

# Short-Term Moderate Weight Loss and Resistance Training Do Not Affect Insulin-Stimulated Glucose Disposal in Postmenopausal Women

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**OBJECTIVES** — Moderate weight loss and exercise have been proposed as important tools in the treatment and prevention of type 2 diabetes. Therefore, we tested the hypothesis that short-term (4 weeks) moderate energy restriction ( $-750$  kcal/day) would result in a significant increase in insulin-stimulated glucose disposal ( $40 \text{ mU} \cdot \text{m}^{-2} \cdot \text{min}^{-1}$  hyperinsulinemic-euglycemic clamp) in moderately overweight postmenopausal women and that when combined with resistance training (RT) an even greater effect would be seen.

**RESEARCH DESIGN AND METHODS** — Older women were randomly assigned to energy restriction (WLoss group;  $n = 9$ ) or energy restriction plus RT (RT + WLoss group;  $n = 10$ ).

**RESULTS** — For the WLoss versus the RT + WLoss groups, changes in body weight ( $-3.0 \pm 0.2$  kg vs.  $-3.2 \pm 0.3$  kg), fat mass (FM) ( $-3.0 \pm 0.3$  kg vs.  $-3.2 \pm 0.3$  kg), and percent body fat (BF) ( $-2.1 \pm 0.4$  vs.  $-2.4 \pm 0.3\%$ ) were not different between groups. Muscle mass (group-by-time interaction,  $P = 0.04$ ) was preserved in RT + WLoss ( $0.40 \pm 0.40$  kg) and reduced in WLoss ( $-0.64 \pm 0.18$  kg). There were no changes in fat-free mass (FFM) and waist-to-hip ratio in either group. Whole body glucose disposal (WLoss  $6.14 \pm 0.57$  vs.  $6.03 \pm 0.53$ , RT + WLoss  $5.85 \pm 0.60$  vs.  $6.09 \pm 0.56$  mg/kg of FFM/min) did not change in either group.

**CONCLUSIONS** — The results of this study demonstrate that short-term energy restriction resulting in moderate decreases in body weight ( $4.0 \pm 0.3\%$ ) and FM ( $8.2 \pm 0.7\%$ ) did not improve insulin-stimulated glucose disposal. The addition of RT to the hypoenergetic diet preserved muscle mass but provided no synergistic effect on insulin action. These results suggest that a greater change in body weight or FM may be necessary to observe a significant improvement in insulin action.

*Diabetes Care* 24:1863–1869, 2001

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Received for publication 1 March 2001 and accepted in revised form 23 July 2001.

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**Abbreviations:** BF, body fat; EGP, endogenous glucose production; FFA, free fatty acids; FFM, fat-free mass; FM, fat mass; OGTT, oral glucose tolerance test; 1RM, one-repetition maximum; RT, resistance training.

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

Overweight postmenopausal women are at a high risk for developing complications that lead to premature morbidity and mortality from metabolic diseases (1). The increased frequency of obesity in older women (2,3), particularly abdominal obesity, is closely associated with an increase in insulin resistance (4–6). Both obesity and insulin resistance are independent risk factors for the development of glucose intolerance and type 2 diabetes. Therefore, a successful treatment to slow or deter the progression to metabolic disorders would be a substantial health benefit for older women. Weight loss is perhaps the most effective treatment for impaired glucose tolerance and the prevention of type 2 diabetes. Much of the literature on the effects of weight loss (7–12) have used interventions that lasted 6–9 months, with a target weight loss of  $>10\%$  of initial body weight. Because of the difficulty in achieving and maintaining a large weight loss, moderate short-term weight loss has been recommended to establish glycemic control in individuals with diabetes (13–15), as an effective treatment for impaired glucose tolerance (16). The effectiveness of moderate energy restriction, resulting in small but significant weight loss, on insulin action is not clear. We hypothesized that short-term moderate energy restriction would result in a significant improvement in insulin action in a group of nondiabetic moderately overweight postmenopausal women.

Resistance training (RT) increases insulin sensitivity in older men and women (17–20). Combining moderate energy restriction with resistance training preserves lean tissue mass and substantially reduces body fat mass (FM) (21,22). Therefore, we also hypothesized that resistance training along with moderate energy restriction would preserve muscle mass and produce a greater effect on insulin action than weight loss alone. Because negative energy balance improves

insulin action (11,12), subjects in the present study were fed a eucaloric diet before and after adherence to a hypocaloric diet designed to produce moderate amounts of weight loss. In this way, the effects of the weight loss and the resultant changes in body composition could be distinguished from that of the hypocaloric diet.

## RESEARCH DESIGN AND METHODS

**Subjects.** A total of 22 postmenopausal Caucasian women, aged  $63 \pm 2$  years (range 55–79), with a BMI of  $29.9 \pm 0.7$  kg/m<sup>2</sup> (25–34), and who were not actively involved in any physical training, volunteered to participate in this 7-week outpatient study. The women were recruited from the Little Rock, Arkansas, region via advertisements in local newspapers. Those who responded were contacted by telephone and invited to the laboratory to determine eligibility. Before the initial screening procedure, each woman signed a screening consent form in accordance with the University of Arkansas for Medical Sciences Institutional Review Board. The screening procedures included a medical history questionnaire, resting electrocardiogram, routine blood and urine chemistries, and a physician-administered physical examination to exclude people with clinically abnormal heart, kidney, liver, or thyroid function before admission into the study. Other entry criteria for inclusion into the study included the following: sedentary for the previous 6 months, nondiabetic (women with normal to impaired glucose tolerance as diagnosed from an oral glucose tolerance test [OGTT]), at least 120–140% ideal BMI, and no evidence of ischemic heart disease. Women who met entrance criteria were notified, signed a consent form, and were randomly assigned to either an energy restriction only (WLoss) or an energy restriction plus resistance training (RT + WLoss) group. Of the 19 women who completed the study, 10 were taking premarin for at least 5 years, 3 were on synthroid for at least 10 years, 4 were treated for hypertension and were on the same medication for at least 5 years (1 on Dyazide, 1 on Vasotec, 1 on cardura, and 1 on a combination of Cardizem, Prosolec, and Zolofit). Three women (two from the WLoss and one from RT + WLoss group) did not com-

plete the study because of unsuccessful attempts to place the retrograde hand line for blood sampling before the start of the baseline glucose clamp procedure and did not voluntarily drop out from this study.

During the initial screening, an OGTT (75-g glucose solution; Fisher Scientific, Pittsburgh, PA) was administered in the postabsorptive state after an overnight 12-h fast to determine whether a prospective subject was diabetic. The National Diabetes Data Group (23) 1997 guidelines were used for the diagnosis of type 2 diabetes and impaired glucose tolerance. The 19 women who completed the study were classified as follows: 17 women with normal ( $<6.10$  mmol/l) and 2 women with impaired ( $6.10$ – $7.00$  mmol/l) fasting plasma glucose; 9 women with normal ( $<7.76$  mmol/l) and 10 women with impaired ( $7.77$ – $11.09$  mmol/l) 2-h plasma glucose during the OGTT. Subjects considered diabetic by the new criteria were excluded from the study.

The women were considered weight-stable at the time of the study if they reported no more than a 2-kg weight loss or gain over the previous 6-month period before they enrolled in the study.

**Experimental design.** The study period lasted for 7 weeks. For weeks 1 and 2, the women consumed a weight-maintenance diet by which the total energy intake was calculated from a measured fasting resting metabolic rate  $\times 1.75$  for an estimation of habitual daily activity (24). A portion of the eucaloric diet included a 3,138-kJ (750 kcal) protein-free beverage. All baseline measurements were assessed during or at the end of the second week. Starting at week 3, a 3,138-kJ/day deficit designed to induce 0.5–0.7 kg of weight loss per week was introduced to both groups by removing the protein-free beverage. During week 7, the 3,138-kJ protein-free beverage was reintroduced to reestablish a eucaloric state. After the subjects had consumed this eucaloric diet for 5 days, all baseline measurements were reassessed.

**Diet composition.** All foods and beverages (except for water) were prepared and provided by our metabolic research kitchen. The women came to the metabolic kitchen each weekday to pick up the prepared food. The food for the weekend was picked up every Friday. During the weekday, the women consumed breakfast in the metabolic kitchen and took home their lunch and dinner. Each morning, the dietitian met with each woman to en-

sure that they were compliant with the requirements of the study. Body weights were measured daily and assessed at the end of the week to ensure that the women were losing weight during the energy-restriction phase and maintaining weight during the maintenance phase. The “non-protein energy” for the entire diet was provided as 65% carbohydrate and 35% fat. During weeks 1, 2, and 7, 3,138 kJ (750 kcal) of the total energy intake was provided as a protein-free formula beverage (65% carbohydrate and 35% fat). The controlled diet consisted of a 3-day rotating menu designed to provide 15, 55, and 30% of total energy as protein, carbohydrate, and fat, respectively, during maintenance weeks. During the energy-restriction phase (weeks 3–6), the amount of protein consumed was the same as the amount consumed during the maintenance phase. Total energy intake was calculated using Nutritionist IV software (version 4.0; N-Squared Computing, First Data Bank, San Bruno, CA) assuming metabolizable energy values for protein, carbohydrate, and fat of 16.7, 16.7, and 37.7 kJ/g, respectively.

**Hyperinsulinemic-euglycemic clamp.** Each subject completed a hyperinsulinemic-euglycemic clamp procedure at the end of weeks 2 and 7. The subjects were tested at 7:00 A.M. in the postabsorptive state after an overnight 12-h fast. For the RT + WLoss group, the week-7 clamp was performed 3 days after the last exercise session. The hyperinsulinemic-euglycemic clamps were performed according to the technique described by DeFronzo et al. (25). Endogenous glucose production (EGP) was determined using a primed constant infusion of [ $6,6$ - $^2\text{H}_2$ ]glucose (Mass Trace, Somerville, MA) prepared in 0.9% NaCl. At time 0, a primed continuous infusion of insulin (Humulin; Eli Lilly, Indianapolis, IN) was started, and the infusion rate from 10–120 min was  $40 \text{ mU} \cdot \text{m}^{-2} \cdot \text{min}^{-1}$ . The plasma glucose level was maintained at 90 mg/dl (5 mmol/l) during the insulin infusion by determining the plasma glucose concentrations every 5 min and adjusting the infusion rate of a 20% dextrose-in-water solution.

Indirect calorimetry was performed before the start of the clamp and during the last 30 min of the clamp to estimate glucose oxidation and storage. The intra- and intervariability of the method for determination of the respiratory quotient for

an alcohol burn were 1.12 and 2.27%, respectively. Nonoxidative glucose disposal was determined by subtracting carbohydrate oxidation rates from the rate of infusion of exogenous glucose. Carbohydrate oxidation rates were calculated based on rates of gas exchange (26).

Plasma glucose concentration was measured using an oxidase method standard to the glucose analyzer (Beckman Glucose Analyzer 2, model #6517; Brea, CA). Plasma insulin was analyzed as previously described (27). The isotope enrichment of plasma  $[6,6^2\text{H}_2]\text{glucose}$  was determined using a Hewlett-Packard 5890 gas chromatography-electron impact-quadrupole-mass spectrometry with a 5970 mass selective detector.

**Resistance training protocol.** For those women assigned to the RT + WLoss group, the training program consisted of 4 weeks of progressive resistance training three times per week with a minimum of 1 day rest in between training sessions, as previously described (28). The first two sets consisted of eight repetitions at 80% of one-repetition maximum (1RM), and the third set was continued until voluntary muscular fatigue or until 12 repetitions were completed. 1RM is defined as the maximum amount of weight that can be lifted once through the full range of motion. Five exercises were performed using Keiser pneumatic variable resistance machines as follows (Keiser pneumatic resistance equipment; Keiser Sports Health Equipment, Fresno, CA): unilateral knee extension (1), unilateral knee flexion (2), double leg press (3), seated chest press (4), and seated arm pull (5). All of the women in the exercise group completed all 12 RT sessions (100% compliance).

Baseline strength (1RM) for each exercise was assessed during week 2. 1RM assessments were repeated at study week 7. Total body strength is reported as the sum of 1RM measurements for right and left unilateral leg extension, right and left unilateral leg curl, double leg press, chest press, and arm pull.

**Body composition.** All body composition measurements were performed in the postabsorptive state after a 12-h overnight fast at weeks 2 and 7. Fasting body weight was measured each weekday during the study period (Model 2181; Toledo Scale, Toledo, OH). Body height, without shoes, was measured to the nearest 0.1 cm

with a wall-mounted stadiometer one morning during week 1.

Skinfold thickness and body circumferences were measured at weeks 2 and 7. Skinfold thickness was measured on the right side of the body with Lange calipers (Cambridge Scientific Industries, Cambridge, MA) to the nearest 0.5 mm at eight sites (biceps, triceps, chest, subscapula, abdomen, suprailiac, mid-axillary, and thigh) by one investigator using standard techniques (29). The sum of skinfolds at these eight sites is reported. Body circumferences were taken with a Gulick tape at the waist (in a horizontal plane at the level of the natural waist, which is the narrowest part of the torso) and hips (in a horizontal plane at the greatest protrusion of the buttocks).

Body density was determined via air-displacement plethysmography using BOD POD (Life Measurements Instruments, Concord, CA) (30). Percent body fat (BF), FM, and fat-free mass (FFM) were estimated from body density using the Siri two-compartment model equation (31).

Muscle mass was calculated from the mean creatinine concentration of three consecutive 24-h urine collections by assuming an equivalence of 17.9 kg muscle/g of urinary creatinine (32). Urine collections were made during weeks 2 and 7. The intra- and intervariability for creatinine concentration assay were 3.3 and 3.7%, respectively.

**Statistical analyses.** Values are reported as means  $\pm$  SEM. At baseline, the difference for a given parameter between the WLoss and RT + WLoss groups was determined using Student's unpaired *t* test (two-tailed). The main effects of time and the interactions between the groups over time for each of the dependent variables were determined by using repeated measures analysis of variance. Analysis of variance was also used to determine significant differences within groups for a given parameter. All data processing and calculations were performed by using JMP Statistical Discovery Software (SAS Institute, Cary, NC). Statistical significance was assigned at  $P < 0.05$ .

## RESULTS

### Subjects

A total of 19 postmenopausal (aged  $63 \pm 2$  years) overweight to obese ( $\text{BMI } 29.9 \pm 0.7 \text{ kg/m}^2$ ) Caucasian women completed this study. Of the women who completed the study, 10 were glucose intolerant by an OGTT, 4 were on hypertensive medication, and 10 were on hormone-replacement therapy.

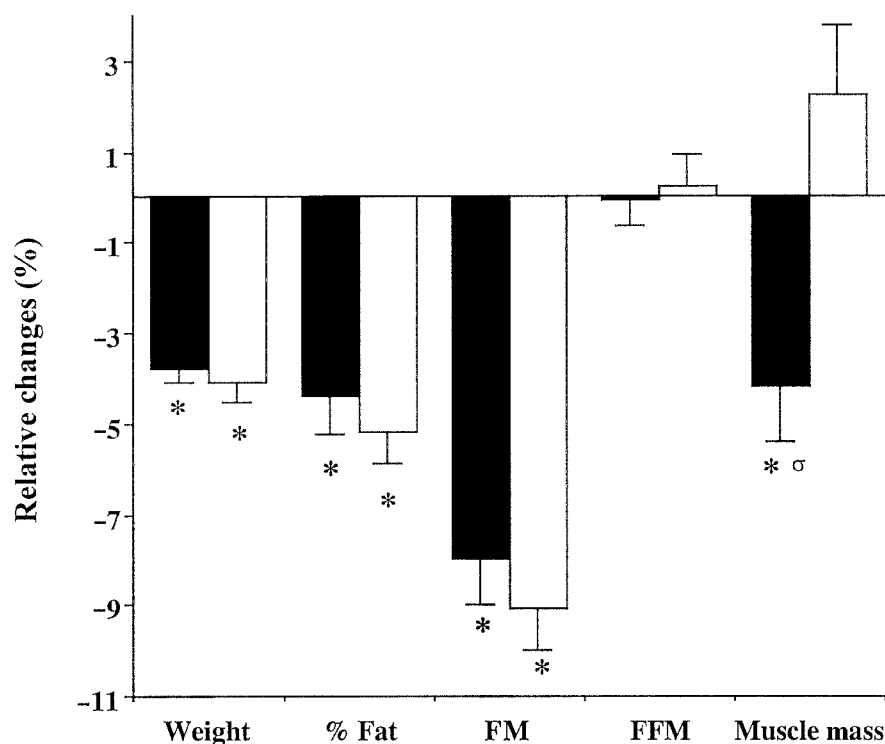
### Changes in body composition

At baseline, there was no difference between the WLoss and RT + WLoss groups regarding the degree of obesity (Table 1). There was no difference in body weight at the end of week 1 or the day of

**Table 1—Characteristics and body composition before and after moderate weight loss**

	WLoss		RT + WLoss	
	Baseline	Week 7	Baseline	Week 7
Age (years)	$61 \pm 2$	$61 \pm 2$	$65 \pm 2$	$65 \pm 2$
Height (cm)	$163.1 \pm 2.6$	$163.1 \pm 2.6$	$163.2 \pm 1.6$	$163.2 \pm 1.6$
Weight (kg)*	$80.8 \pm 2.6$	$77.8 \pm 2.7^\dagger$	$78.2 \pm 2.1$	$75.0 \pm 2.2^\dagger$
BMI ( $\text{kg/m}^2$ )*	$30.4 \pm 1.0$	$29.3 \pm 1.0^\dagger$	$29.4 \pm 0.9$	$28.2 \pm 0.9^\dagger$
BF (%)*	$47.2 \pm 1.4$	$45.2 \pm 1.6^\dagger$	$47.0 \pm 1.4$	$44.6 \pm 1.4^\dagger$
FM (kg)*	$38.3 \pm 2.1$	$35.3 \pm 2.2^\dagger$	$36.9 \pm 1.9$	$33.7 \pm 1.9^\dagger$
FFM (kg)	$42.5 \pm 1.3$	$42.4 \pm 1.3$	$41.2 \pm 0.6$	$41.3 \pm 0.7$
MM (kg)†	$16.0 \pm 1.3$	$15.4 \pm 1.3^\dagger$	$17.9 \pm 0.8$	$18.3 \pm 0.8$
Waist circumference (cm)*	$97.3 \pm 2.7$	$93.3 \pm 2.2^\dagger$	$90.9 \pm 2.1$	$88.2 \pm 2.2^\dagger$
Waist-to-hip ratio	$0.86 \pm 0.02$	$0.85 \pm 0.01$	$0.81 \pm 0.02$	$0.80 \pm 0.02$
Sum skinfolds (cm)*	$238.8 \pm 10.6$	$221.5 \pm 10.0^\dagger$	$228.4 \pm 9.2$	$214.7 \pm 10.2^\dagger$

Data are means  $\pm$  SEM. Percent BF, FM, and FFM were calculated from body density values using the Siri two-compartment model. Body density measurements were made via whole-body plethysmography in the postabsorptive state after a 12-h overnight fast. Muscle mass (MM) was estimated from 24-h urinary creatinine excretion. \*Significant time effect for both groups combined ( $n = 19$ ),  $P < 0.001$ ; †significant time effect for respective groups,  $P < 0.001$ ; ‡significant group-by-time interaction,  $P < 0.05$ .



**Figure 1**—Relative changes (percent) in body composition measures in WLoss and RT + WLoss groups after 4 weeks of treatment. Closed bars represent the WLoss group, and open bars represent the RT + WLoss group. \*Significant change from baseline to week 7,  $P < 0.01$ .  $\sigma$ Significant group  $\times$  time interaction demonstrating a difference in response between WLoss and RT + WLoss,  $P < 0.05$ . Values are means  $\pm$  SEM.

metabolic testing at the end of week 2 (WLoss  $80.7 \pm 2.6$  vs.  $80.8 \pm 2.6$  kg; RT + WLoss  $78.5 \pm 2.1$  vs.  $78.2 \pm 2.1$  kg). Also, there was no difference in body weight during the last day of energy restriction during week 6 or the final day of metabolic testing during week 7 (WLoss  $77.5 \pm 2.7$  vs.  $77.8 \pm 2.7$  kg; RT + WLoss  $75.1 \pm 2.2$  vs.  $75.0 \pm 2.2$  kg). As shown in Fig. 1 and Table 1, body weight, BMI, percent BF, FM, waist circumference, and sum of skinfold all decreased with energy restriction. The absolute and relative changes in these parameters were not different between the WLoss and RT + WLoss groups. There were no significant changes in FFM and waist-to-hip ratio in either group. The similar response for all these measured variables resulted in no significant group-by-time interactions between the groups. However, a significant decrease in muscle mass in the WLoss group with no change in the RT + WLoss group resulted in a significant group-by-time interaction ( $P = 0.04$ ).

### Energy intake

The mean values for energy intake were not different for the WLoss and RT + WLoss groups during the weight-maintenance ( $2,206 \pm 86$  and  $2,061 \pm 56$  kcal/day, respectively) and energy-restriction ( $1,457 \pm 105$  and  $1,312 \pm 59$  kcal/day, respectively) phases. There were no differences between the groups during either phase for the percentage of carbohydrate, protein, or fat.

### Strength indexes

Baseline 1RM strength values were not different between the WLoss and RT + WLoss groups. Strength training resulted in significant increases in 1RM strength values for each individual exercise in the RT + WLoss group. Total body strength increased by  $23 \pm 2\%$  ( $235 \pm 19$  to  $289 \pm 18$  kg,  $P < 0.001$ ) in the RT + WLoss group with no changes in the WLoss group ( $2 \pm 2\%$ ).

### Hyperinsulinemic-euglycemic clamp

At baseline, the mean values relating to glucose and insulin metabolism were not

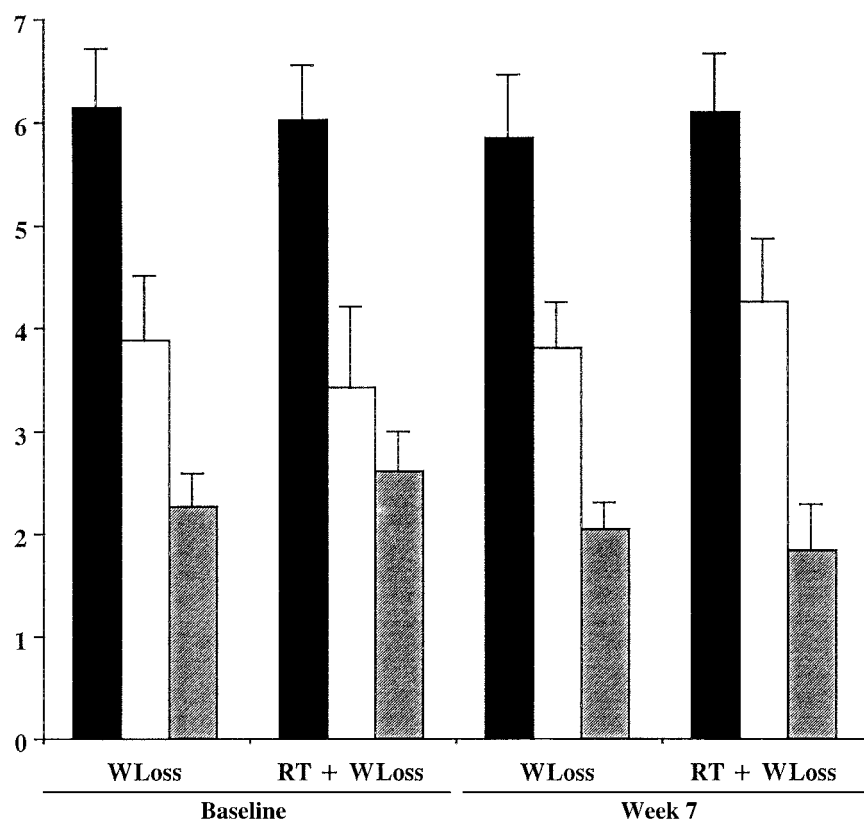
different between groups. During the hyperinsulinemic-euglycemic clamp, the plasma glucose coefficient of variation was within 2% of the desired value of 5 mmol/l [90 mg/dl] before and after the intervention.

There were no changes over time in either group with respect to insulin-stimulated glucose disposal, glucose oxidation, or glucose storage (Fig. 2). Basal endogenous glucose production was reduced in the WLoss ( $3.15 \pm 0.16$  to  $2.88 \pm 0.10$   $\text{mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ;  $P < 0.05$ ) but not in the RT + WLoss ( $2.93 \pm 0.09$  to  $2.86 \pm 0.09$   $\text{mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) group. There was no group-by-time interaction for endogenous glucose production ( $P = 0.11$ ). Hepatic glucose production was completely suppressed during hyperinsulinemia (data not shown). The addition of resistance training to the energy restriction provided no synergistic effect to any measure relating to glucose metabolism. Therefore, the results of both groups were combined to assess the effect of weight loss on these variables.

For all 19 women combined, there was no change in insulin-stimulated glucose disposal ( $5.99 \pm 0.41$  to  $6.06 \pm 0.38$  mg/kg of FFM per min;  $P = 0.78$ ). When glucose disposal was partitioned into oxidative and nonoxidative disposal, there was no change in mean glucose oxidation ( $2.14 \pm 0.20$  to  $2.20 \pm 0.31$  mg/kg of FFM per min;  $P = 0.40$ ) or storage ( $3.85 \pm 0.36$  to  $3.86 \pm 0.49$  mg/kg of FFM per min;  $P = 0.31$ ).

**CONCLUSIONS**— Weight loss is the most common recommendation to improve glucose tolerance and to decrease the risk of developing type 2 diabetes. As a result of the difficulty in achieving a substantial decrease in body weight, small-to-moderate weight loss is often prescribed. However, the effects of small-to-moderate amounts of weight loss on insulin action have not been examined. The results of this study demonstrate that 4 weeks of moderate energy restriction, resulting in a 4% decrease in body weight, did not improve insulin-stimulated glucose disposal in a group of nondiabetic postmenopausal women. Previous studies designed to induce a similar rate of weight loss (0.25–0.5 kg per week) in older individuals reported significant improvements in insulin sensitivity and glucose utilization (8,9,33). The intervention period in those studies





**Figure 2**—Total glucose disposal (M, milligrams per kilograms of FFM per minute) during hyperinsulinemic-euglycemic clamp before and after 4 weeks of energy restriction with (RT + WLoss) and without (WLoss) resistance training (■). Glucose disposal was partitioned into glucose oxidation (□) and nonoxidative glucose disposal (■) from indirect calorimetry during hyperinsulinemic-euglycemic clamp. No significant differences were seen between groups or as a result of weight loss. Values are means  $\pm$  SEM.

lasted for a period of 4–9 months and resulted in a greater decrease in body weight (10–22%) and absolute FM (19–26%) than the present study. The change in obesity quantified as a reduction in body weight, percent BF, or FM (visceral or subcutaneous) was highly related to the improvements in insulin sensitivity and glucose utilization (8,9,33). This study was specifically designed to examine whether a short-term weight loss program resulting in a moderate amount of weight loss would have a similar effect on insulin action, as reported in studies of longer duration. Collectively, the present data along with previous studies suggest that a greater change in body weight and FM than what was observed in the present study may be necessary to have a significant physiological effect on insulin action and glucose metabolism.

The relation between abdominal fat (especially visceral fat) and insulin resistance underlies the importance of reduc-

ing these fat depots (4,5). It has been hypothesized that the increased visceral fat associated with obesity leads to a reduced rate of plasma free fatty acid (FFA) clearance and higher levels of circulating FFA (34), which can lead to insulin resistance (35). Therefore, perhaps the amount of abdominal fat loss rather than absolute body weight loss is more instrumental in improving insulin sensitivity in long-term weight loss studies (36). Although abdominal FM was not directly assessed in this protocol, it is likely that the 8% decrease in FM did not achieve a sufficient amount of change in abdominal FM to affect insulin-stimulated glucose disposal in this group of nondiabetic older women. Various studies have documented that waist circumference is a very robust predictor of abdominal visceral adipose tissue (37,38). Therefore, one would assume that the 3.5% change in waist circumference is a good estimate of a change in visceral adiposity. However, a

statistically significant decrease in waist circumference did not translate into a significant physiological effect of improving insulin-stimulated glucose disposal. Whereas it is clear that a reduction in abdominal fat is associated with improved insulin actions (36), as with total fat reduction, there may be a threshold of abdominal fat loss (measured directly or indirectly) that is necessary to produce such an effect.

A negative energy balance, independent of the magnitude of weight loss, accounts for the majority of improvement in insulin action observed in the early stages of a weight loss program (11,12). To avoid the confounding effect of being in a hypo-energetic state, the women were fed a eucaloric diet for 5 days before metabolic reevaluation. In addition, the reintroduction of energy prevented any further decrease in body weight and allowed metabolic testing to be performed during a period when body weight was stabilized. However, it is possible that the change in the diet before the hyperinsulinemic clamp could have masked any effect that the weight loss (10,39) or exercise (40) may have had on insulin action. Henry et al. (10) stated that after 5 days of a calculated weight-maintenance diet at the new body weight, glucose levels increased to pre-weight-loss levels without any change in body weight. Mott et al. (39) also reported that increasing energy intake for 2 weeks resulted in a significant decrease in insulin-stimulated glucose storage that the authors associated with a reduction in glycogen synthase activity. Segal et al. (40) also reported that 12 weeks of aerobic training had no effect on insulin action in lean, obese, and type 2 diabetic subjects when the energy expended during exercise training was compensated with diet to prevent weight loss. The authors concluded that the increase in energy intake and the exercise training may have exerted an opposing effect on insulin action and glucose metabolism.

The results of the current study also indicate that the addition of resistance training to a short-term energy restriction program did not improve insulin action in moderately overweight older women. Previous longer-term resistance training studies alone (17,18,20) or in conjunction with energy restriction (19) have demonstrated significant improvements in insulin action and glucose utilization.

One major methodological difference is that metabolic parameters were reassessed 24 h after the last exercise session in those studies, whereas glucose disposal was measured 72 h after resistance training in the current study. There is evidence to show that the time of metabolic reevaluation is important when considering the effect of acute or training exercise on glucose metabolism (41–43). As reported by Mikines et al. (43), one single session of aerobic exercise increased insulin action for up to 48 h after the exercise, with no remaining effect observed after 5 days. Various investigators have also demonstrated that one session of aerobic or resistance exercise and 1 week of vigorous aerobic exercise also decreases the insulin response to a glucose challenge when the measurements were made 24 h after the last exercise session (21,41,42,44). However, the results of this study do not contradict the importance of exercise as a therapeutic tool in the management of glucose metabolism in obese and insulin-resistant individuals. Instead, the data emphasize that the adherence to continuous physical activity (i.e., repeated sessions of acute exercise) is important to observe the beneficial effect of exercise on metabolic parameters.

Despite the fact that muscle mass did not increase in the RT + WLoss group, the current data demonstrate that there was a significant effect of resistance training on muscle mass, assessed by urinary creatinine excretion, when compared with the WLoss group after only 4 weeks of training. The preservation of muscle mass in the RT + WLoss group demonstrates the importance of combining moderate energy restriction with resistance training in the treatment of body weight reduction. Other studies have documented the positive benefits of exercise training with energy restriction (21, 22,45,46). Using magnetic resonance imaging to measure muscle size, Ross et al. (22,45) demonstrated that lean tissue, primarily skeletal muscle mass, was preserved in response to a program that combined moderate energy restriction with resistance training for a period of 16 weeks. In another study, Ryan et al. (46) used dual-energy X-ray absorptiometry to demonstrate a preservation of FFM after 16 weeks of resistance training and moderate energy restriction. Collectively, these results provide evidence that FFM may be maintained during weight reduction

when a more moderate approach to energy restriction is combined with an exercise regimen.

The decrease in basal EGP after weight reduction is in agreement with other energy-restriction studies (11,12). However, in contrast to those studies, the decrease in EGP was not accompanied with a change in circulating postabsorptive glucose concentrations. This is probably because the change in EGP was very small and may not have been of significant magnitude to affect circulating glucose concentrations. In addition, the severity of energy restriction may also dictate the degree of EGP. Kelley et al. (11) and Markovic et al. (12) used a severe energy restriction of >50% of baseline energy intake. These authors reported that energy restriction accounted for the majority of improvement in fasting glucose production and suggested that the dramatic effect on EGP may be because of the expected fall in hepatic glycogen, as a result of the severity of the energy restriction. However, it is important to note that it may be difficult to detect changes in fasting glucose concentrations as a result of alterations in endogenous glucose production in the nondiabetic subjects of the present study.

In conclusion, the results of this study demonstrate that a small-to-moderate amount of weight loss (<5% of initial body weight) had no effect on insulin-stimulated glucose disposal in overweight nondiabetic postmenopausal women. Also, weight loss alone decreased hepatic glucose production, but a greater decrease in EGP may be necessary to affect fasting glucose concentration. Whereas the addition of resistance training preserved muscle mass during weight loss, it provided no additional or synergistic effect to that observed with energy restriction alone when insulin action was assessed 72 h after the last exercise session. More studies are needed to establish whether there is a threshold of weight loss that is necessary to improve insulin action and glucose tolerance and to reduce the risk of type 2 diabetes.

**Acknowledgments**—This study was supported by National Institute on Aging Grants AG 11811, R29 AG13409, T32 AG00048, and AG14928; National Institutes of Health Grant NCRR00954; the American College of Sports

Medicine; and the American Federation for Aging Research.

We extend our sincere and deepest appreciation to all the volunteers for their time and dedication, without which this study would not have been possible. Special thanks to Arlene Sullivan and Michelle Frost for grace and humor in performing all of the medical duties that were required during this project, Dr. James Fluckey for his advice and counseling during data collections, and the staff of the Nutrition, Metabolism, and Exercise Laboratory for assisting with various aspects of this project. We are also grateful to Keiser Sports Health Equipment (Fresno, CA) for donating the RT equipment.

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