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Abbreviations: DA, diet and aerobic exercise; DO, diet only; DR, diet and resistance exercise; MRI, magnetic resonance imaging; OGTT, oral glucose tolerance test; WHR, waist-to-hip ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

RESEARCH DESIGN AND METHODS

Subjects

Subjects were recruited from the general population. Inclusion criteria were that the subjects were upper-body obese (BMI

Table 1—*Descriptive characteristics of subjects at baseline*

	DO	DA	DR
n	13	11	14
Anthropometry			
Age (years)	40.1 ± 6.7	37.5 ± 6.0	34.8 ± 5.8
Weight (kg)	90.8 ± 14.5	99.9 ± 19.9	86.1 ± 10.5
BMI (kg/m^2)	33.7 ± 4.1	36.0 ± 7.1	31.6 ± 4.3
WHR	0.84 ± 0.05	0.81 ± 0.06	0.81 ± 0.04
Waist circumference (cm)	100.8 ± 12.5	101.9 ± 13.9	95.6 ± 9.0
MRI			
Total fat (kg)	41.2 ± 11.3	47.3 ± 15.7	37.8 ± 9.3
Abdominal subcutaneous fat (kg)	6.9 ± 2.5	7.8 ± 3.1	6.2 ± 1.7
at L4-L5 (cm^2)	444 ± 163	356 ± 202	307 ± 75
Visceral fat (kg)	2.27 ± 1.05	1.91 ± 0.94	1.50 ± 0.59
at L4-L5 (cm^2)	131 ± 50	120 ± 42	84 ± 27
Skeletal muscle (kg)	22.8 ± 3.3	24.2 ± 3.8	21.3 ± 2.1
Intermuscular fat (kg)	1.31 ± 0.42	1.54 ± 0.63	1.08 ± 0.41
Metabolic			
Fasting glucose (mmol/l)	5.3 ± 0.5	5.4 ± 0.5	5.2 ± 0.4
Fasting insulin (pmol/l)	138.6 ± 54.0	127.8 ± 86.5	114.2 ± 58.2
Glucose area (mmol · l^{-1} · 3 h^{-1})	17.6 ± 3.3	16.1 ± 3.1	17.1 ± 4.1
Insulin area (pmol · l^{-1} · 3 h^{-1})	1,483 ± 492	1,330 ± 512	1,391 ± 398
Insulin sensitivity index (ml · m^{-2} · min^{-1})	390 ± 47	394 ± 68	398 ± 75
Triglycerides (mmol/l)	1.91 ± 2.00	1.50 ± 0.76	1.45 ± 0.77
Total cholesterol (mmol/l)	5.36 ± 0.88	4.63 ± 0.88	4.94 ± 0.78
LDL cholesterol (mmol/l)	3.41 ± 0.69	2.86 ± 0.71	3.10 ± 0.78
HDL cholesterol (mmol/l)	1.08 ± 0.25	1.08 ± 0.26	1.16 ± 0.24
Total-to-HDL cholesterol ratio	5.37 ± 2.22	4.44 ± 1.10	4.46 ± 1.35
Apolipoprotein B (g/l)	1.18 ± 0.30	1.08 ± 0.25	1.10 ± 0.33
Apolipoprotein A (g/l)	1.27 ± 0.19	1.27 ± 0.24	1.21 ± 0.09
Apolipoprotein B–to–LDL cholesterol ratio	0.35 ± 0.09	0.38 ± 0.05	0.35 ± 0.07

Data are means ± SD.

>27.0 kg/m^2; waist-to-hip ratio [WHR; using umbilicus waist circumference] >0.85), had a stable weight (+2 kg) in the 6 months before the study, took no medications (e.g., oral contraceptives), consumed on average less than two alcoholic beverages per day, were premenopausal, and had a regular menstrual cycle. Those subjects meeting the criteria were randomly assigned to one of three treatments: diet only (DO), diet and aerobic exercise (DA), or diet and resistance exercise (DR). A total of 38 women completed the study. The descriptive characteristics for all groups are presented in Table 1 (DO, $n = 13$; DA, $n = 11$; DR, $n = 14$). There were no group differences for any of the body composition or metabolic variables before treatment ($P > 0.05$). All subjects gave their written informed consent to participate in the study, which was conducted according to the ethical guidelines of Queen's University.

Measurement of total and regional fat and skeletal muscle by magnetic resonance imaging

Whole-body (41 images) magnetic resonance imaging (MRI) data were obtained with a Siemens 1.5-Tesla scanner (Erlangen, Germany) using an established protocol (27). The MRI data were transferred to a stand-alone work station (Silicon Graphics, Mountain View, CA) for analysis using special software (TomoVision, Montreal, Canada) as described elsewhere (27,28). Total fat (subcutaneous + visceral + intrapelvic + intrathoracic + intermuscular), intermuscular fat (fat intertwined between the bundles of skeletal muscle fibers that was visible on the MRI images), and skeletal muscle mass were determined using all 41 images. Visceral and abdominal subcutaneous fat were calculated using the five images extending from 5 cm below to 15 cm above L4-L5. Volume units (liters) was converted to mass units (kg) by multiplying the volumes by the assumed constant densities of 0.92 for adipose tissue and 1.04 for skeletal muscle (29). With the exception of intermuscular fat, a detailed description of the MRI results is published elsewhere (30).

We have previously reported that the mean difference for repeat measurements of total, abdominal subcutaneous, and visceral fat are <3, 1, and <6%, respectively (31). We have also shown that MRI-measured intermuscular fat is strongly correlated ($r = 0.92$, $P < 0.001$) with intermuscular fat measured in corresponding cadaver sections (28). However, the standard error of the estimate for repeated measures of intermuscular fat is 30% (28).

Anthropometric variables

Body mass was measured to the nearest 0.1 kg with the subjects dressed in light

clothing. Standing height was measured to the nearest 0.1 cm using a stadiometer. Circumference measurements were taken with the subjects in a standing position at the level of the last rib and hip (32).

Metabolic variables

All biochemical studies were performed within the first 10 days of the subjects' menstrual cycle after an overnight fast. The posttreatment measurements were obtained 5–13 days after completing the treatment while the subjects were consuming a weight maintenance diet. Glucose and insulin levels were also measured in response to a 75-g oral glucose tolerance test (OGTT). Blood samples were collected at 0, 60, 120, and 180 min. Glucose and insulin areas under the curve were determined using a trapezoid model (33). The OGTT insulin sensitivity index was determined using the glucose and insulin levels at 0, 120, and 180 min according to the method of Mari et al. (34). The OGTT insulin sensitivity index is highly reproducible (7% coefficient of variation) and is correlated ($r = 0.77$, $P < 0.001$) with insulin sensitivity measured by the hyperinsulinemic-euglycemic clamp (34). The OGTT plasma samples for four subjects (two DO and two DA) were damaged during shipment. Therefore, OGTT data are only presented for 11 subjects in the DO group and 9 subjects in the DA group.

Serum total cholesterol and triglyceride levels were determined using standard techniques. HDL cholesterol was assayed after isoelectric-polyanionic precipitation of HDL cholesterol. The LDL cholesterol was subsequently determined using the following equation: LDL cholesterol = cholesterol − [HDL cholesterol + (0.46 × triglycerides)]. Apolipoprotein A and B levels were determined by rate nephelometry using reagents obtained from Beckman Instruments (Fullerton, CA). Blood glucose was measured using the glucose oxidase method (Beckman Glucose Analyzer; Beckman Instruments), and plasma insulin was measured by radioimmunoassay (35).

Diet and exercise regimens

Dietary protocol. The subjects' energy requirements were estimated by multiplying the Harris-Benedict equation (36) by a factor of 1.5, which is within ~8% of actual energy requirements (37). A weight maintenance diet was followed at this energy intake for 2 weeks before the pretreatment testing. For the 16-week treatment, the subjects in all three groups were asked to reduce their weight maintenance energy intake by 1,000 kcal/day. All foods were self-selected, store bought, and prepared by the subjects, and no supplements were prescribed. All subjects were required to keep daily diet records for the duration of the study and to limit their dietary fat intake to <30%. The diet records were reviewed using standard food tables (38). All subjects attended weekly meetings to obtain dietary counsel and discuss success strategies. After the 16-week treatment period, the energy intake for weight maintenance was recalculated and prescribed until completion of the posttest measurements.

Aerobic exercise protocol. A total of 11 women performed aerobic exercise 5 days per week in addition to the energy restriction. The exercise sessions lasted ~15 min at the beginning and progressed to a maximum of 60 min based on the subject's capabilities. The mode of aerobic exercise was determined by the subject and consisted of either walking on a motorized treadmill (Quinton Instruments, Seattle, WA), cycling on a cycle ergometer (Monark, Stockholm, Sweden), or stair stepping on an electronic stairmaster (StairMaster 4000; Tri-Tech, Tulsa, OK). Exercise intensity was monitored using a heart rate monitor (Polar USA, Stanford, CT) and progressed from 50 to 85% of the maximal heart rate that was achieved during the maximal oxygen uptake test. All of the exercise sessions were by appointment and were supervised by a physical educator.

Resistance training protocol. In addition to the energy deficient diet, 14 women performed resistance exercise 3 days per week using Nautilus equipment (Nautilus, Deland, FL). Training sessions began with a 5- to 10-min warm-up of low-intensity cycling. Seven exercises were performed in each session: leg extension, leg flexion, super pullover (latissimus dorsi), bench press, shoulder press, triceps extension, and biceps curl. One set of 8–12 repetitions were performed to the point of volitional fatigue (i.e., the individual could not complete any more repetitions). For each repetition, the concentric contraction phase was performed in ~2 s and the eccentric contraction phase in ~4 s. As soon as 12 repetitions could be performed at a given weight with good form, the weight was increased by an amount (i.e., one plate) that permitted ~8 repetitions to be performed. Sit-ups were also performed for the abdominal muscles. Each session lasted ~30 min. All exercise sessions were supervised by a physical educator who provided verbal encouragement to help ensure that physiological failure was reached and that proper lifting techniques were used.

With the exception of the exercise programs in the DA and DR groups, no physical activity prescription was given, and all women were asked to maintain their normal (i.e., prestudy) physical activity patterns for the duration of the study.

Evaluation of training performance

Cardiorespiratory fitness (Vo_{2max}). Vo_{2max} was determined using a treadmill test that used a constant walking speed. For the initial 2 min, the grade was set at 0%, after which time it was increased to 2% for the third minute and by 1% every minute thereafter until fatigue was reached. Standard open-circuit spirometry techniques using a Beckman metabolic measurement cart (Sensormedics, Fullerton, CA) were used to determine oxygen uptake.

Muscular strength. Increases in strength were determined using the following formula: $[(a - b)/a] \times 100$, where a equals the weight lifted at the beginning of week 4, and b equals the weight lifted at the completion of the program. Week 4 was chosen as the initial week to represent changes in muscular strength that were primarily due to skeletal muscle hypertrophy, thereby omitting initial increases in strength that were predominately attributable to neuromuscular factors (39). A linear relationship between the seven- to ten-repetition maximum and the one-repetition maximum both before ($r = 0.94$) and after training ($r = 0.95$) have been shown with a Nautilus training program (40). Increases in upper-body strength were calculated using the bench press and super pullover exercises, whereas lower-body strength changes were determined using the leg extension and leg curl exercises.

Energy cost of exercise

Aerobic exercise. The energy expenditure of treadmill walking and stationary cycling were determined using the Amer-

ican College of Sports Medicine equations (41). Because energy expenditure values with a StairMaster 4000 are ~20% lower that those determined using the equation provided by the equipment manufacturer (42), energy expenditure values obtained with the stair stepper were reduced by 20%.

Resistance exercise. The energy expenditure was estimated to be 120 kcal per session of resistance exercise (43).

Statistical analysis

The normality of distribution of each variable was tested, and log-transformed data were used when necessary. A one-way ANOVA, with the pretreatment score acting as the dependent variable, was performed to examine differences between the groups before the intervention. Paired *t* tests were used to assess within-group changes (pre- to posttreatment) for all dependent variables. Bonferonni adjustments ($P < 0.02$, 0.05/number of groups) were used to interpret all *t* test results. A two-way repeated measures ANOVA, with the pre- and posttreatment scores acting as the dependent variables, was used to evaluate treatment effects for all dependent variables. When the ANOVA *P* value was <0.05, a Scheffé post hoc comparison test was used to locate specific pretreatment differences and main treatment effects. Pearson product-moment correlations were used to determine the simple relationship between the different MRI and metabolic variables. Multiple regression analysis was used to determine whether visceral fat predicted the metabolic variables after controlling for total, abdominal subcutaneous, and intermuscular fat. Statistical procedures were performed using SYSTAT (SYSTAT, Evanston, IL). All data are presented as means ± SD.

RESULTS

Evaluation of diet and exercise

Dietary analysis. With few exceptions (<2%), complete dietary intake records were submitted, as required by all subjects. The daily diet records indicated that the average dietary-induced energy deficit for the DO, DA, and DR groups were 1,222 ± 293, 1,299 ± 215, and 1,209 ± 211 kcal/day for the 16-week treatment period. The corresponding fat intakes were 21 ± 5, 25 ± 5, and 22 ± 5%. There were no group differences for the energy deficit or fat intakes ($P > 0.1$).

Aerobic exercise. Attendance for the exercise sessions averaged 92% (range 85–98%) in the DA group. The duration of the exercise sessions was 34 ± 6 min at an intensity of 77 ± 4% of the maximal heart rate. The total energy expenditure for the DA group was 19,167 ± 4,461 kcal. In response to the aerobic exercise program, $V_{O_{2max}}$ (l/min) increased ($P < 0.02$) by 9 ± 9%. $V_{O_{2max}}$ did not change in the DO or DR groups ($P > 0.02$).

Resistance exercise. For the DR group, attendance for the exercise sessions averaged 94% (79–100%). The estimated total energy expenditure for the DR group was 5,348 ± 318 kcal. In response to the resistance exercise program, lower-body and upper-body training load increased by 29 ± 15 and 38 ± 15%, respectively ($P < 0.01$).

Effects of weight loss on anthropometric variables

Body weight and waist circumference were reduced within each group ($P < 0.001$) (Table 2); however, these changes were not different across treatment ($P > 0.1$). WHR did not change ($P > 0.1$) within any group (Table 2).

Effects of weight loss on MRI variables

As indicated in Table 2, significant reductions in total, abdominal subcutaneous, visceral, and intermuscular fat were observed within each group ($P < 0.01$). The changes in these fat depots were not different across treatment ($P > 0.05$). The observations for visceral and abdominal subcutaneous fat area (cm^2) at the L4-L5 image were the same as those for visceral and abdominal mass (kg) calculated using all five abdominal images. Skeletal muscle mass was preserved within the DA and DR groups ($P > 0.1$); however, a significant ($P < 0.001$) reduction in skeletal muscle mass was observed in the DO group (Table 2).

Pretreatment metabolic variables

None of the subjects had impaired glucose tolerance before treatment (44). Three subjects started with high-risk total cholesterol values (≥6.2 mmol/l), and 14 subjects started with borderline high-risk total cholesterol values (5.1–6.1 mmol/l). Three subjects started with very high-risk (≥4.9 mmol/l), nine subjects with high-risk (4.1–4.8 mmol/l), and 19 subjects with borderline high-risk (3.3–4.0 mmol/l) LDL cholesterol values. Eleven subjects started with high-risk (<1.0 mmol/l) HDL cholesterol values. One subject started with very high-risk triglyceride values (≥5.1 mmol/l), and five subjects started with high-risk triglyceride values (2.3–5.6 mmol/l). All of the remaining total, LDL, and HDL cholesterol and triglyceride values were within the desirable range (45).

Effects of weight loss on metabolic variables

Fasting glucose and insulin. Independent of treatment, fasting plasma glucose levels did not change ($P > 0.1$). Fasting insulin was reduced in response to DO ($P = 0.002$) and DR ($P = 0.007$) but not DA ($P = 0.18$) (Table 2). These changes were not different across treatment ($P > 0.1$).

OGTT. OGTT glucose area was reduced in response to DR ($P = 0.017$); however, OGTT glucose area did not change in response to DO ($P = 0.14$) or DA ($P = 0.14$) (Table 2). OGTT insulin area and the insulin sensitivity index improved in all groups ($P < 0.02$) (Table 2). The changes in glucose area, insulin area, and insulin sensitivity index were not different across treatment ($P > 0.1$).

Plasma lipids and lipoproteins. Changes in the plasma lipids and lipoproteins are given in Table 2. Total cholesterol and apolipoprotein B were reduced ($P < 0.02$) in all groups. The reduction in LDL cholesterol was significant in the DO ($P = 0.001$) and DR ($P = 0.02$) groups alone. A slight (7%) but significant ($P = 0.01$) reduction in HDL cholesterol was observed in the DR group. Independent of treatment, there were no changes in any of the other plasma lipid or lipoprotein variables ($P > 0.05$). Without exception, there were no treatment differences for the changes in the plasma lipid/lipoprotein levels ($P > 0.1$).

Relationship between body composition and metabolic variables

Pretreatment visceral fat was significantly ($P < 0.05$) correlated with OGTT glucose area ($r = 0.51$), fasting insulin ($r = 0.49$), OGTT insulin area ($r = 0.44$), insulin sensitivity index ($r = -0.44$), and plasma triglycerides ($r = 0.32$) in all 38 subjects. These correlations persisted throughout the treatment because the posttreatment values for visceral fat were significantly ($P < 0.05$) related to the posttreatment

Table 2—*Changes in anthropometric, MRI, and metabolic variables*

	DO		DA		DR	
	Absolute	%	Absolute	%	Absolute	%
Anthropometry						
Weight (kg)	−10.0 ± 3.9*	11 ± 3	−11.1 ± 4.4*	11 ± 4	−10.0 ± 3.0*	12 ± 4
BMI (kg/m^2)	−4.0 ± 1.4*	11 ± 3	−4.2 ± 1.2*	11 ± 4	−3.9 ± 1.0*	12 ± 4
WHR	−0.01 ± 0.04	1 ± 5	−0.01 ± 0.02	1 ± 3	−0.01 ± 0.01	1 ± 1
Waist circumference (cm)	−7.5 ± 4.6*	7 ± 4	−7.3 ± 5.4*	7 ± 5	−8.5 ± 2.3*	9 ± 2
MRI						
Total fat (kg)	−7.8 ± 3.1*	19 ± 5	−9.9 ± 4.6*	21 ± 10	−8.6 ± 2.4*	24 ± 8
Abdominal subcutaneous fat (kg)	−1.3 ± 0.6*	19 ± 7	−1.6 ± 0.8*	22 ± 10	−1.7 ± 0.7*	29 ± 11
at L4-L5 (cm^2)	−82 ± 66*	15 ± 15	−60 ± 22*	22 ± 10	−26 ± 11*	19 ± 6
Visceral fat (kg)	−0.65 ± 0.37*	29 ± 11	−0.61 ± 0.41*	31 ± 18	−0.42 ± 0.21*	31 ± 9
at L4-L5 (cm^2)	−51 ± 21*	37 ± 11	−39 ± 24*	29 ± 16	−19 ± 16*	24 ± 15
Skeletal muscle (kg)	−1.1 ± 0.8*	5 ± 3	−0.6 ± 1.1	2 ± 4	−0.4 ± 1.1	2 ± 5
Intermuscular fat (kg)	−0.22 ± 0.19*	17 ± 12	−0.38 ± 0.40*	24 ± 26	−0.12 ± 0.14*	10 ± 12
Metabolic						
Fasting glucose (mmol/l)	−0.1 ± 0.4	1 ± 8	−0.1 ± 0.5	2 ± 9	−0.1 ± 0.4	2 ± 8
Fasting insulin (pmol/l)	−48.1 ± 45.5*	27 ± 28	−17 ± 39	5 ± 36	−33.0 ± 38.9*	19 ± 29
Glucose area (mmol · l^{-1} · 3 h^{-1})	−1.0 ± 2.0	5 ± 11	−1.0 ± 1.8	5 ± 10	−1.8 ± 2.5*	9 ± 11
Insulin area (pmol · l^{-1} · 3 h^{-1})	−328 ± 549*	17 ± 36	−445 ± 490*	23 ± 36	−321 ± 354*	17 ± 20
Insulin sensitivity index (ml · m^{-2} · min^{-1})	31 ± 30*	9 ± 8	36 ± 39*	11 ± 12	40 ± 36*	12 ± 11
Triglycerides (mmol/l)	−0.52 ± 1.55	12 ± 27	−0.26 ± 0.49	11 ± 31	−0.35 ± 0.82	15 ± 30
Total cholesterol (mmol/l)	−0.83 ± 0.36*	16 ± 7	−0.42 ± 0.55*	9 ± 11	−0.60 ± 0.43*	12 ± 9
LDL cholesterol (mmol/l)	−0.55 ± 0.49*	16 ± 17	−0.28 ± 0.42	9 ± 14	−0.34 ± 0.50*	10 ± 16
HDL cholesterol (mmol/l)	−0.05 ± 0.24	2 ± 25	−0.03 ± 0.18	3 ± 15	−0.09 ± 0.11*	7 ± 11
Total-to-HDL cholesterol ratio	−0.76 ± 1.71	10 ± 19	−0.17 ± 0.62	4 ± 13	−0.21 ± 0.61	4 ± 10
Apolipoprotein B (g/l)	−0.11 ± 0.09*	10 ± 8	−0.17 ± 0.14*	17 ± 14	−0.16 ± 0.13*	14 ± 10
Apolipoprotein A (g/l)	−0.01 ± 0.17	5 ± 2	−0.14 ± 0.25	10 ± 20	−0.05 ± 0.16	4 ± 14
Apolipoprotein B–to–LDL cholesterol ratio	0.03 ± 0.01	10 ± 17	−0.03 ± 0.05	6 ± 12	0.02 ± 0.07	2 ± 18

Data are means ± SD. *Significant within-group change ($P < 0.017$, paired t test with Bonferonni adjustments).

values for OGTT glucose area ($r = 0.33$), fasting insulin ($r = 0.52$), OGTT insulin area ($r = 0.37$), and insulin sensitivity index ($r = -0.44$). Furthermore, when the posttreatment values for visceral fat were plotted against OGTT glucose, fasting insulin, OGTT insulin, and the insulin sensitivity index, the relationships fell along the same regression lines as the corresponding pretreatment values. Both before and after treatment, the correlations for visceral fat remained significant after controlling for total, abdominal subcutaneous, and intermuscular fat (data not shown). With the exception of total fat, which was related to the OGTT insulin sensitivity index ($r = -0.34$, $P = 0.05$), none of the other body fat variables were related to any of the metabolic variables (i.e., glucose, insulin, lipids/lipoproteins) before treatment ($P > 0.05$). None of the change scores for the body fat variables were related to the change scores for any of the metabolic variables ($P > 0.05$). Without exception, the observations for visceral and abdominal subcutaneous fat area (cm^2) at the L4-L5 level were the same as those for visceral and abdominal mass (kg) calculated using all five abdominal images.

CONCLUSIONS — The effects of weight loss alone or weight loss combined with aerobic or resistance training on metabolic risk factors and abdominal adiposity were studied in obese premenopausal women. The findings demonstrate that a moderate weight loss (~10 kg or 10%) was associated with a significant reduction in numerous metabolic risk factors, which appeared to be partially mediated by the corresponding reductions in visceral fat. However, the addition of aerobic or resistance exercise to the energy-restrictive diet did not enhance the improvement in the metabolic profile.

In this study, weight loss was associated with reduced levels of total and LDL cholesterol, apolipoprotein B, and fasting insulin. This is noteworthy because these variables are independent predictors of ischemic heart disease (46,47) and thus reinforce the importance of weight loss in the treatment of dyslipidemia and hyperinsulinemia. That weight loss had no effect on plasma triglycerides, HDL cholesterol, or glucose variables may be explained by the relatively normal lipid and glucose tolerance levels for most subjects before treatment. Indeed, the reductions observed for many of the metabolic variables were positively correlated with pretreatment values (data not shown), a finding in agreement with previous studies wherein the effectiveness of weight loss as a therapeutic strategy was particularly useful for individuals with dyslipidemia and/or glucose intolerance (3,48).

In agreement with previous studies in

overweight premenopausal women (13–15,49), postmenopausal women (17,50), and men (15,51), in this study, the addition of aerobic or resistance exercise to the energy-restrictive diet did not enhance the changes in the lipid profile. Common to these studies, diet and exercise combined was not associated with an increase in weight loss compared with diet alone. Given the importance of weight and/or fat loss in the treatment of disturbances in plasma lipids and lipoproteins, it is not unreasonable to assume that the inability of exercise to induce an added benefit is at least partially explained by the inability of exercise to increase the reduction in total or abdominal adiposity. This is consistent with the observation that exercise in the absence of weight loss has little or no effect on the plasma lipid profile (12,15,52,53). In this way, it is suggested that improvement in obesity-related dyslipidemias may best be accomplished by the prescription of prolonged (30–60 min/day) low-intensity (50–60% $V_{O_{2max}}$) exercise on all or most days of the week (24,54–56). In as much as weight loss contributes to improvements in lipid profile, a regimen of this nature is more likely to result in exercise-induced weight loss that is associated with reduction in obesity and related comorbidities (24,55).

Consistent with our findings for lipid profile, we observed no clear benefit of aerobic or resistance exercise on glucose tolerance or insulin action. These observations agree with earlier findings in pre- (16) and postmenopausal (17) overweight women. However, this is contrary to our recent observation in obese men wherein the combination of diet and aerobic or resistance exercise induced a two-fold greater improvement in insulin action when compared with diet alone (18). Because the baseline insulin levels for the men and women within the respective studies were similar, the study designs (i.e., diet and exercise regimens) were identical, and the relative reduction in total and regional adiposity by comparison to the DO groups were not different, a rationale that explains the equivocal findings is unknown. Moreover, we are unaware of mechanisms (e.g., estrogen) that would support the view that sex independently contributes to the effects of exercise alone on insulin sensitivity.

That exercise did not enhance the improvement in the metabolic profile observed in response to diet alone does not argue against a role for exercise in improving health risk. On the contrary, it is well established that elevated levels of physical activity (57,58) and fitness (58,59) are inversely related to morbidity and mortality independent of obesity and disturbances in metabolic risk factors. Furthermore, a single bout of exercise reduces plasma triglycerides, increases HDL cholesterol, and improves insulin sensitivity for up to 72 h (60–62). Accordingly, because we acquired our metabolic measurements at least 96 h after exercise, our findings reinforce the notion that in the absence of changes in total or regional fat, the positive effects of exercise on metabolic risk factors attenuate quickly. Thus, adherence to exercise is required to maintain the improvement in metabolic profile.

A secondary aim of this study was to investigate the influence of weight loss on the relationships between visceral fat, abdominal subcutaneous fat, intermuscular fat, and metabolic risk factors. The principal finding was that visceral fat was uniquely related to a number of the metabolic variables both before and after treatment. Furthermore, when plotting visceral fat against the metabolic variables (e.g., insulin sensitivity index), the posttest regression lines fell essentially on top of the pretest regression lines. Although this result does not infer a cause-and-effect relationship, it does suggest that the relationship between visceral fat and metabolic risk factors persists after weight loss. This finding agrees with previous observations in both sexes (18,23–25) and reinforces the importance of decreasing visceral fat in the treatment of the metabolic syndrome. That the pretreatment and changes in abdominal subcutaneous fat were not related to metabolic risk factors is consistent with findings in obese women (5,63,64) but disagrees with findings in obese men (18).

Lipid accumulation within skeletal muscle is also altered in obesity and is linked to insulin resistance (22,65,66). In the present study, glucose and insulin variables were not related to skeletal muscle composition, as determined by the amount of intermuscular fat. This observation may reflect limitations inherent to the MRI technique used to measure muscle composition. We have previously reported that the error for estimating intermuscular fat by MRI approximates 30% (28). Because the reduction in intermuscular fat approximated 24%, our study may lack the power required to detect relationships between corresponding changes in intermuscular fat and metabolic risk factors.

Summary

The results of this study demonstrate that a ~10 kg (10%) weight loss is associated with reductions in total and LDL cholesterol, apolipoprotein B, and insulin action in obese premenopausal women. However, no additional benefit of aerobic or resistance exercise training on metabolic risk factors was observed. It would appear that the failure of exercise to enhance diet-induced improvements in insulin and glucose metabolism may be sex-dependent. Accordingly, there is a need for well-controlled randomized trials wherein the influence of sex on the effects of exercise on obesity and related comorbidities is compared. Finally, the findings reinforce the importance of diminished visceral fat in the reduction of insulin resistance.

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