

Effects of Exercise Modality on Insulin Resistance and Functional Limitation in Older Adults

A Randomized Controlled Trial

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Background: Authorities advocate that resistance and aerobic exercise are essential for reducing risk factors for chronic disease and disability in older adults. However, the incremental effects of combined resistance and aerobic exercise compared with either modality alone on risk factors for disease and disability is generally unknown.

Methods: Participants were 136 sedentary, abdominally obese older men and women recruited from September 30, 2002, through November 15, 2006, at Queen's University. Participants were randomized to 1 of the following 4 groups for 6 months: resistance exercise, aerobic exercise, resistance and aerobic exercise (combined exercise), or nonexercise control. Primary outcomes were analyzed by an intent-to-treat model and included changes in insulin resistance by hyperinsulinemic-euglycemic clamp and functional limitation using the average change in 4 tests combined (average z score).

Results: After controlling for age, sex, and baseline value, insulin resistance improved compared with controls in the aerobic exercise and the combined exercise groups but not in the resistance exercise group. Improvement (mean [SE]) in the combined exercise group was greater

than in the resistance exercise group (9.2 [1.3] vs 1.8 [1.3] mg/mL/ μ IU per kilogram of skeletal muscle per minute $\times 100$ [$P < .001$]) but not in the aerobic exercise group (9.2 [1.3] vs 6.5 [1.3] mg/mL/ μ IU per kilogram of skeletal muscle per minute $\times 100$ [$P = .46$]). Functional limitation improved significantly in all groups compared with the control group. Improvement in the combined exercise group was greater than in the aerobic exercise group (0.5 [0.1] vs -0.0 [0.1]; standard units, z score [$P = .003$]) but not in the resistance exercise group. Improvement in the resistance exercise group was not different from the aerobic exercise group.

Conclusion: The combination of resistance and aerobic exercise was the optimal exercise strategy for simultaneous reduction in insulin resistance and functional limitation in previously sedentary, abdominally obese older adults.

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THE PREVALENCE OF CHRONIC disease and physical disability among obese elderly persons is high and increasing.^{1,2}

The economic burden associated with chronic disease or disability is substantial.²⁻⁴ Although the elderly currently constitute less than 13% of the total population,⁵ they account for approximately 35% of the total personal health care costs.⁶ Projections indicating that the US population 65 years and older will increase from 12% in 2000 to 20% in 2030⁵ underscore the urgent need to develop effective strategies designed to manage the risk factors for disease and disability and thereby improve the overall health and quality of life of older adults.

Recent public health guidelines from the American Heart Association and the American College of Sports Medicine advocate that regular physical activity, in-

cluding aerobic and resistance exercise, is essential for healthy aging.⁷ Specifically, it is recommended that older adults engage in both exercise modalities to reduce the risk factors for chronic disease and disability. With respect to risk factors for disease, it is well established that aging is associated with a marked increase in insulin resistance,⁸ a primary defect that precedes serious diseases, including diabetes,⁹ stroke,¹⁰ and coronary heart disease independent of other major cardiovascular disease risk factors.^{11,12} Aging is also associated with a progressive increase in functional limitations that affect activities of daily living and quality of life¹³ and that are highly predictive of subsequent disability.¹⁴ To our knowledge, there are no randomized controlled studies that have simultaneously investigated the incremental effects of combined aerobic and

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Table 1. Description of Exercise Interventions

	Study Group			
	Control	Resistance Exercise	Aerobic Exercise	Combined Exercise
No. of weekly visits	1	3 ^a	5	3 ^a
Type of exercise				
Aerobic	None	None	30 min of moderate-intensity treadmill walking (measured heart rate to ensure 60%-75% $\dot{V}O_2$ peak range obtained from GXT) ^b	30 min of moderate-intensity treadmill walking (measured heart rate to ensure 60%-75% $\dot{V}O_2$ peak range obtained from GXT) ^b
Resistance	None	1 Set of 9 exercises, each to volitional fatigue ^c : chest press, shoulder raise, shoulder flexion, leg extension, leg flexion, triceps extension, biceps curl, abdominal crunches, modified push-ups; approximate duration each session, 20 min	None	1 Set of 9 exercises, each to volitional fatigue ^c : chest press, shoulder raise, shoulder flexion, leg extension, leg flexion, triceps extension, biceps curl, abdominal crunches, modified push-ups; approximate duration each session, 50 min
Total weekly exercise duration, min	None	60	150	150

Abbreviations: GXT, graded exercise test; $\dot{V}O_2$, oxygen consumption per unit of time.

^aSessions were performed on nonconsecutive days of the week. All exercise sessions were by appointment and supervised.

^bThe GXTs for measurement of $\dot{V}O_2$ peak were performed using a treadmill protocol with a constant walking speed, progressive increases in treadmill grade, and the use of standard open-circuit spirometry techniques at baseline, during the second month of exercise, and in the final week of the intervention. Aerobic exercise intensity was monitored every 5 minutes using an automated heart rate monitor (Polar Oy, Kempele, Finland).

^cThe weight lifting was increased when 15 repetitions were completed with good form. To account for neuromuscular adaptations, relative strength increases were assessed by subtracting the average weight lifted during the fourth week from the average weight lifted during the final week of the trial and was expressed as a percentage of the fourth week's weight.

resistance exercise compared with either modality alone on these risk factors in older men and women. Thus, the following questions with important practical and clinical implications remain unanswered: "Is resistance or aerobic exercise alone an effective strategy for simultaneous reduction in risk factors for disease and disability?" and "Is the combination of aerobic and resistance exercise a better treatment strategy for simultaneous reduction of risk factors for disease and disability than either modality alone?" Answers to these questions are important and would lend empirical support to current public health guidelines for physical activity in older adults.

We therefore performed a randomized controlled trial to investigate the independent and combined effects of resistance and aerobic exercise on insulin resistance and functional limitations in abdominally obese older men and women. We chose to study abdominally obese elderly subjects because they are at substantially increased risk for insulin resistance¹⁵ and functional limitations,¹⁶ and because it is estimated that 62% of men and 74% of women aged 60 to 69 years in the United States are abdominally obese.¹⁷

METHODS

DESIGN

We conducted a 6-month, single-center, randomized controlled trial with a parallel group design. Previously sedentary, abdominally obese older men and women were randomly assigned to 1 of the following 4 groups: resistance exercise, aerobic exercise, a combination of resistance and aerobic exercise (combined exercise), or nonexercise control (**Table 1**). Randomized group assignment was issued on completion of baseline assessments and was not revealed to those conducting baseline tests. The randomization procedure was stratified

by sex, but without any blocking. Participants and exercise supervision personnel could not feasibly be blinded to group assignment after randomization; however, the main study outcomes were measured by blinded technologists using objective assessments. The study was approved by the Queen's University Health Sciences Research Ethics Board. All participants received medical clearance from their personal physician and gave informed consent before participation.

PARTICIPANTS

Abdominally obese adults aged 60 to 80 years who did not smoke were recruited using a wide variety of techniques, including newspapers, radio, mailers, and posters. Inclusion criteria required a waist circumference of at least 102 cm in men and at least 88 cm in women and stable weight (± 2 kg) for 6 months before study entry. Potential participants were excluded if they reported a history of heart disease, stroke, diabetes mellitus, or any condition that would prevent them from engaging in an exercise study; if they were currently dieting or intended to diet; if they were already engaging in 2 or more planned exercise sessions per week; or if they were taking any medication to lower glucose levels. Blood pressure and medications to lower lipid levels were allowed if the regimen was maintained throughout the trial.

DIETARY AND EXERCISE INTERVENTIONS

During the baseline period, participants were instructed by a nutritionist to continue a diet that would maintain baseline body weight through maintenance of calorie intake while recording their daily consumption of self-selected foods. A healthy diet composition was encouraged, and body weight was monitored for approximately 4 weeks to determine the daily calorie intake required for weight maintenance. During the intervention, to help ensure that the negative energy balance was induced by the exercise modality alone, participants were instructed to maintain the calorie intake targets determined at baseline unless the weight change differed substantively from

that predicted by exercise-induced energy expenditure. If the weight change deviated substantively (approximately ± 1 kg) from expectation, individual sessions with the study nutritionist were scheduled to identify the reason for the deviation. Participants attended 9 individual 1-hour seminars in which the nutritionist taught healthy food selection and preparation according to Canada's Food Guide (<http://www.hc-sc.gc.ca/fn-an/food-guide-aliment/index-eng.php>). Participants continued to keep and analyze daily food records throughout the study. On completion of the study, 2 weeks of records were analyzed using a computerized program (Food Processor; ESHA Research, Salem, Oregon) to assess the accuracy of self-reported records. All exercise interventions are described in Table 1.

ANTHROPOMETRIC MEASUREMENTS

Anthropometric measurements were taken at baseline and the last week of the intervention. Body mass was measured with participants dressed in standard T-shirts and shorts. Waist circumference was obtained in a standing position using the mean of 2 measures obtained at the superior edge of the iliac crest.¹⁸

MEASUREMENT OF TOTAL AND REGIONAL FAT AND SKELETAL MUSCLE MASS

Adiposity (fat) and skeletal muscle mass were measured by means of magnetic resonance imaging and analyzed using standard procedures.^{19,20} Visceral and abdominal subcutaneous fat depots were calculated using 5 images from 5 cm below to 15 cm above the L4-5 intervertebral space.¹⁹

MEASUREMENT OF INSULIN RESISTANCE AND GLUCOSE TOLERANCE

Insulin resistance was assessed by means of a 3-hour hyperinsulinemic-euglycemic clamp.²¹ Postintervention insulin resistance was assessed 36 to 48 hours after the final exercise session. Glucose tolerance was measured at baseline by means of a 2-hour glucose tolerance test.²¹ Participants whose plasma glucose levels exceeded 200 mg/dL (to convert to millimoles per liter, multiply by 0.0555) at 120 minutes were considered to have diabetes, referred for medical follow-up, and were excluded from the study.

MEASUREMENT OF FUNCTIONAL LIMITATION AND CARDIORESPIRATORY FITNESS

Functional limitation was evaluated using 4 of the 6 tests designed by Rikli and Jones²² to assess physiological variables associated with independent living in older adults. Items consisted of the maximal number of chair stands performed in 30 seconds (the number of times the subject stood up from a chair); the 2-minute step (the number of steps in place in 2 minutes); the 8-ft up-and-go (the time needed to get out of a chair, walk 2.4 m, and return to the seated position in the chair); and the seated arm curl (the number of times a hand weight [2.25 kg for women and 3.6 kg for men] could be curled through a full range in 30 seconds). We chose to evaluate the effects of exercise modality on functional limitation using predominantly lower extremity exercise tests because they predict subsequent disability in nondisabled older adults.¹⁴ Functional limitation was determined for each subject by averaging the improvement (difference between scores obtained before and after the intervention) for all 4 tests. Because the unit measurement is not equivalent across tests, a composite score was calculated by normalizing the change for each test using *z* scores and averaging them. Cardiorespiratory fitness (measured as oxy-

gen consumption per unit of time [peak $\dot{V}O_2$]) was determined using results of a maximal treadmill test combined with standard open-circuit spirometry techniques (SensorMedics Corp, Yorba Linda, California) at baseline.²³

ESTIMATION OF AEROBIC AND RESISTANCE EXERCISE ENERGY EXPENDITURE

Oxygen cost of aerobic exercise was determined using the relationship between heart rate and oxygen consumption obtained from the graded exercise test results (peak $\dot{V}O_2$). Oxygen consumption during resistance exercise was estimated to be 45% of maximal.²⁴ Energy expenditure for both exercise modalities was determined by multiplying oxygen consumption by 5.04 kcal/L.

STATISTICAL ANALYSIS

We selected the sample size to provide a statistical power of 80% to detect a difference of 1.5 mg/kg of muscle per minute in insulin resistance between any 2 groups at 6 months using analysis of covariance (ANCOVA) at an α of .05.²⁵ We estimated that the improvement in insulin resistance would range from 3.5 to 5.0 (SD, 2.5) mg/kg of muscle per minute,²⁶ with a correlation of 0.7 between baseline and posttreatment insulin resistance measurements. To allow for this scenario, a minimum of 23 patients was required in each group (to detect a difference of 1.5 mg/kg of muscle per minute between any 2 groups). We exceeded this sample size to allow for withdrawals.

We evaluated the effect of the intervention by means of intent-to-treat analysis. Subjects for whom follow-up data were unavailable were included in a multiple-imputations procedure that estimated the missing data values randomly based on the multivariate normal distribution of the data within each sex-specific intervention group.²⁷ We used analysis of variance to determine differences between means of the treatment groups at baseline and to describe changes in ancillary variables such as muscular strength, cardiorespiratory fitness, energy intake, and energy expenditure. All treatment-related changes in primary and secondary outcomes were adjusted for baseline values, age, and sex using ANCOVA. The ANCOVA model was extended to include the sex and treatment \times sex interaction terms to determine whether the effects of treatment varied by sex. We performed Tukey post hoc tests with adjustment for multiple comparisons to determine differences between intervention groups.

To examine the relationship between changes in total and abdominal fat and skeletal muscle and changes in functional limitation, subjects with complete body composition data before and after the intervention were cross-classified according to tertiles of change in fat and muscle mass, creating 9 different categories. Improvement in functional limitation was calculated for each of the 9 groups, and *P* values for trend were calculated to determine whether fat and muscle change tertiles were independently related to improvements in functional limitation. *P* values of less than .05 were accepted to indicate statistical significance. All analyses were performed using commercially available software (SAS, version 9.1; SAS Institute Inc, Cary, North Carolina). Unless otherwise indicated, data are expressed as mean (SE).

RESULTS

Of the 136 men and women randomized, 117 completed their assigned treatment (**Figure 1**). Discontinuation owing to musculoskeletal pain was primarily due to preexisting arthritic joint injuries that were exacerbated by exercise. Those who did not complete the trial

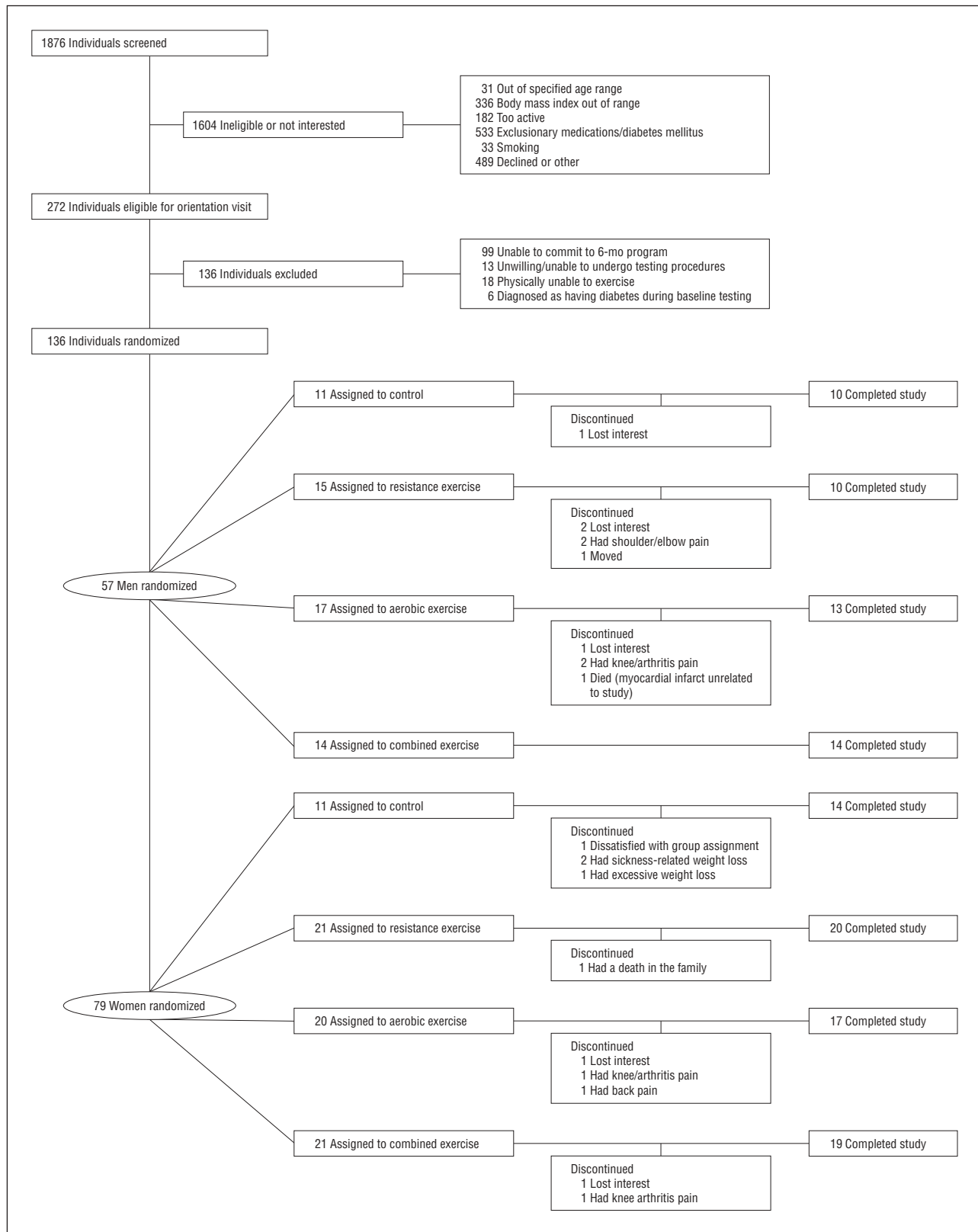


Figure 1. Participant flow diagram. All subjects assigned to each treatment (including those who discontinued the study) were included in the primary intent-to-treat analyses.

did not differ significantly in any baseline anthropometric variable from those who completed. The study sample was 98.5% white; 33.1% were receiving medication for

control of blood pressure; and 19.1% were taking medications to lower lipid levels. No participant reported taking any medication to lower glucose levels.

Table 2. Subject Characteristics at Baseline

Characteristic	Study Group, Mean (SD)									
	Women					Men				
	Control (n=17)	Resistance Exercise (n=21)	Aerobic Exercise (n=20)	Combined Exercise (n=21)	All (n=79)	Control (n=11)	Resistance Exercise (n=15)	Aerobic Exercise (n=17)	Combined Exercise (n=14)	All (n=57)
Anthropometric										
Age, y	66.7 (3.7)	67.6 (4.2)	69.1 (6.5)	66.5 (5.3)	67.5 (5.1)	67.4 (3.8)	67.4 (5.7)	68.8 (6.0)	67.1 (4.5)	67.7 (5.1)
BMI	30.4 (3.2)	30.0 (3.4)	29.2 (3.7)	29.5 (3.0)	29.7 (3.3)	30.5 (2.0)	30.1 (2.6)	29.9 (3.0)	31.1 (3.1)	30.4 (2.7)
Waist circumference, cm	104.9 (7.4)	104.3 (8.5)	104.2 (10.4)	102.8 (9.6)	104.0 (9.0)	112.8 (5.3)	111.0 (5.4)	113.0 (7.9)	114.1 (8.3)	112.7 (6.9) ^a
MRI										
Skeletal muscle, kg	20.6 (2.6)	19.9 (2.5)	19.3 (3.6)	19.0 (2.1)	19.7 (2.8)	29.5 (3.7)	32.2 (4.1)	30.3 (3.6)	30.0 (3.6)	30.6 (3.8) ^a
Total fat, kg	38.1 (7.5)	36.4 (6.7)	34.9 (7.2)	34.9 (6.8)	36.0 (7.0)	34.0 (6.1)	31.5 (4.5)	33.0 (9.2)	34.9 (6.8)	33.3 (6.9) ^a
Fat to muscle ratio	1.9 (0.3)	1.8 (0.3)	1.8 (0.3)	1.8 (0.4)	1.8 (0.3)	1.2 (0.2)	1.0 (0.2)	1.1 (0.3)	1.2 (0.2)	1.1 (0.2) ^a
Total abdominal fat, kg	8.5 (2.0)	7.8 (1.8)	7.6 (2.2)	7.5 (1.5)	7.8 (1.9)	9.0 (1.6)	8.2 (1.4)	8.9 (2.5)	9.1 (2.1)	8.8 (2.0) ^a
Visceral fat, kg	2.7 (1.0)	2.5 (1.0)	2.6 (1.0)	2.3 (0.7)	2.5 (0.9)	4.3 (1.3)	4.6 (1.1)	4.6 (0.9)	4.7 (1.1)	4.6 (1.1) ^a
Abdominal subcutaneous fat, kg	5.9 (1.5)	5.3 (1.1)	5.0 (1.5)	5.1 (1.2)	5.3 (1.4)	4.6 (0.9)	3.6 (0.7)	4.3 (2.2)	4.4 (1.4)	4.2 (1.5) ^a
Metabolic										
Fasting glucose level, mg/dL	84.7 (9.8)	84.0 (6.9)	86.7 (11.9)	76.5 (15.9)	82.8 (12.2)	85.3 (7.3)	86.5 (8.3)	87.0 (10.5)	85.6 (10.7)	86.2 (9.2)
2-h glucose level, mg/dL	121.5 (22.6)	136.8 (35.6)	130.7 (29.4)	119.9 (36.0)	127.4 (32.0)	108.4 (26.2)	126.5 (28.8)	136.2 (32.2)	120.8 (33.3)	124.5 (31.3)
Fasting insulin level, μ IU/mL	9.7 (6.0)	11.4 (6.7)	8.5 (4.4)	7.4 (3.6)	9.3 (5.4)	10.5 (8.4)	9.6 (3.5)	11.0 (4.7)	11.7 (4.5)	10.7 (5.2)
Insulin sensitivity, M/I	30.4 (11.0)	23.8 (11.1)	30.7 (14.1)	34.4 (15.0)	30.0 (13.4)	26.6 (9.9)	22.0 (10.1)	21.5 (11.1)	18.6 (9.6)	21.8 (10.3) ^a
Functional limitation^b										
No. of chair stands	12.5 (2.6)	12.3 (3.3)	11.4 (3.8)	13.8 (3.4)	12.5 (3.4)	15.6 (3.6)	16.3 (3.7)	14.7 (3.9)	15.2 (3.2)	15.4 (3.6) ^a
No. of arm curls	17.1 (3.6)	14.4 (2.4)	13.9 (3.7)	16.2 (3.0)	15.3 (3.4)	19.9 (3.9)	20.6 (4.3)	19.5 (4.0)	19.3 (3.0)	19.8 (3.8) ^a
2-min step test, No. of steps	100.6 (24.3)	82.8 (16.3)	88.2 (15.8)	92.3 (21.5)	90.5 (19.1)	110.3 (14.4)	116.0 (14.0)	110.9 (13.2)	114.9 (19.2)	113.1 (15.1) ^a
8-ft up-and-go, s	5.2 (0.7)	5.3 (0.8)	5.2 (0.9)	5.0 (0.8)	5.2 (0.8)	4.0 (0.5)	4.0 (0.5)	4.2 (0.6)	4.2 (0.8)	4.1 (0.6) ^a
Cardiorespiratory fitness										
$\dot{V}O_{2max}$, L/min	1.7 (0.3)	1.7 (0.3)	1.7 (0.3)	1.8 (0.4)	1.7 (0.3)	2.6 (0.4)	2.6 (0.5)	2.5 (0.4)	2.7 (0.5)	2.6 (0.5) ^a
$\dot{V}O_{2max}$, mL/kg/min	21.1 (2.6)	21.0 (3.9)	21.8 (3.1)	23.5 (5.2)	21.9 (4.0)	28.3 (5.3)	27.8 (5.2)	26.9 (4.0)	28.1 (6.2)	27.7 (5.1) ^a

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); M/I, rate of glucose uptake per unit of insulin per kilogram of skeletal muscle per minute \times 100; MRI, magnetic resonance imaging; $\dot{V}O_{2max}$, maximum oxygen consumption.

SI conversion factors: To convert glucose to millimoles per liter, multiply by 0.0555; insulin to picomoles per liter, multiply by 6.945.

^aBaseline mean values for all men are significantly different from those for all women ($P < .05$).

^bTests are described in the "Measurement of Functional Limitation and Cardiorespiratory Fitness" subsection of the "Methods" section.

Mean attendance at the exercise sessions was 91% (9%) and did not vary by sex or exercise group. Aerobic exercise intensity did not differ between the aerobic exercise and the combined exercise groups (mean exercise heart rate was 80% of the predicted maximum in both groups). More than 80% of the daily food intake records were completed by 90 of 136 participants during the 6-month intervention. An additional 34 completed records at a rate of approximately 2 to 3 days per week. Computer analysis of diet records for a subset of 84 subjects verified self-reported results for 2 of the 24 weeks and confirmed that the total calorie and fat content of the diet was not different from nutritional recommendations.

Despite significant sex differences for several baseline characteristics, there were no significant differences between groups within each sex for any baseline variable (**Table 2**). With the exception of a greater reduction of total and visceral fat in men than women in the aerobic exercise group only, men and women within the same treatment group did not differ significantly in their response to exercise for any variable (data not shown). Therefore, all treatment-induced changes are shown collapsed across sex.

Compared with the control group, cardiorespiratory fitness increased in the aerobic and combined exercise groups but not in the resistance exercise group (**Table 3**). The mean increase in the aerobic exercise group was greater than that in the resistance exercise group (3.9 [3.0] vs 1.1 [3.3] mL/kg/min [$P = .007$]), but not in the combined exercise group (3.9 [3.0] vs 3.7 [4.4] mL/kg/min

[$P = .99$]). Muscular strength measures increased independently of exercise in the resistance exercise and combined exercise groups (**Table 3**). Compared with resistance exercise, total exercise-induced energy expenditure was greater within the aerobic exercise and combined exercise groups, but the aerobic and combined exercise groups did not differ from each other (mean [SD], 30 699 [9129] vs 27 764 [7000] kcal [$P = .49$]) (**Table 3**). There were no between-group differences for adherence to the recommended calorie intake targets (**Table 3**).

PRIMARY OUTCOME ANALYSES

Compared with the control group, insulin resistance improved in the aerobic exercise and combined exercise groups, whereas insulin resistance did not change in the resistance exercise group (**Table 4**). The improvement in insulin resistance in response to combined exercise was greater than the improvement in response to resistance exercise (9.22 [1.29] vs 1.84 [1.28] mg/mL/ μ IU per kilogram of skeletal muscle per minute \times 100 [$P < .001$]), but not aerobic exercise (9.22 [1.29] vs 6.51 [1.27] mg/mL/ μ IU per kilogram of skeletal muscle per minute \times 100 [$P = .46$]) (**Figure 2**).

Compared with the control group, functional limitation improved significantly in all exercise groups independent of the test (**Table 4**). Improvement within the combined exercise group was greater than that in the aerobic exercise group (0.52 [0.10] vs -0.01 [0.10] standard units, z score [$P = .003$]), but not the resistance exercise group.

Table 3. Changes in Muscle Strength, Cardiorespiratory Fitness, Energy Expenditure, and Energy Intake in Study Completers After 6 Months^a

Characteristic	Study Group, Mean (SD)			
	Control (n=24)	Resistance Exercise (n=30)	Aerobic Exercise (n=30)	Combined Exercise (n=33)
Muscle strength measures, kg				
Pectoralis	...	13.6 (13.4) ^b	...	15.7 (10.5) ^b
Shoulder abductors	...	20.8 (17.5) ^b	...	20.4 (12.5) ^b
Lateralis	...	14.0 (7.6) ^b	...	15.7 (14.6) ^b
Elbow extensors	...	27.0 (27.6) ^b	...	34.7 (28.8) ^b
Elbow flexors	...	14.8 (11.9) ^b	...	11.5 (10.5) ^b
Knee extensors	...	29.1 (19.5) ^b	...	28.7 (21.0) ^b
Knee flexors	...	26.7 (31.3) ^b	...	27.3 (32.5) ^b
Cardiorespiratory fitness				
Peak $\dot{V}O_2$, L/min	-0.10 (0.25)	0.05 (0.26)	0.25 (0.22) ^{c,d}	0.23 (0.35) ^{c,d}
Peak $\dot{V}O_2$, mL/kg/min	-1.1 (2.9)	1.1 (3.3)	3.9 (3.0) ^{c,d}	3.7 (4.4) ^{c,d}
Energy expenditure				
Aerobic exercise, kcals/1000	30.7 (9.1)	20.5 (5.0) ^e
Resistance exercise, kcals/1000	...	6.6 (2.3)	...	7.2 (2.2)
Total exercise, kcals/1000	...	6.6 (2.3)	30.7 (9.1) ^d	27.8 (7.0) ^d
Energy intake, kcal/d ^f	-28.1 (122.6)	-51.9 (130.7)	-6.9 (136.8)	-50.6 (120.0)

Abbreviations: $\dot{V}O_2$, oxygen consumption per unit of time; ellipses, not applicable.

^aValues were derived from subjects with complete preintervention and postintervention data. Muscular strength increase was calculated by subtracting the weight lifted in the fourth week from the weight lifted in the final week of the intervention.

^bIndicates significant ($P < .001$) strength improvements from weeks 4 to 24, as determined by paired t test.

^cIndicates pairwise group comparisons, using analysis of variance (ANOVA) with Tukey studentized range tests adjusted for multiple comparisons, with statistically significant differences ($P < .05$) compared with the control group.

^dIndicates pairwise group comparisons, using ANOVA with Tukey studentized range tests adjusted for multiple comparisons, with statistically significant differences ($P < .05$) compared with the resistance exercise group.

^eIndicates pairwise group comparisons, using ANOVA with Tukey studentized range tests adjusted for multiple comparisons, with statistically significant differences ($P < .05$) compared with the aerobic exercise group.

^fAnalyzed on a subset of 84 completers (20 in the control group, 21 in the resistance exercise group, 22 in the aerobic exercise group, and 21 in the combined exercise group). Change data are shown as the difference between recorded calorie consumption and the prescribed maintenance target established under stable weight conditions.

The improvement in functional limitation in the resistance exercise group was not different from that in the aerobic exercise group independent of the test (Table 4).

SECONDARY OUTCOME ANALYSES

Total fat decreased in the aerobic and combined exercise groups compared with the resistance exercise and control groups, but the aerobic and combined exercise groups did not differ from each other (Table 4 and **Figure 3**). Compared with the control group, abdominal and visceral fat decreased in the aerobic exercise (-0.84 [0.13] vs -0.05 [0.12] and -0.43 [0.08] vs -0.02 [0.06] kg, respectively [both $P < .001$]) and the combined exercise groups (-0.76 [0.10] vs -0.05 [0.12] and -0.35 [0.05] vs -0.02 [0.06] kg, respectively [both $P < .001$]). Total, abdominal, and visceral fat did not change significantly in the resistance exercise group.

Skeletal muscle mass increased within the resistance exercise and combined exercise groups compared with the aerobic exercise and control groups, but the resistance and combined exercise groups did not differ from each other (Table 4 and Figure 3). Skeletal muscle mass did not change in the aerobic exercise group. The ratio of fat to skeletal muscle mass decreased within all exercise groups compared with the control group, but the decrease was greater in the combined exercise group than in the resistance exercise group (-0.19 [0.02] vs -0.12

[0.01] [$P < .05$]) or the aerobic exercise group (-0.19 [0.02] vs -0.13 [0.02] [$P < .05$]). The decrease in the ratio of fat to skeletal muscle mass was not different between the resistance and aerobic exercise groups (Table 4).

Figure 4 depicts the relationship between changes in functional limitation and changes in skeletal muscle and total or abdominal fat by subdividing the subjects with complete data ($n = 117$) according to change tertiles for total skeletal muscle and total or abdominal fat. Skeletal muscle and total or abdominal fat change tertiles were independent predictors of improvement in functional limitation. For a given change in total or abdominal fat, the improvement in functional limitation increased when moving from low to high tertiles of muscle gain. Similarly, for a given change in skeletal muscle, the improvement in functional limitation increased when moving from low to high tertiles of total or abdominal fat loss.

COMMENT

The primary finding of this randomized controlled trial is that the combination of resistance and aerobic exercise is the optimal exercise strategy for simultaneous improvement of insulin resistance and functional limitation in older men and women. That these observations were obtained in response to 90 minutes of moderate-intensity aerobic exercise combined with 60 minutes of resistance exercise

Table 4. Change in Primary and Secondary Outcome Variables

Characteristic	Study Group, Mean (SE) ^a			
	Control (n=24/ITT=28)	Resistance Exercise (n=30/ITT=36)	Aerobic Exercise (n=30/ITT=37)	Combined Exercise (n=33/ITT=35)
Anthropometric				
Body weight, kg	0.28 (0.37)	-0.64 (0.37)	-2.77 (0.33) ^{b,c}	-2.31 (0.33) ^{b,c}
BMI	0.10 (0.13)	-0.26 (0.12)	-0.96 (0.12) ^{b,c}	-0.84 (0.12) ^{b,c}
Waist circumference, cm	-0.28 (0.53)	-3.18 (0.49) ^b	-5.08 (0.46) ^{b,c}	-4.61 (0.47) ^b
MRI				
Skeletal muscle, kg	-0.01 (0.18)	0.97 (0.20) ^{b,d}	-0.06 (0.19)	0.62 (0.15) ^{b,d}
Upper body muscle, kg	-0.07 (0.11)	0.61 (0.16) ^{b,d}	-0.31 (0.11)	0.38 (0.09) ^{b,d}
Lower body muscle, kg	0.05 (0.11)	0.39 (0.12)	0.24 (0.12)	0.24 (0.10)
Total fat, kg	-0.52 (0.38)	-1.56 (0.36)	-3.03 (0.39) ^{b,c}	-3.38 (0.34) ^{b,c}
Total abdominal fat, kg	-0.05 (0.12)	-0.42 (0.11)	-0.84 (0.13) ^b	-0.76 (0.10) ^b
Visceral fat, kg	0.02 (0.06)	-0.21 (0.06)	-0.43 (0.08) ^b	-0.35 (0.05) ^b
Abdominal subcutaneous fat, kg	-0.04 (0.07)	-0.21 (0.07)	-0.40 (0.07) ^b	-0.40 (0.06) ^b
Fat to muscle ratio	-0.02 (0.02)	-0.12 (0.01) ^b	-0.13 (0.02) ^b	-0.19 (0.02) ^{b,d}
Metabolic				
Fasting insulin level, $\mu\text{U/mL}$	-0.29 (0.63)	-0.97 (0.57)	-1.43 (0.63)	-1.49 (0.53)
Insulin resistance, M/I	0.29 (1.59)	1.84 (1.29)	6.51 (1.27) ^{b,c}	9.22 (1.33) ^{b,c}
Functional limitation^e				
No. of chair stands	0.36 (0.56)	4.3 (0.56) ^b	4.00 (0.50) ^b	5.89 (0.52) ^{b,d}
No. of arm curls	0.15 (0.84)	6.2 (0.79) ^b	5.11 (0.67) ^b	7.85 (0.69) ^{b,d}
2-min step test, No. of steps	1.77 (2.35)	19.58 (2.34) ^b	17.00 (1.99) ^b	26.88 (2.02) ^{b,d}
8-ft up-and-go, s	-0.05 (0.08)	-0.56 (0.08) ^b	-0.45 (0.07) ^b	-0.60 (0.07) ^b
Combined (all 4 tests) improvement, z score	-1.01 (0.12)	0.17 (0.12) ^b	-0.01 (0.10) ^b	0.52 (0.10) ^{b,d}

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ITT, intent-to-treat; M/I, rate of glucose uptake per unit of insulin per kilogram of skeletal muscle per minute $\times 100$; MRI, magnetic resonance imaging; $\text{VO}_{2\text{max}}$, maximum oxygen consumption.

SI conversion factor: To convert insulin to picomoles per liter, multiply by 6.945.

^aAdjusted for baseline value, age, and sex. Pairwise comparisons among groups were tested for statistical significance using Tukey studentized range tests.

^bSignificant preintervention vs postintervention treatment differences compared with the control group ($P < .05$).

^cSignificant preintervention vs postintervention treatment differences compared with the resistance exercise group ($P < .05$).

^dSignificant preintervention vs postintervention treatment differences compared with the aerobic exercise group ($P < .05$).

^eTests are described in the "Measurement of Functional Limitation and Cardiorespiratory Fitness" subsection of the "Methods" section.

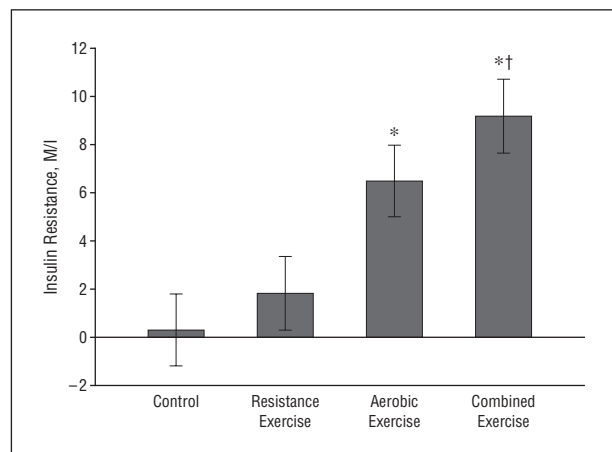


Figure 2. Absolute improvement in insulin resistance for each intervention group. Combined exercise indicates a combination of resistance and aerobic exercise. Data represent least squares means (SEs) adjusted for age, sex, and baseline value and are expressed as M/I (the rate of glucose uptake per unit of insulin per kilogram of skeletal muscle per minute $\times 100$). Pairwise group comparisons using Tukey studentized range tests adjusted for multiple comparisons indicate statistical differences. * $P < .05$ vs the control group. † $P < .05$ vs the resistance exercise group.

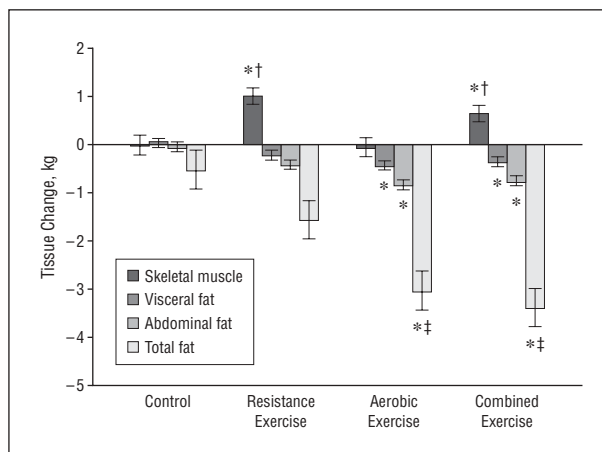


Figure 3. Absolute change in total, abdominal, and visceral fat and in skeletal muscle for each intervention group. Combined exercise indicates a combination of resistance and aerobic exercise. Data represent least squares means (limit lines are standard error) adjusted for age, sex, and baseline value. Pairwise group comparisons using Tukey studentized range tests adjusted for multiple comparisons indicate statistical differences. * $P < .05$ vs the control group. † $P < .05$ vs the aerobic exercise group. ‡ $P < .05$ vs the resistance exercise group.

performed across 3 days each week is promising and suggests that substantial improvement in overall health through effective management of risk factors for disease and disability can be achieved in a pragmatic manner. These ob-

servations lend empirical support to the recently revised public health guidelines for physical activity in older adults endorsed by the American Heart Association and the American College of Sports Medicine.⁷

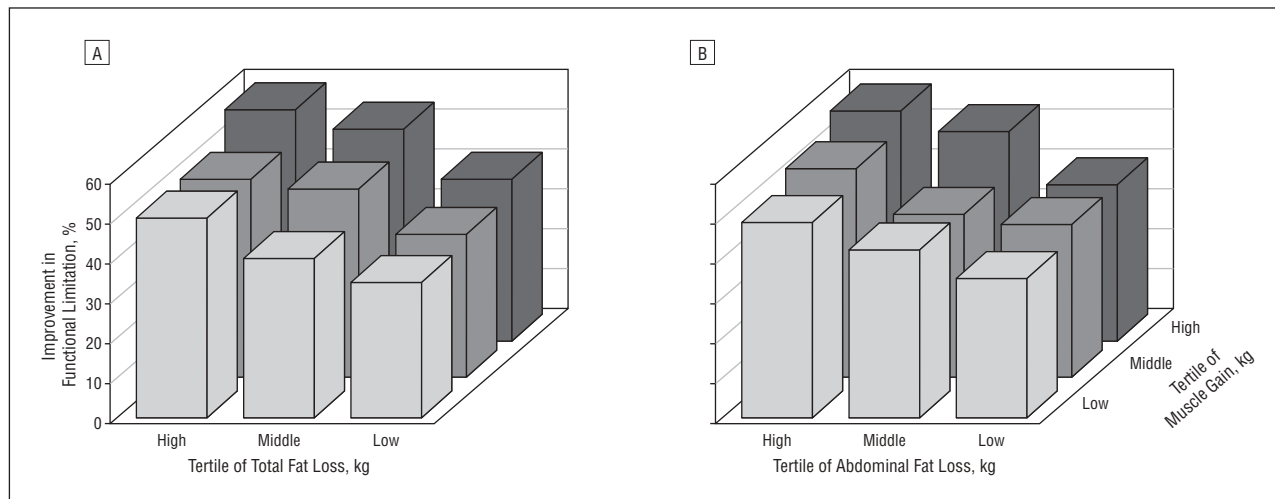


Figure 4. Percentage of improvement in functional limitation by tertiles of fat loss and muscle gain. Percentage improvement in functional limitation according to tertiles of skeletal muscle and total fat loss (A) and abdominal fat loss (B). Tertiles of fat loss (total and abdominal) and skeletal muscle gain were independent predictors of improvement in functional limitation ($P \leq .001$ for trend).

Although our findings demonstrate that the combination of resistance and aerobic exercise is the optimal exercise strategy for simultaneous improvement of insulin resistance and functional limitation, considerable improvement in both risk factors was observed in response to aerobic exercise alone. Combined with the observation that cardiorespiratory fitness, a significant predictor of mortality risk in older adults,²⁸ was substantially increased in the aerobic and combined exercise groups, it is apparent that either exercise strategy is associated with a marked improvement in health-related quality of life in older adults. These findings provide treatment options for clinicians who seek lifestyle-based strategies for simultaneously reducing the risk of disease and disability in older men and women.

To our knowledge, this is the first randomized trial to investigate the effects of combined aerobic and resistance exercise compared with either modality alone on insulin resistance in nondiabetic older subjects. The observed improvement within the aerobic exercise group was impressive (31%) and similar to corresponding improvements in insulin resistance observed in response to aerobic exercise in younger adults.²¹ This finding extends the observations of Dengel et al,²⁹ who reported that 10 months of aerobic exercise was associated with a 22% increase in insulin sensitivity in 10 older men compared with controls, and Frank et al,³⁰ who showed significant improvement in homeostatic assessment model algorithm-measured insulin action in 87 older women who performed moderate-intensity aerobic exercise for 1 year. The improvement in insulin resistance within the combined exercise group, although substantial (43%), was not greater than that within the aerobic exercise group. This finding was not surprising given that the improvement in insulin resistance within the resistance exercise group did not reach statistical significance. This agrees with Hersey et al,³¹ who conducted a 6-month randomized controlled trial in 52 older adults and reported that aerobic but not resistance exercise was associated with decreases in fasting insulin and glucose tolerance compared with control conditions. Thus, despite the re-

peated observation that resistance exercise alone is associated with improvements in insulin action³² and glycemic control^{33,34} in older diabetic subjects, the utility of this modality to improve insulin resistance in nondiabetic older adults is not convincing.

The negative energy balance induced within the aerobic and combined exercise groups was not different, and thus the reduction in abdominal and visceral fat was not different. Because reducing abdominal and visceral fat is a primary conduit by which exercise improves insulin resistance,^{15,35} this at least partially explains why the improvement in insulin resistance did not differ between these 2 groups. These observations underscore the importance of reducing abdominal and visceral fat if exercise-based strategies are to effectively manage insulin resistance in the elderly. Accordingly, given the relatively low energy expenditure associated with resistance exercise, significant and sustained reduction of abdominal fat in older adults may require the simultaneous prescription of a calorie-reduced diet.

Our study provides evidence that functional limitation is substantively improved in response to resistance or aerobic exercise and that the combination of the 2 modalities provides additional improvement compared with aerobic exercise alone. These results are consistent with those of Wood et al,³⁶ who studied 36 elderly subjects and reported that 12 weeks of resistance or aerobic exercise was associated with similar improvements in functional limitation compared with controls and that the 2 modalities combined may provide additional improvement compared with either modality alone. Changes in skeletal muscle and fat mass in response to intervention may provide a partial explanation for our findings. Evidence from cross-sectional studies suggest that, in older adults, the ratio of lean mass to fat mass is a stronger predictor of functional limitations³⁷ and frailty³⁸ than fat mass or lean mass alone. Thus, it is the relative, not the absolute, amount of lean mass that best predicts functional limitation. Our results extend these observations because the greatest change in the ratio of fat to skeletal muscle was observed in the combined exercise group. On

the other hand, because the increase in relative skeletal muscle mass in response to combined exercise was greater than that in response to resistance exercise, despite similar improvement in functional limitation, alternative explanations must be considered.

The tests of functional limitation we used are designed for gauging improvement in muscular strength and aerobic capacity.²² Although it could be argued that inclusion of the 6-minute walk test instead of the 2-minute step test in our test battery may have helped to realize the potential benefit of aerobic exercise for improving functional limitation, Rikli and Jones²² report that the 6-minute walk test and the 2-minute step test relate to criterion measures of aerobic capacity by a similar magnitude. Indeed, in our study the association between cardiorespiratory fitness and the 2-minute step test was quite strong before ($R=0.62$ [$P<.001$]) and after ($R=0.56$ [$P<.001$]) the intervention. Thus, we do not have a ready explanation for why improvement in functional limitation in response to combined exercise was not greater than that in response to resistance exercise. Nevertheless, given the observation that aerobic exercise attenuates disability and maintains independent living in older adults,³⁹ simultaneous improvement in cardiorespiratory fitness and functional limitation in response to exercise may be the optimal measure for establishing the utility of lifestyle-based strategies to improve functional limitation and attenuate disability risk in older adults.

Our findings counter the position that caloric restriction needs to be a principal component of exercise strategies designed to reduce abdominal obesity and associated risk factors for disease and disability in older adults.⁴⁰ Indeed, although the 3% weight loss observed in the aerobic exercise or the combined exercise group is considered modest, abdominal and visceral fat were reduced by approximately 13% and total fat by 10%, and the relative amount of skeletal muscle mass increased in both groups. These observations suggest that the goal to reduce body weight by 10% to 15% commonly recommended for younger obese adults^{18,41} may not be required to observe significant reduction in abdominal obesity and associated risk factors among the elderly. This observation has implications for older adults who may find achieving substantial weight loss difficult because changing lifelong habits of nutrition and exercise may cause distress and anxiety.⁴²

Our findings suggest that as little as 90 minutes of aerobic exercise combined with 60 minutes of resistance exercise performed across 3 days each week (eg, the same 3 days) is associated with considerable health benefit. Indeed, combined exercise was associated with marked improvement in insulin resistance and functional limitation, reduction of abdominal and visceral fat, and an increase in relative and absolute skeletal muscle mass. Combined with the 18% improvement in cardiorespiratory fitness, it is difficult to imagine a more effective strategy for improving overall health in the elderly.

The strengths of our study include excellent adherence to the exercise regimens and a low dropout rate, which attests to the feasibility of the exercise performed. Additional strengths include the tight control of all exercise sessions performed under direct supervision with automated monitoring of heart rate during each

aerobic exercise session and ensurance of good form during each resistance exercise session. Monitoring of dietary intake for each participant helped to ensure that the composition and caloric intake of the prescribed diet was maintained throughout the intervention and, consequently, that the treatment effects were attributable to the exercise modality. That aerobic exercise frequency was reduced from 5 to 3 days a week when combined with resistance exercise enhanced the palatability of the combined intervention. This approach ensured that the total energy expenditure or dose of exercise performed between the aerobic exercise and combined exercise groups was not different, thereby allowing us to isolate the effects of exercise modality. The efficacy of the exercise modalities, demonstrated under strictly controlled conditions, sets the stage for the development of effectiveness studies designed to determine the extent to which our findings can be generalized.

Limitations include the study of a relatively homogeneous sample of abdominally obese, white men and women, and thus we do not know whether our findings apply to other elderly men and women. However, because 62% and 74% of US elderly women and men, respectively, are abdominally obese, it is likely that a sizeable proportion of the older adult population would benefit from the exercise modalities studied. Our study was conducted in ideal circumstances with motivated men and women who were supervised during all exercise sessions and were encouraged to strictly follow their individualized diet plans.

In conclusion, the combination of resistance and aerobic exercise combined with a balanced diet was the optimal strategy for the simultaneous improvement of insulin resistance and functional limitation in previously sedentary, abdominally obese older men and women. Health care providers are encouraged to promote performance of resistance and aerobic exercise by older adults for simultaneous reduction of insulin resistance and functional limitations, established risk factors for disease and disability.

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