Research Article

Effects of Caloric Restriction on Cardiorespiratory Fitness, Fatigue, and Disability Responses to Aerobic Exercise in Older Adults With Obesity: A Randomized Controlled Trial

Barbara J. Nicklas, PhD,^{1,2} Tina E. Brinkley, PhD,¹ Denise K. Houston, PhD,¹ Mary F. Lyles, MD,¹ Christina E. Hugenschmidt, PhD,¹ Kristen M. Beavers, PhD,² and Xiaoyan Leng, PhD³

¹Section on Gerontology and Geriatric Medicine, Department of Internal Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina. ²Department of Health and Exercise Science, Wake Forest University, Winston-Salem, North Carolina. ³Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, North Carolina.

Address correspondence to: Barbara J. Nicklas, PhD, Section on Gerontology and Geriatric Medicine, Department of Internal Medicine, Wake Forest School of Medicine, Winston-Salem, NC 27157. E-mail: bnicklas@wakehealth.edu

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Abstract

Background: Obesity compounds aging-related declines in cardiorespiratory fitness, with accompanying fatigue and disability. This study determined the effects of two different levels of caloric restriction (CR) during aerobic training on cardiorespiratory fitness, fatigue, physical function, and cardiometabolic risk.

Methods: The INFINITE study was a 20-week randomized trial in 180 older (65–79 years) men and women with obesity (body mass index = 30–45 kg/m²). Participants were randomly assigned to (i) aerobic training (EX; treadmill 4 days/wk for 30 minutes at 65%–70% of heart rate reserve), (ii) EX with moderate (–250 kcal/d) CR (EX + Mod-CR), or (iii) EX with more intensive (–600 kcal/d) CR (EX + High-CR). Cardiorespiratory fitness (peak aerobic capacity, VO₂ peak, primary outcome) was determined during a graded exercise test.

Results: One hundred and fifty-five participants returned for 20-week data collection (87% retention). VO₂ peak increased by 7.7% with EX, by 13.8% with EX + Mod-CR, and by 16.0% with EX + High-CR, and there was a significant treatment effect (EX + High-CR = 21.5 mL/kg/min, 95% confidence interval = 19.8–23.2; EX + Mod-CR = 21.2 mL/kg/min, 95% confidence interval = 19.4–23.0; EX = 20.1 mL/kg/min, 95% confidence interval = 18.4–21.9). Both CR groups exhibited significantly greater improvement in self-reported fatigue and disability and in glucose control, compared with EX.

Conclusion: Combining aerobic exercise with even moderate CR is more efficacious for improving cardiorespiratory fitness, fatigue and disability, and glucose control than exercise alone and is as effective as higher-dose CR.

Keywords: Caloric restriction, Clinical trials, Exercise, Functional performance

Nearly 40% of adults aged more than 65 years are classified as obese according to body mass index criteria (1,2). An adverse consequence of obesity in this age group is an extremely low cardiorespiratory fitness (CRF) (3), which is associated with compromised physical function, greater fatigue, and earlier mobility disability (4–8). Although declines in CRF are inherent to aging, gains in fat mass with age can compound this decline (9,10). Excess adiposity predisposes to low CRF through both central and peripheral mechanisms and through biomechanical and biochemical factors (3). Therefore, the ability to consume, deliver, and metabolize oxygen

needed to perform specific tasks is particularly compromised in this population.

Presently, regular aerobic exercise is the only therapy known to consistently improve CRF and delay the onset of disability (6,11–13). However, the efficacy of exercise for enhancing CRF and other outcomes may be compromised in those with obesity (14–17). The current public health exercise recommendation (18)—without concurrent reductions in energy intake—is not of sufficient volume to elicit substantial weight or fat loss, especially in older adults. Thus, prescribing caloric restriction (CR) may be necessary to optimize the

benefits of exercise. Presently, CR—even in conjunction with exercise—is not widely prescribed to older adults due to the uncertainty of whether any functional and metabolic benefits outweigh the risks, including nutritional concerns and loss of muscle mass and strength (19). In addition, current obesity treatment guidelines recommend prescribing a reduced calorie diet (20), but the most efficacious level of energy deficit to elicit risk factor improvements, and whether there is a dose–response effect of different intensities of CR, are not known.

This study determined the effects of adding no CR, moderate CR (–250 kcal/day), or more intensive CR (–600 kcal/day) on the magnitude of improvement in the primary outcome of CRF in response to aerobic training in older adults with obesity. We hypothesized that the more intensive CR group would experience the greatest improvement in CRF, followed by the moderate CR group, and then the exercise only group. Secondary goals were to examine the effects of both CR doses on fatigue, disability, body composition, physical function, and cardiometabolic risk.

Methods

Trial Design and Participants

This study (INFINITE) was a 20-week, three-group, single-blind, randomized trial (Trial Registration: NCT01048736). The study was approved by the WFSM Institutional Review Board, and participants provided written informed consent. Men and women were enrolled based on these criteria: (i) age 65–79 years, (ii) sedentary, (iii) body mass index = 30–45 kg/m², (iv) nonsmoking for more than 1 year, (v) less than 5% weight change in past 6 months, and (vi) no insulin-dependent diabetes, osteoporosis, cognitive impairment (Mini-Mental State Exam Score < 24), or clinical evidence of depression, heart disease, cancer, liver, renal, or chronic pulmonary disease, uncontrolled hypertension, major physical impairment, or contraindication for exercise or weight loss.

A total of 1,318 participants were screened by phone (Figure 1); 239 participants were invited for a clinical screening. Of these, 180 participants met all entry criteria and were tested on study outcomes by blinded assessors prior to being randomly assigned to either (i)

aerobic training (EX only), (ii) EX with moderate (–250 kcal/d deficit) CR (EX + Mod-CR), or (iii) EX with intensive (–600 kcal/d deficit) CR (EX + High-CR).

Interventions

Aerobic training

All participants underwent supervised aerobic training 4 days/wk on treadmills according to current recommendations (18). Blood pressure and heart rate (HR) were measured before each session and participants warmed up by walking at a slow pace. Duration progressed from 15 to 20 minutes at 50% HR reserve the first week to 30 minutes at 65%–70% HR reserve by the end of the sixth week. At least two HR readings were taken during each session and used to monitor compliance to intensity; speed and grade were adjusted by study staff based on these HR values. HR readings, speed, grade, exercise duration, and the amount of energy expended (American College of Sports Medicine metabolic calculations using weekly measured body weight) were recorded for each session.

Caloric restriction

Participants assigned to EX were instructed to maintain their regular dietary intake. Those assigned to EX + Mod-CR or EX + High-CR were provided with two meals/day (lunch and dinner) prepared by a metabolic kitchen and picked up three times per week. The diet contained greater than 30% calories from fat and at least 0.8 g protein/kg body weight. Participants were allowed two “ad lib” days per month. They met weekly with a registered dietitian to facilitate compliance and were provided menus for their breakfast, which were consistent with the prescribed calorie level. They were instructed to consume only the food given to them or approved from the menu. Participants were asked to keep a diet log which was reviewed by the registered dietitian to verify compliance. Body weight was measured weekly.

The individual calorie level assigned was derived from subtracting 250 kcal (Mod-CR) or 600 kcal (High-CR) from estimated daily energy needs for weight maintenance. Energy needs were calculated from the direct measurement of resting metabolic rate (RMR), applying an activity factor based on daily activities (1.2 for sedentary, 1.3 for lightly active). No woman was provided with less than 1,100 kcal/day and no man less than 1,300 kcal/day.

Outcomes

All assessments took place in the WFSM Geriatric Research Center by examiners blinded to participant treatment assignment. The pre-specified primary outcome of *peak aerobic capacity* (VO_2 peak) was determined on a treadmill during an exercise test to exhaustion. A ramp protocol was used—the speed was set at a constant rate according to individual ability, and the incline increased at small intervals throughout the test. Ventilatory and gas exchange responses were measured on a breath-by-breath basis (MGC Diagnostics, St. Paul, MN). All participants reached a respiratory exchange ratio greater than 1.10 during their initial test; thus, none were retested to obtain a valid measure of VO_2 peak.

Body composition

Whole body fat mass, lean mass, and percent fat were measured by dual-energy X-ray absorptiometry (Hologic Delphi QDR, Bedford, MA). RMR was measured after an overnight fast by indirect calorimetry (MGC Diagnostics) (21). *Lipid and glucose risk factors* were measured in blood samples drawn after an overnight fast by a

Figure 1. CONSORT diagram. BMI = body mass index; EX = aerobic training; EX + Mod-CR = EX with moderate caloric restriction; EX + High-CR = EX with more intensive caloric restriction.

clinical laboratory (LabCorp, Burlington, NC). Two-hour postprandial glucose and insulin were measured in samples drawn after a 75-g glucose ingestion. The homeostasis model assessment (HOMA2-IR) score was calculated (22).

Physical function/disability/fatigue

Lower-extremity function was assessed with the Short Physical Performance Battery (SPPB) involving a standing balance test, 4-m gait speed, and repeated chair rises (23). Walking mobility was measured using a 400-m walk test for time. Self-reported disability was measured using a 19-item questionnaire that asks about perceived difficulties in activities of daily living during the last month (24); higher scores indicate greater disability. Fatigue was assessed using the Vitality domain on the Medical Outcomes Study 36-item short-form (SF-36) measure (25), which consists of an average of four items assessing vitality/fatigue levels in the past month on a 6-point scale. Higher scores indicate higher vitality or less fatigue.

Statistical Analysis

Analysis of covariance, using SAS 9.4 (Cary, NC), was used to compare treatment effects, adjusting for age, gender, and baseline value. Postintervention least square means and 95% confidence intervals (CI) were estimated. Pairwise comparisons of postintervention least square means were also based on the analysis of covariance models. Paired *t* tests were used to assess change within groups. Due to a malfunction with the oxygen analyzer during the study, VO₂ peak values were missing for 13 participants at baseline (EX = 5, EX + Mod-CR = 4, EX + High-CR = 4) and 12 participants at follow-up (EX = 3, EX + Mod-CR = 4, EX + High-CR = 5); therefore, multiple imputations (*m* = 5) were used to impute these values. Because the pattern of missingness was arbitrary, fully conditional specification

methods using regression were applied (26). Imputation regression was based on age, gender, baseline (weight, height, VO₂ peak, treadmill speed, and elevation), and postintervention (VO₂ peak, treadmill speed and elevation, and lean mass) measures, respectively. All analyses for VO₂ peak values were repeated for each of the '*m*' imputed datasets, and the results were then pooled to get the mean, variance, and confidence interval (27). All tests were two sided at a significance level of .05.

Results

Baseline Characteristics and Retention

Table 1 shows the mean age was 69.2 ± 3.5 years, three fourths of the study sample were women and reported their race as white, and all could be classified as obese. A total of 155 (87% retention) returned for final data collection (Figure 1). Baseline characteristics of those who dropped out were not different from those who completed. There were eight minor intervention-related adverse events (all musculoskeletal complaints); these included one in EX, four in EX + Mod-CR, and three in EX + High-CR. All returned to intervention, and exercise and CR were extended if needed to complete the 20 weeks (for 1–2 weeks for three participants and 6 weeks for one participant).

Intervention Adherence

Adherence to the exercise prescription and the number of calories expended per session did not differ by group (Table 2). For the CR intervention, we implemented a 1,100 kcal/day minimum for women and a 1,300 kcal/day minimum for men. Thus, for individuals with lower calorie needs (eg, lower RMR), the provided diets did not reach the planned level of CR. In EX + Mod-CR,

Table 1. Baseline Demographic and Health Characteristics by Intervention Group

	EX (N = 61)	EX + Mod-CR (N = 60)	EX + High-CR (N = 59)
Age, y	69.1 (3.7)	68.8 (3.1)	69.6 (3.8)
Female, N (%)	46 (75%)	45 (75%)	45 (76.3%)
White, N (%)	46 (75%)	45 (75%)	40 (67.8%)
Education (> high school)	49 (80%)	49 (77%)	48 (81%)
MMSE score	28.1 (1.6)	28.0 (1.7)	27.7 (1.8)
Height, cm	165.8 (9.1)	163.3 (9.3)	164.6 (8.4)
Body mass, kg	95.2 (13.6)	92.4 (12.2)	93.4 (13.9)
Body mass index, kg/m ²	34.6 (3.1)	34.7 (3.7)	34.4 (3.7)
Percent body fat, %	44.5 (5.1)	44.6 (6.7)	43.0 (6.5)
Waist to hip ratio	0.89 (0.09)	0.87 (0.10)	0.89 (0.09)
Resting seated blood pressure			
Systolic, mmHg	134 (14)	137 (18)	137 (19)
Diastolic, mmHg	74 (10)	75 (10)	75 (10)
Self-reported comorbidity, N (%)			
Hypertension	36 (59%)	35 (58%)	37 (63%)
Noninsulin-treated diabetes	12 (20%)	5 (8%)	13 (22%)
Sleep apnea	19 (31%)	25 (42%)	20 (34%)
Osteoarthritis	46 (75%)	42 (70%)	39 (66%)
Osteopenia	10 (16%)	8 (13%)	7 (12%)
Medication use, N (%)			
Antihypertensive	41 (67%)	43 (72%)	39 (66%)
Cholesterol lowering	27 (44%)	20 (33%)	32 (54%)
Glucose control	11 (18%)	4 (7%)	13 (22%)
Antidepressant/mood	21 (34%)	22 (37%)	15 (25%)

Notes: EX = aerobic training; EX + Mod-CR = EX with moderate caloric restriction; EX + High-CR = EX with more intensive caloric restriction; MMSE = Mini-Mental State Exam. Values are mean (SD) or N (%).

Table 2. Study Intervention Process and Adherence Data

	EX (N = 44)	EX + Mod-CR (N = 58)	EX + High-CR (N = 53)
Exercise intervention			
Prescribed intensity (70% of HR reserve, beats/min)	120 (9)	118 (10)	116 (10)
Prescribed duration (min/day)	40	40	40
Prescribed frequency (day/wk)	4	4	4
Actual exercise performed			
Intensity level (HR at midpoint, beats/min)	119 (9)	117 (11)	116 (9)
Percent of days $\geq$ prescribed HR (%)	75.7 (24.8)	75.1 (25.1)	72.6 (25.2)
Duration (min/day)	36.8 (2.3)	37.4 (1.7)	37.5 (1.0)
Frequency (day/wk)	3.31 (0.68)	3.50 (0.47)	3.55 (0.38)
Percent attendance (% of possible sessions)	85.8 (16.3)	89.9 (11.5)	91.2 (8.6)
Exercise volume (mean kcal/session)	221 (76)	235 (66)	225 (81)
Dietary intervention			
Baseline weight maintenance calorie level (kcal/day) ^a		1,750 (354)	1,776 (429)
Prescribed calorie level (kcal/day)		1,512 (334)	1,283 (240)
Absolute caloric reduction (kcal/day) ^b		238 (50)	493 (242)
Relative caloric reduction (%) ^b		13.8 (3.7)	26.6 (7.9)
Recorded dietary compliance (%) ^c		99.2 (4.8)	100.2 (4.1)

Notes: EX = aerobic training; EX + Mod-CR = EX with moderate caloric restriction; EX + High-CR = EX with more intensive caloric restriction; HR = heart rate. Values are mean (SD).

^aEstimated from measurement of resting metabolic rate times activity factor of 1.2–1.3 (sedentary/light activity). ^bAbsolute and relative daily caloric intake reduction from weight maintenance level. ^cReported deviation from provided kilocalorie level is calculated from daily food logs.

nine participants were prescribed less than the 250 kcal/day deficit, and in EX + High-CR, 28 participants were prescribed less than the 600 kcal/day deficit. Nevertheless, there was an approximately twofold greater absolute (weight maintenance minus prescribed calorie level) and relative (percent reduction from weight maintenance calorie level) caloric deficit between EX + Mod-CR and EX + High-CR (Table 2).

Treatment Effects on CRF, Physical Function, and Fatigue Measures

CRF measured as peak oxygen consumption (VO_2 peak, mL/kg/min) increased significantly by 7.7% (95% CI: 4.5% to 10.8%) with EX, by 13.8% (95% CI: 9.7% to 18.0%) with EX + Mod-CR, and by 16.0% (95% CI: 12.0% to 20.0%) with EX + High-CR (Supplementary Table 1). There was a significant treatment effect for CRF—higher postintervention VO_2 peak (adjusted for age, gender, and baseline VO_2 peak) was observed in both CR groups compared with EX (Table 3). There was no difference in postintervention CRF between CR groups.

There were no significant treatment effects on the secondary measures of exercise performance, although peak workload measured in metabolic equivalent of task levels and total exercise time to exhaustion at postintervention tended ($p < .10$) to be higher in the CR groups (Table 3 and Supplementary Table 1). There were no treatment effects on the objective physical function measures (Table 3); all groups showed similar improvements in 400-m walk time and lower extremity function (Supplementary Table 1).

Treatment group differences were observed for the self-report measures of fatigue and disability, with both EX + Mod-CR and EX + High-CR exhibiting greater improvement than EX (Table 3). Within-group analyses showed that only the CR groups reported significantly less disability after treatment. Although all groups reported feeling significantly less fatigued after treatment, the CR groups showed an approximate twofold larger improvement in the SF-36 Vitality score than EX (Supplementary Table 1).

Treatment Effects on Body Mass, Body Composition, and Cardiometabolic Risk Factors

The CR groups lost more body mass than EX (–1.5%, 95% CI: –2.6% to –0.3%); however, the amount of total mass lost was not significantly different between EX + Mod-CR (–8.5%, 95% CI: –9.7% to –7.2%) and EX + High-CR (–9.4%, 95% CI: –10.5% to –8.3%; Table 4 and Supplementary Table 2). Likewise, decreases in body fat mass, lean mass, and percent fat were all greater with CR compared with EX, but did not differ between CR groups (Table 4 and Supplementary Table 2).

There was no treatment effect on RMR (Table 4). However, RMR was unchanged with EX (0.8%, 95% CI: –6.6% to 5.1%), whereas it decreased significantly by 3.6% (95% CI: –7.7% to 0.5%) with EX + Mod-CR and by 5.2% with EX + High-CR (95% CI: –9.0% to –1.4%; Supplementary Table 2).

There were no treatment effects on any of the lipid values (Table 4 and Supplementary Table 2), but both CR groups experienced greater decreases in fasting glucose and insulin and in 2-hour glucose values compared with EX. The 2-hour insulin values tended to be lower in both CR groups compared with EX. The HOMA2-IR score was markedly improved in both CR groups relative to EX, but there were no differences between CR groups.

Discussion

This trial is the first to compare the effects of two levels of CR during aerobic training on CRF, as well as other patient-centered and clinically relevant outcomes, in older adults with obesity. The results showed that either a moderate or more intensive energy deficit during the current exercise recommendation for this population augmented (by nearly twofold) the improvement in peak oxygen uptake, a physiological measure of functional ability. Importantly, disability and fatigue decreased more when either dose of CR was added to exercise, suggesting the improvement in CRF with CR translated into feeling less fatigue and more able to perform daily tasks.

Table 3. Treatment Effects on VO₂ peak and Secondary Exercise and Physical Function Outcomes

	Postintervention LS Means (95% CI)			<i>p</i> Value	Postintervention LS Mean Differences (95% CI)			
	Overall Baseline Mean (<i>SD</i>)	EX (<i>N</i> = 42–44)	EX + Mod-CR (<i>N</i> = 54–58)		EX + High-CR (<i>N</i> = 50–53)	EX + Mod-CR – EX	EX + High-CR – EX + Mod-CR	
Peak exercise outcomes								
VO ₂ peak, mL/kg/min	18.4 (3.3)	20.1 (18.4 to 21.9)	21.2 (19.4 to 23.0)	21.5 (19.8 to 23.2)	.02	1.1 (0.1 to 2.1)*	1.4 (0.4 to 2.4)**	0.3 (–0.8 to 1.3)
VO ₂ peak, mL/min	1,724 (406)	1,891 (1,679 to 2,102)	1,852 (1,646 to 2,058)	1,861 (1,664 to 2,059)	.65	–39 (–119 to 41)	–29 (–112 to 53)	10 (–75 to 94)
Peak MET level	5.1 (0.9)	5.7 (5.4 to 6.0)	6.0 (5.8 to 6.3)	6.1 (5.8 to 6.3)	.09	0.3 (0.0 to 0.7)	0.3 (0.0 to 0.7)	0.0 (–0.3 to 0.3)
Peak RER	1.2 (0.1)	1.1 (1.1 to 1.2)	1.1 (1.1 to 1.2)	1.2 (1.1 to 1.2)	.29	0.0 (0.0 to 0.1)	0.0 (0.0 to 0.1)	0.0 (0.0 to 0.0)
Peak HR, beats/min	142 (13)	141 (138 to 145)	144 (141 to 146)	143 (140 to 146)	.59	2.1 (–2.0 to 6.1)	1.4 (–2.7 to 5.4)	–0.7 (–4.5 to 3.1)
Total exercise time, min	6.1 (1.3)	6.8 (6.4 to 7.2)	7.2 (6.9 to 7.5)	7.3 (7.0 to 7.7)	.08	0.4 (–0.1 to 0.9)	0.5 (0.1 to 1.0)	0.1 (–0.3 to 0.6)
Physical function outcomes								
400-m walk time, s	337 (62)	306 (297 to 316)	302 (293 to 310)	303 (295 to 311)	.72	–5 (–17 to 7)	–3 (–15 to 8)	1 (–10 to 13)
Usual gait speed, m/s	1.0 (0.2)	1.1 (1.0 to 1.1)	1.1 (1.0 to 1.1)	1.1 (1.0 to 1.1)	.55	–0.0 (–0.1 to 0.1)	0.0 (–0.1 to 0.0)	–0.0 (–0.1 to 0.0)
Chair rise time, s	13.1 (3.9)	11.7 (10.9 to 12.4)	11.5 (10.8 to 12.2)	10.6 (9.9 to 11.3)	.07	–0.2 (–1.1 to 0.8)	–1.0 (–2.0 to 0.1)	–0.9 (–1.8 to 0.0)
SPPB (0–12)	10.5 (1.5)	10.9 (10.6 to 11.2)	11.0 (10.7 to 11.3)	10.9 (10.6 to 11.2)	.74	0.1 (–0.3 to 0.6)	0.0 (–0.4 to 0.4)	–0.1 (–0.5 to 0.3)
Self-reported disability	1.4 (0.4)	1.3 (1.2 to 1.4)	1.2 (1.1 to 1.3)	1.2 (1.1 to 1.3)	.04	–0.1 (–0.2 to –0.0)*	–0.1 (–0.2 to –0.0)*	0.0 (–0.1 to 0.1)
SF-36 Vitality score	69.2 (18.8)	74.4 (70.9 to 78.0)	80.0 (76.8 to 82.5)	79.3 (76.0 to 82.5)	.04	5.5 (1.1 to 10.0)*	4.9 (0.3 to 9.4)*	–0.7 (–5.0 to 3.6)

Notes: CI = confidence interval; EX = aerobic training; EX + Mod-CR = EX with moderate caloric restriction; EX + High-CR = EX with more intensive caloric restriction; HR = heart rate; LS = least squares; MET = metabolic equivalent; RER = respiratory exchange ratio; SPPB = Short Physical Performance Battery. Data are LS means for post-treatment values, adjusted for age, gender, and baseline value of each outcome. Self-reported disability: scaled as 1 (usually did with no difficulty) to 5 (unable to do); higher scores indicate greater disability. SF-36 Vitality: scaled as 0 (fatigued) to 100 (energetic); higher scores indicate feeling more energetic/less fatigued. ***p* < .01 and **p* < .05 using analysis of covariance (ANCOVA) to compare treatment effects, adjusting for age, gender, and baseline value (corrected for three comparisons using Bonferroni method).

Table 4. Treatment Effects on Body Mass, Body Composition, and Cardiometabolic Risk Factors

	Overall Baseline Mean (SD)	Postintervention LS Means (95% CI)			p Value	Postintervention LS Mean Differences (95% CI)		
		EX (N = 32-44)	EX + Mod-CR (N = 50-57)	EX + High-CR (N = 36-53)				
						EX + Mod-CR - EX	EX + High-CR - EX	EX + High-CR - EX + Mod-CR
Body mass, kg	94.1 (13.3)	92.2 (90.9 to 93.5)	85.7 (84.6 to 86.9)	84.7 (83.6 to 85.9)	<.001	-6.4 (-8.1 to -4.8)*	-7.4 (-9.1 to -5.8)*	-1.0 (-2.5 to 0.6)
Fat mass, kg	41.4 (7.6)	39.6 (38.6 to 40.6)	35.2 (34.3 to 36.1)	34.3 (33.4 to 35.2)	<.001	-4.4 (-5.6 to -3.1)*	-5.3 (-6.6 to -4.0)*	-0.9 (-2.1 to 0.3)
Lean mass, kg	50.5 (10.0)	50.5 (49.7 to 51.2)	48.7 (48.1 to 49.3)	48.4 (47.7 to 49.1)	<.001	-1.8 (-2.6 to -0.9)*	-2.1 (-2.9 to -1.2)*	-0.3 (-1.1 to 0.5)
Body fat, %	44.1 (6.1)	42.9 (42.1 to 43.7)	40.9 (40.2 to 41.5)	40.4 (39.6 to 41.1)	<.001	-2.0 (-2.9 to -1.1)*	-2.5 (-3.5 to -1.6)*	-0.5 (-1.4 to 0.4)
RMR, kcal/d	1,377 (295)	1,404 (1,348 to 1,461)	1,354 (1,305 to 1,404)	1,358 (1,307 to 1,410)	.31	-50 (-119 to 20)	-46 (-117 to 24)	3.7 (-63 to 71)
Triglycerides, mg/dL	127 (58)	119 (108 to 131)	106 (96 to 116)	112 (102 to 123)	.19	-14 (-28 to 1.1)	-7.1 (-22 to 7.7)	6.4 (-7.5 to 20)
Total C, mg/dL	194 (40)	185 (178 to 191)	174 (168 to 181)	176 (170 to 183)	.06	-10 (-19 to -1.4)	-8.1 (-17 to 0.9)	2.0 (-6.5 to 11)
LDL-C, mg/dL	112 (34)	106 (100 to 112)	100 (95 to 106)	100 (95 to 106)	.30	-5.7 (-14 to 2.2)	-5.5 (-14 to 2.7)	0.2 (-7.5 to 8.0)
HDL-C, mg/dL	57 (16)	56 (53 to 58)	54 (52 to 56)	54 (52 to 56)	.36	-1.8 (-4.6 to 0.9)	-1.7 (-4.5 to 1.1)	0.1 (-2.5 to 2.8)
Glucose, mg/dL	103 (19)	102 (99 to 105)	97 (94 to 100)	96 (94 to 99)	.01	-4.7 (-8.5 to -0.9)*	-5.4 (-9.2 to -1.5)*	-0.7 (-4.3 to 3.0)
Insulin, μ U/mL	18.0 (10.5)	17.3 (15.3 to 19.3)	11.5 (9.7 to 13.3)	12.0 (10.2 to 13.8)	<.001	-5.8 (-8.4 to -3.2)*	-5.3 (-7.8 to -2.7)*	0.5 (-1.9 to 3.0)
HOMA2-IR	2.0 (1.2)	1.9 (1.7 to 2.2)	1.3 (1.1 to 1.5)	1.3 (1.1 to 1.5)	<.001	-0.6 (-0.9 to -0.3)*	-0.6 (-0.9 to -0.3)*	0.0 (-0.2 to 0.3)
2-h glucose, mg/dL ^a	116 (50)	116 (108 to 124)	104 (98 to 111)	99 (91 to 107)	.01	-11.7 (-21.9 to -1.5)*	-16.8 (-27.9 to -5.8)*	-5.1 (-15.1 to 4.8)
2-h insulin, μ U/mL ^a	111 (106)	98 (75 to 121)	83 (63 to 102)	61 (40 to 83)	.07	-15.4 (-44.5 to 13.7)	-36.5 (-67.5 to -5.6)	-21.1 (-49.2 to 6.9)

Notes: CI = confidence interval; EX = aerobic training; EX + Mod-CR = EX with moderate caloric restriction; EX + High-CR = EX with more intensive caloric restriction; HDL-C = high-density lipoprotein cholesterol; HOMA2-IR = homeostatic model assessment of insulin resistance; LDL = low-density lipoprotein cholesterol; LS = least squares; RMR = resting metabolic rate. Data are LS means for post-treatment values, adjusted for age, gender, and baseline value of each outcome.

^aTwo-hour glucose/insulin not conducted in those with diabetes.

**p* < .05 using analysis of covariance (ANCOVA) to compare treatment effects, adjusting for age, gender, and baseline value (corrected for three comparisons using Bonferroni method).

Our study adds to the growing body of literature examining the benefits and risks of prescribing CR for intentional weight loss to older adults. We show that even moderate CR has additive benefits to exercise, which should reduce reluctance to recommend CR to older adults with obesity to augment their exercise efforts. These results are consistent with those from a prior trial in older adults with obesity, which showed that a high level of CR (prescribed 500–750 kcal/d deficit) induced an approximate 10% loss of body mass and improved CRF more than exercise alone (28).

The metabolic cost of specific activities is higher with increased age (29,30), and daily tasks, such as housework and carrying groceries, can require 40%–50% of peak oxygen consumption in older adults (31). Activities with even higher energy requirements, such as stair climbing, are much more difficult for those with a lower VO_2 peak, leading to a cycle of greater fatigue, followed by less movement, and eventual disability. This strongly emphasizes the importance of a higher peak ability to utilize oxygen for maintaining independence. Because a VO_2 peak of less than 18 mL/kg/min is a cut point for distinguishing those with the ability to perform daily activities (32), the baseline VO_2 peak of 18.4 mL/kg/min of participants in this study places them at a tipping point for eventual disability. Thus, the improvement of 2.5–2.8 mL/kg/min observed in the CR groups is particularly relevant to the fatigue and disability levels of these older adults. Interestingly, both CR groups reported about twofold less perceived fatigue and disability, despite not performing better on the laboratory-based assessments of function, relative to the exercise group. The absence of group differences in usual gait speed and SPPB may have been due to a lack of room for much improvement in these measures; however, we were surprised that there were no effects of adding CR to exercise on 400-m walk time.

This study is also the first to show beneficial effects of both levels of CR on glucose metabolism. There is no doubt that CR resulting in weight loss improves glucose tolerance, insulin sensitivity, and lipid profiles in younger individuals, but data from the few prior trials that examined these outcomes in adults greater than 65 years are scarce and inconsistent (19). The Diabetes Prevention Program and the Look AHEAD trials showed a beneficial effect of lifestyle intervention for reducing risk of diabetes and related complications in older adults, but these interventions involved CR and physical activity without a physical activity only comparison group, so the independent effects of CR cannot be distinguished (33,34). Our results showing improved glucose control with higher-dose CR are in agreement with another study using a similar CR dose (500–750 kcal/d deficit) in older individuals (35). Our findings of no effects of CR on total, low-density lipoprotein, or high-density lipoprotein cholesterol in this population confirm the results from another group (35), as well as the results from our prior study of adding CR to resistance training (36).

One of the major strengths of this study was the tight control of the dietary and exercise treatments. Interestingly, despite a twofold difference in both absolute (kcal/day deficit) and relative (% reduction) energy reduction, the two levels of CR did not result in differential weight or fat loss. This finding suggests there may be a threshold level of CR for maximizing weight loss and that a higher-intensity CR may not be necessary or advised. Without being able to account for the dynamic changes in energy balance that occur during active weight loss, it would appear that the moderate-CR group lost more weight than expected, but the reasons for this are unknown. There may have been group differences in reporting errors of energy intake, or other components of energy expenditure, to account for the similar loss of body weight, but research that includes precise measures

of energy balance is needed to determine this. It is also worth considering that, since the mean exercise energy expenditure over the 20 weeks of training was similar between groups, the CR groups may have experienced a slightly greater training workload (~20 kcal differential in training volume over the 40 minutes) given that they were moving less mass during the training sessions.

In conclusion, adding CR during an aerobic exercise program is well tolerated in older, sedentary adults with obesity and potentiates the benefits of their exercise. Even a moderate deficit of ~240 kcal/day is more efficacious for improving CRF, perceptions of fatigue and disability, and glucoregulatory control than exercise alone and is as effective as more intensive CR.

Supplementary Material

Supplementary data is available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

None reported.

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