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Caloric Restriction with or without Exercise: The Fitness vs. Fatness Debate

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Abstract

There is debate over the independent effects of aerobic fitness and body fatness on mortality and disease risks.

PURPOSE—To determine whether a 25% energy deficit that produces equal change in body fatness leads to greater cardiometabolic benefits when aerobic exercise is included.

METHODS—Thirty-six overweight participants (16 males/20 females) 39±1 y; 82±2kg; BMI=27.8 ±0.3 Kg/m^2, mean±SEM) were randomized to one of three groups (N=12 for each) for a 6-month intervention: control (CO: weight-maintenance diet), caloric restriction (CR: 25% reduction in energy intake) or caloric restriction plus aerobic exercise (CR+EX: 12.5% reduction in energy intake plus 12.5% increase in exercise energy expenditure). Food was provided during weeks 1–12 and 22–24. Changes in fat mass, visceral fat, VO_{2peak} (graded treadmill test), muscular strength (isokinetic knee extension/flexion), blood lipids, blood pressure and insulin sensitivity/secretion were compared.

RESULTS—As expected, VO_{2peak} was significantly improved after 6 months of intervention in CR +EX only (22±5% vs. 7±5% in CR and −5±3% in CO) whereas isokinetic muscular strength did not change. There was no difference in the losses of weight, fat mass or visceral fat and changes in systolic BP between the intervention groups. However, only CR+EX had a significant decrease in diastolic BP (−5±3% vs. −2±2% in CR and −1±2% in CO), in LDL-cholesterol (−13±4% vs. −6±3% in CR and 2±4% in CO), and a significant increase in insulin sensitivity (66±22% vs. 40±20% in CR and 1±11% in CO).

CONCLUSIONS—Despite similar effect on fat losses, combining CR with exercise increased aerobic fitness in parallel with improved insulin sensitivity, LDL-cholesterol and diastolic BP. The results lend support for inclusion of an exercise component in weight loss programs to improve metabolic fitness.

Key Terms

exercise training; maximal aerobic fitness; energy restriction; blood pressure; blood lipids

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Introduction

Paragraph 1

Numerous studies have linked increased adiposity (17,32) and reduced physical activity (17) and/or fitness (32,35) to increased risk of cardiovascular disease (CVD) and overall mortality. However, because of the strong link between physical fitness -particularly of aerobic nature- and reduced prevalence of obesity (35,38), there is debate about the potential independent effects of aerobic fitness and adiposity (i.e., fatness) on CVD and metabolic health risk factors. For example, it is generally recognized that the benefits of increased physical activity on CVD risks include decreased platelet aggregation, enhanced fibrinolysis, decreased susceptibility to malignant ventricular arrhythmias, improved endothelial function and myocardial oxygen delivery, along with reduced obesity (12). The detriments of increased fatness on the other hand, include increased renin-angiotensin system activation(10), low grade inflammation(2, 39), and chronic oxidative stress (20) which result in reduced nitric oxide availability, increased vascular tone and arterial stiffening and increased systolic and pulse pressures (8,29). Furthermore, both fatness and poor fitness are linked with insulin resistance, elevated blood pressure and elevated total and LDL cholesterol concentrations (12), all of which improve with weight loss and enhanced fitness. These links are of course complicated by the strong negative relation between fitness and fatness.

Paragraph 2

While several large studies (18) including the Nurses Health Study (17) and the Lipid Research Clinic Study (32) have provided evidence supporting independent contributions of both decreased physical activity/fitness and increased fatness on mortality, there are several reports predominately from Blair’s group (4,5,23,33,34) suggesting that aerobic fitness can negate the adverse effects of fatness on mortality (4,33,34). Such results have often been interpreted that reducing fatness is not necessary in light of adequate fitness (24). The majority of previous studies, however, have been criticized for inclusion of mostly relatively young healthy white individuals rather than a more ethnically representative sample of aging individuals (38). In contrast, analysis from the LOOK Ahead Trial in a large ethnically diverse sample of overweight individuals with type 2 diabetes, found that both fitness and fatness are related to CVD risk factors, but that the strength of the association for fitness vs. fatness was different for different risk factors (38). These results along with a few other trials (3,19) suggest that both fitness and reduced fatness are important for reducing overall morbidity and mortality.

Paragraph 3

An interesting question still up for debate is whether improvements in fitness or fatness independently alter risk factors for CVD and the metabolic syndrome, particularly during caloric restriction. Prolonged caloric restriction increases life span in rodents and other shorter-lived animal species (36), but the addition of exercise improves average lifespan but not maximal life span (16). In humans, caloric restriction has been shown to impact several biomarkers of longevity including fasting insulin concentration, body core temperature (14), DNA damage (14) and markers of atherosclerosis (9). It is however not known, if in a prospective design, the addition of exercise training will yield extra health benefit in the face of similar weight and fat loss. In other words, does caloric restriction with or without exercise result in different improvements in cardiometabolic risk factors which could ultimately improve longevity. The purpose of this analysis was to determine whether a deficit by energy restriction or energy restriction plus aerobic exercise that produces equal change in fatness (26) leads to greater cardiometabolic benefits when exercise is included.

Research Methods and Procedures

Paragraph 4

This evaluation was performed as part of a randomized clinical trial designed to examine the effects of caloric restriction on markers of longevity in non-obese humans referred to as the CALERIE study (Comprehensive Assessment of Long term Effects of Reducing Intake of Energy; Trial registration: ClinicalTrials.gov Identifier: NCT00099151). Details of the study have been published elsewhere (14). Briefly, we enrolled overweight men and women (25≤ screening BMI<30 kg/m^2) aged 25–45 y for women, and 25–50 y for men with no personal history of type 2 diabetes, cardiovascular disease, high blood pressure (>160/90mmHg), liver disease or obesity, no psychiatric or eating disorders, alcoholism or substance abuse; and not taking any medication. The study was approved by our Institutional Review Board and all participants gave written informed consent before participation.

Paragraph 5

Intervention—Following a 5-week baseline assessment, 36 participants were randomized into one of three groups (n=12 for each): 25% caloric restriction (CR) from baseline energy requirements; 12.5% CR + 12.5% increase in total energy expenditure through structured exercise (CR+EX); and control (CO) with weight-maintenance by a healthy diet (American Heart Association Step 1 diet). An additional 12 subjects were also randomized into a low-caloric diet (LCD) rapid weight loss group (15%), but this group is not included in the current analysis as the participants did not exercise and lost a greater amount of body weight. Subjects were stratified according to sex, race and screening BMI before sequential randomization. Baseline energy requirements were determined from individual free-living energy expenditure assessed over four weeks using doubly labeled water (14).

Paragraph 6

Diets—All diets were based on the American Heart Association Step 1 recommendations (≤30% fat; ≤10% saturated-fat) and provided the RDA for all essential vitamins and minerals. For the first 12 weeks after randomization, the diet for all groups was provided by our Metabolic Kitchen (14). During weeks 13–22, participants self-selected their own diet based on their individual caloric target, before returning to the in-feeding protocol for weeks 22–24.

Paragraph 7

Structured Exercise—Except for the CR+EX group, other participants were not permitted to modify their physical activity patterns. The CR+EX group was required to increase energy expenditure by 12.5% above baseline requirements by undergoing structured aerobic exercise (i.e., walking, running or stationary cycling) five days per week according to an individualized exercise prescription. The target energy cost of the exercise sessions was calculated from the weekly desired energy cost divided by five days per week. Five rather than seven days per week of exercise was selected to comply with the American College of Sports Medicine (ACSM) recommendations of 3–5 days per week of aerobic exercise (1). Individual exercise prescriptions to meet target goals were calculated by measuring the oxygen cost (V-Max 29 Series, SensorMedics, Yorba Linda, CA) during three individually-prescribed levels of activity (i.e., walking at 3.0, 3.5 and 4.0 MPH), generating an energy cost equation from the workload vs. oxygen cost above rest (i.e., net oxygen consumption), and assigning exercise duration according to target energy expenditure and self selected workload. Energy equivalents were determined using the calculated food quotient of 4.89 kcal/liter of oxygen consumed.

Paragraph 8

To prevent skeletal muscle soreness and injury, the exercise load was progressively increased during the initial 6 weeks while energy intake was adjusted so that the energy deficit always equaled 25% of daily energy requirements. Following week 6, participants were allowed to select his/her exercise intensity (as long as their heart rate was within 65% to 90% of maximal heart rate (1)), and exercise duration was adjusted to maintain the target energy expenditure. During the first 6 weeks, all exercise sessions were conducted at the PBRC Health and Fitness Center under supervision. For weeks 7 – 24, at least three of the five weekly sessions were conducted at the Center under supervision. A wireless heart rate monitor (Polar S-610, Polar Beat, Port Washington, NY) was used to record exercise duration and average heart rate during both supervised and unsupervised sessions. The average energy cost throughout the intervention was 403 ± 63 kcal per session for women and 569 ± 118 kcal per session for men which resulted in an average exercise duration of 53 ± 11 min and 45 ± 14 min per session for women and men, respectively.

Paragraph 9

Behavior and Compliance Strategies—Cognitive-behavioral techniques were used to foster adherence to diet and exercise prescription, including self monitoring and stimulus control (14). All participants attended weekly group meetings and were contacted once per week via telephone to address any adherence problems quickly. Both direct observation and heart rate data (from both supervised and unsupervised sessions) were used to assess exercise compliance.

Paragraph 10

Metabolic testing—Subjects were tested during a 5-d admission to the clinical research center at baseline (month 0) and month 6 (14) (Figure 1). Testing included dual energy x-ray absorptiometry (DXA) to assess total body composition (Hologic QDR 4500A; QDR for Windows Version 11.1.2, Hologics, Bedford, MA); multislice computed tomography (CT) scanning of the abdominal region to assess total, visceral and subcutaneous abdominal adipose tissue (31); and a frequently sampled intravenous glucose tolerance test (28,37) to assess insulin sensitivity. More specifically, abdominal fat was measured on a GE LightSpeed Plus CT scanner (General Electric Medical Systems, Milwaukee, WI). Eight contiguous images (1 cm slice thickness) were acquired every 5 cm - 5 above and 2 below a slice centered on the Lumbar 4-Lumbar 5 inter-vertebral disc using 170mA, a scan time of 1 s, and a 512 × 512 matrix. Total, visceral and subcutaneous abdominal fat were defined using Analyze 3.0 (Biomedical Imaging Resource - Mayo Clinic, Rochester, MN), by selecting regions of interest as previously described in detail (31). Briefly, total abdominal fat was defined as the sum of adipose tissue pixels (−30 to −190 Hounsfield Units) inside a line tracing the skin whereas visceral abdominal fat was segmented by drawing a line around the interior of the peritoneal cavity and summing all adipose tissue pixels within the area. Subcutaneous abdomen fat was calculated as the difference between total abdominal fat and visceral abdominal fat. Measurements of systolic and diastolic blood pressure were taken twice, 5 minutes apart, in a quite room at thermo-neutrality from the participant’s right arm with a manual sphygmomanometer by a certified staff member after 10 minutes of seated rest. A fasting blood sample was also drawn for determination of serum lipids. Several days before the inpatient admission, aerobic fitness was assessed by a progressive treadmill test to exhaustion (VO_{2peak} test) and isokinetic muscle “strength” and endurance of the quadriceps was measured using a Cybex II Isokinetic Dynamometer, (Cybex Division of Lumex, Inc, Ronkonkoma, NY USA)

Paragraph 11

Aerobic Fitness—Maximal oxygen uptake (VO_{2peak}) was performed in the morning after an overnight fast by a progressive treadmill test to exhaustion (1). Following a 6-minute warm-up, subjects began walking or running (depending on their fitness level) at a pace that elicited a heart rate of between 120 and 140 bpm after which the workload was progressively increased by 2% in grade every minute until volitional fatigue. O_2 consumption (VO_2) and CO_2 production (VCO_2) were measured continuously using a metabolic cart (V-Max 29 Series, SensorMedics, Yorba Linda, California) that was calibrated before each test. Heart rate was monitored continuously using a portable heart rate monitor (Polar S-610, Polar Beat, Port Washington, NY). The highest VO_2, respiratory exchange ratio (RER) and heart rate achieved over a 20-s period within the last 2-min of exercise were recorded as the maximum values.

Paragraph 12

Muscle Strength—Isokinetic strength and endurance were measured using a Cybex II Isokinetic Dynamometer, (Cybex Division of Lumex, Inc, Ronkonkoma, NY USA) during knee extension and flexion. The procedure involved an initial test of 3 repetitions at 60 degrees/sec to measure peak force and power followed by a test to fatigue at 180 degrees/sec. Prior to testing, subjects underwent a familiarization trial.

Paragraph 13

Serum Lipids—Total cholesterol, LDL- Cholesterol and Triglycerides were analyzed according to standardized procedures (25) and LDL- cholesterol was calculated using the Friedwald equation.

Paragraph 14

Statistical Analysis—Data are expressed as means ± SEM and the level of significance for all statistical tests was set at $p<0.05$. SAS Version 9.1 was used for analysis and all analyses were performed by a biostatistician. The change and percent change from baseline to month 3 and month 6 were computed for all variables and analysis of variance of the changes was used to determine differences. The factors tested in the model were treatment (CR, CR+EX, control), time (month 3, month 6) and sex, and their interactions. Baseline values were included in the models as covariates. The statistical significance for all multiple comparisons was adjusted with respect to the Tukey-Kramer method to control for Type I errors. One participant in the control group withdrew during the study (before month 3) for personal reasons. Data is therefore presented for 35 subjects.

Results

Paragraph 15

Baseline Characteristics—The characteristics of the 35 subjects and their cardiometabolic parameters at baseline have been previously published (14,22,25,26) but are described in Table 1. As expected, there was no difference among treatment groups at baseline.

Paragraph 16

Effect of Caloric Restriction on Body Weight and Body Composition—Details on the change in body weight and body composition have been previously reported (14,22,26). Briefly, and as summarized in Figures 2 and 3, body weight was significantly reduced from baseline ($p<0.001$) by ~10% in both the CR and CR+EX groups at the end of the 6-month intervention (Figure 2). Total body fat mass and visceral abdominal fat were significantly ($p<0.005$) but similarly reduced in both intervention groups (by ~25%) and unchanged in controls (Figure 3).

Paragraph 17

Effect of Caloric Restriction on Aerobic Fitness and Isokinetic Strength—The change in maximal aerobic fitness ($V0_{2peak}$) and isokenetic strength in the control, CR and CR +EX groups are summarized in Table 2. Absolute VO_{2peak} (l/min) was significantly increased vs. baseline by 10±4% ($p<0.01$) in the CR+EX group and slightly but insignificantly ($p=0.36$) decreased by −4±5% and −6±3% in the CR and control groups, respectively. When adjusted for body weight, VO_{2peak} was significantly improved by 22±5% in the CR+EX group ($p<0.0001$), slightly but non-significantly increased (7±5%; $p=0.06$) in CR (mainly as a function of body mass reduction) and slightly but not significantly decreased) in the control group (−5±3%; $p>0.20$). Findings were similar when expressed as METs. In the CR+EX group METS increased by 18±6% ($p<0.001$) but the change in METs was not significant from baseline in the CR group (7±6%) or control (−2±5%). There were no changes in peak torque or average power during isokinetic quadriceps flexion or extension.

Paragraph 18

Caloric Restriction and Cardiometabolic Risk Factors—The change in systolic blood pressure, diastolic blood pressure, total cholesterol, LDL-Cholesterol, HDL-Cholesterol and insulin sensitivity have been previously reported (14,22,25) and are summarized in Figure 4. While HDL was significantly ($p<0.05$) increased in all treatment groups (including the control), diastolic blood pressure, total cholesterol, LDL-cholesterol and insulin sensitivity were significantly ($p<0.02$) improved vs. baseline only in the CR+EX group but not in the CR or control groups. Systolic blood pressure was not changed by any of the treatments. Fasting serum triglyceride concentration (not shown) increased significantly ($p<0.05$) by 28±11% in the control group but decreased −21±5% and −15±6%, respectively, in both CR and CR + EX groups ($P<0.001$ vs. baseline and vs. Control).

Discussion

Paragraph 19

In this randomized clinical trial, we tested the effect of body weight and body fat loss with or without improvement in physical fitness on cardiometabolic risk factors in overweight men and women who underwent a 6 months caloric restriction regimen with or without regular aerobic exercise. While both intervention groups experienced similar reductions in total body mass, fat mass and visceral abdominal mass, the caloric restricted plus exercise group experienced greater improvement in insulin sensitivity, LDL-cholesterol and diastolic blood pressure than the caloric restriction by diet alone group. Our results strongly suggest that inclusion of regular aerobic exercise (or training) in a weight loss program yields cardiometabolic health benefits beyond those of weight loss alone. Our results further support the argument that both fitness and fatness are important for reducing cardiometabolic risks, particularly during caloric restriction, and may shed some light on how fitness or fatness may contribute to overall mortality.

Paragraph 20

The main difference between the two caloric restricted groups was that one group was 25% caloric restricted by diet alone (i.e., consuming 75% of requirement) while the other group was in 25% energy deficit, 12.5% by decreasing food intake and 12.5% by increasing energy expended through regular aerobic exercise. Not surprisingly, the caloric restricted plus exercise group experienced significant improvements in aerobic fitness with an average 10% improvement in absolute VO_{2peak} (l/min) and an average 22% improvement in VO_{2peak} relative to body weight. Of interest, however, is the slight albeit not statistically significant decrease in absolute aerobic fitness that occurred over the 6 month period in both the non-exercise groups. In comparison, Ross and colleagues (27) found that weight loss induced by a 700 kcal daily energy deficit by diet resulted in a 5% decrease in aerobic fitness while weight loss induced by a 700 kcal increase in exercise resulted in a 13% improvement in VO_{2peak}. In the current study, however, caloric restriction either by diet or diet plus exercise did not result in any significant changes in leg muscle peak power or endurance. Importantly, our data demonstrates that caloric restriction does not lead to reduced overall strength or functionality in humans when fed a nutritionally sound diet.

Paragraph 21

A unique aspect and strength of the study is that weight loss was achieved through provision of isoenergetic deficits (regardless of exercise) which resulted in almost identical reductions in total body weight and total and visceral adiposity (26). Such design allows us to tease out the additional influence of exercise which according to our results is a necessary part of the prescription in order to gain full cardiometabolic improvements including improved insulin sensitivity and lowered LDL-cholesterol and diastolic blood pressure. The statistically significant improvement in insulin sensitivity only in the CR +EX but not CR group is not surprising given the well-documented insulin sensitizing effect of aerobic exercise (15) driven predominantly by increased GLUT4 expression and trafficking in exercised skeletal muscle (11). Increased fatness, on the other hand, is associated with increased ectopic fat deposition in skeletal muscle and liver (22) which may influence the insulin signaling cascade (30) and impact circulating lipids (30). Somewhat surprising, however, is that inclusion of aerobic exercise did not result in additional improvements in HDL-cholesterol (21) and to a lesser extend systolic blood pressure (13). Such lack of effect may be related to our selection of healthy overweight rather than obese volunteers (who had relatively normal blood pressure values) and our administration of a tightly controlled AHA-Step1 diet which provided 30% of calories from fat.

Paragraph 22

The results of the current study along with those of a previous analysis reporting larger reduction in 10-year cardiovascular disease risk (38% in CR + EX vs. 29% in CR and no change in controls) (25) when exercise was included suggest that improvements in both fitness and fatness are needed for optimally reducing overall morbidity and mortality. Results are in agreement with cross-sectional analysis of the Look AHEAD study in which fitness and fatness had different impacts on CVD risk factors even though these two variables are clearly strongly related (38). Specifically, aerobic fitness (assessed by VO_{2peak}) had stronger associations than fatness with the Framingham Risk Score (model used to identify healthy individuals at risk for cardiovascular disease), the ankle/brachial index (average ankle systolic blood pressure/arm systolic blood pressure; a physiological marker of cardiovascular risk), and hemoglobin A1C concentration (a marker of diabetes control). Our results further suggest that regular aerobic exercise which improves VO_{2peak} also improves peripheral resistance during diastole above that noted with a reduction in fatness (25). Even though it is clearly established that elevated systolic blood pressure is a more powerful predictor of cardiovascular events than diastolic pressure (6,7), increased diastolic blood pressure causes an increased risk for end organ failure (7), cardiovascular death (6), and could indeed be an important reason why fitness is associated with reduced overall mortality.

Paragraph 23

Another important health benefits exerted by regular exercise beyond those of weight loss include its impact on aerobic capacity, particularly in relation to daily functionality and overall mortality. Aerobic capacity has been shown to be a more powerful predictor of mortality among both healthy men and those with cardiovascular disease than other established risk factors with each 1 MET increase in aerobic capacity conferring a 12% increase in survival. Based on these reported statistics, our CR+EX group, who improved their aerobic capacity by an average 1.6 METS would have an estimated 19.2% increase in survival. By contrast, the improvement in the aerobic capacity of the CR+EX group was parallel with an alarming tendency of absolute aerobic capacity to decline over the 6-month period in both the CR and control treated groups.

Paragraph 24

While this randomized clinical trial is in support of the argument that exercise training offers benefits beyond improved fatness, it was conducted in a small sample (relative to epidemiological trials) of 35 healthy overweight volunteers with limited health risk factors and without groups such as exercise alone (25% energy deficit via exercise energy expenditure) or exercise without weight loss (12.5% increase in energy expenditure with 12.5% increase in energy intake). Such groups would have helped to distinguish between the metabolic effects of fitness compared to fatness alone. Both groups, however, would have been almost impossible: for example, participants in the caloric restriction plus structured exercise group exercised an average of 45–53 minutes at least 5 days a week to achieve the 12.5% of energy expenditure which would have had to be doubled to promote 25% energy expenditure. Unfortunately, our relatively small sample size of mostly healthy overweight volunteers also limited our power to detect differences among treatments for improvements in cardiometabolic risk factors (22). These limitations, however, were compensated in part by the very tight control of the intervention and control groups including the rigorously controlled diet and structured exercise program.

Paragraph 25

Results of the current study suggests that beyond changes in fatness, combining caloric restriction with exercise is important for increasing aerobic fitness and optimizing improvements in risk factors for diabetes and cardiovascular disease, including improved insulin sensitivity, LDL-Cholesterol, and diastolic blood pressure, that are beyond those of body weight/body fat reduction alone. Improvements in other cardiometabolic risk factors, however, such as systolic blood pressure and HDL-cholesterol might only be associated with changes in fatness and/or consumption of a healthy diet.

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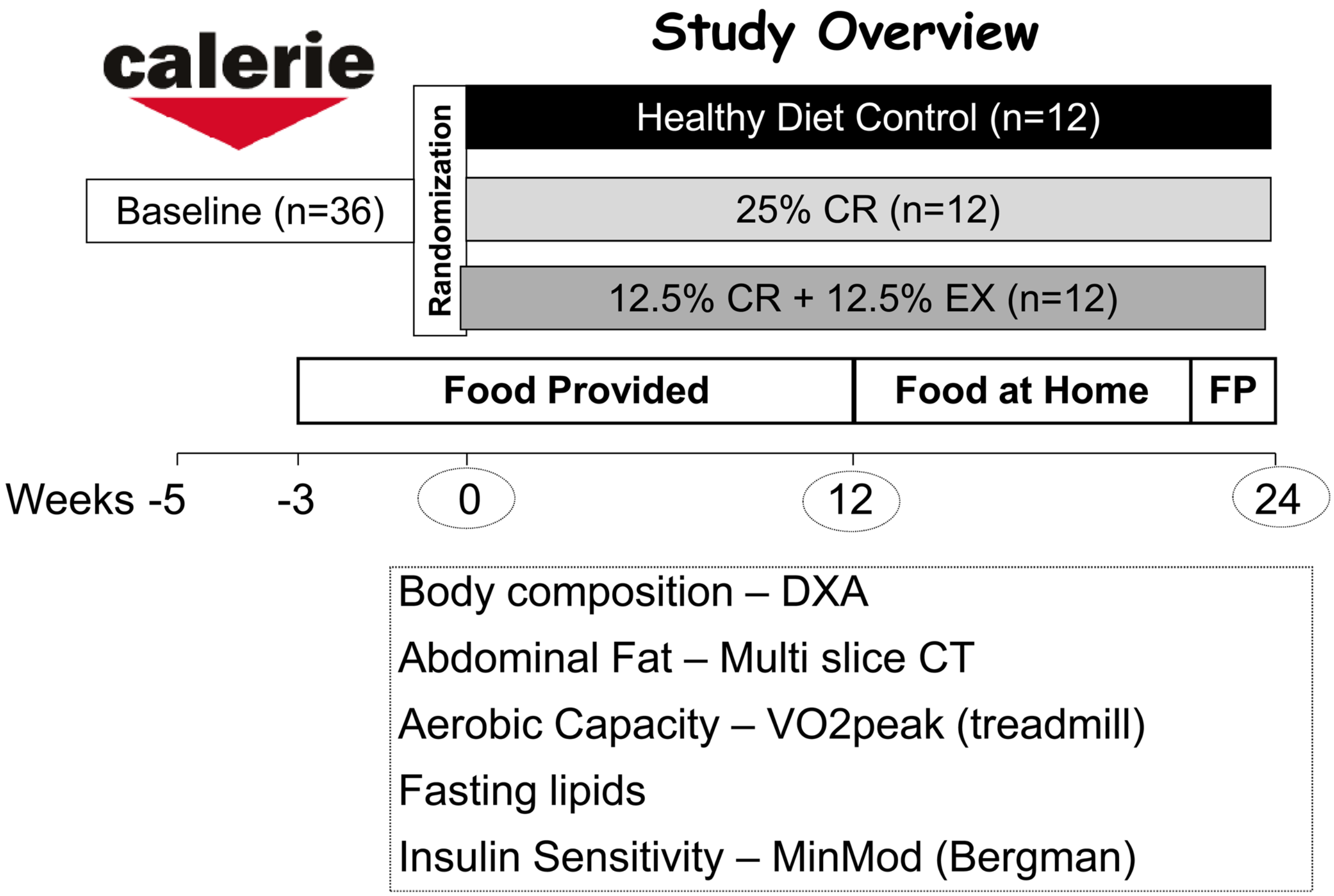

Figure 1.
Overview of CALERIE Study.

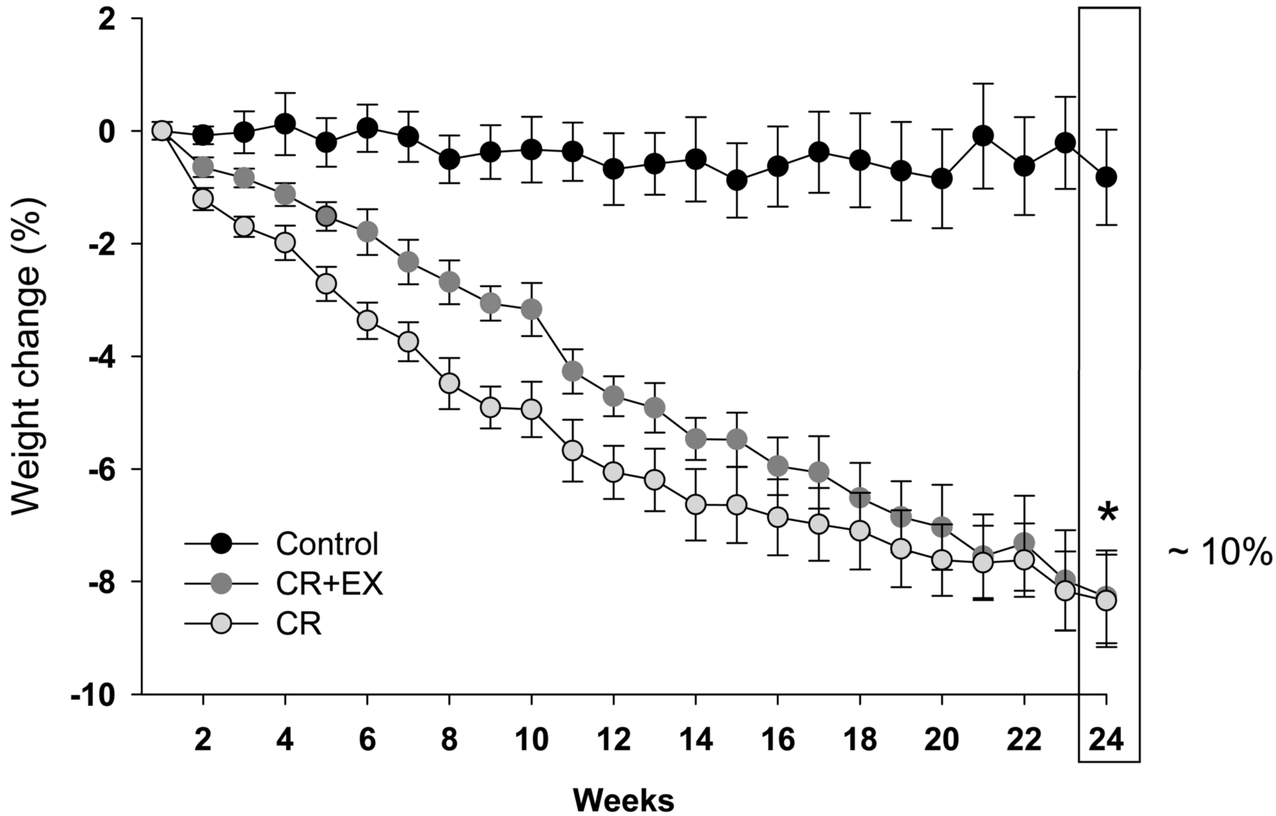

Figure 2.

Change in body mass over the 6 months of treatment with control, caloric restriction (CR), and caloric restriction structured aerobic exercise (CR+EX). There were no significant differences between CR and CR+EX treatments. *Significant ($p<0.005$) change from baseline.

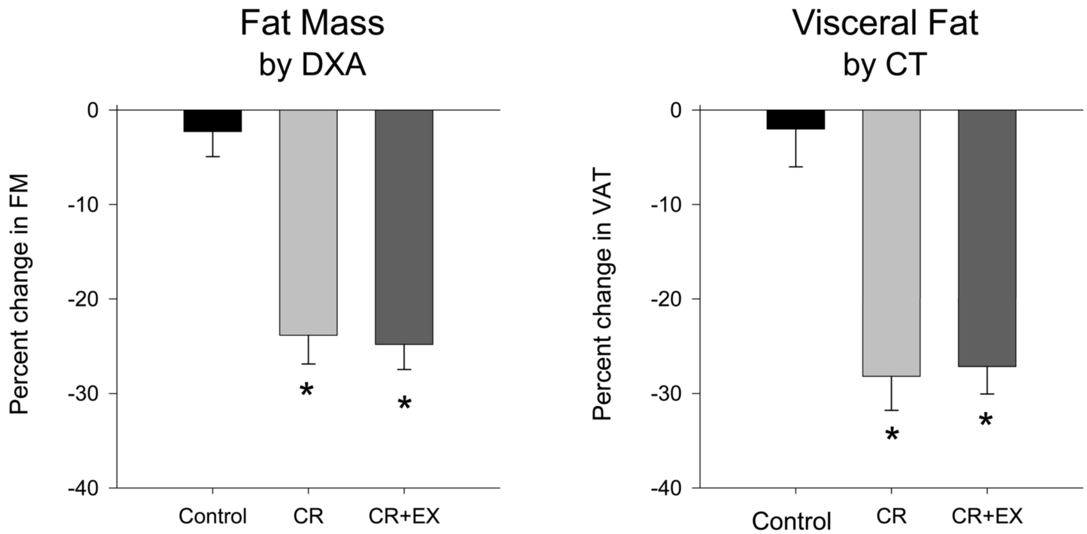

Figure 3.
Change in whole body fat mass and visceral fat stores after 6 months of treatment with control, caloric restriction (CR), and caloric restriction and structured aerobic exercise (CR+EX). There were no significant differences between CR and CR+EX treatments; *Significant (P<0.005) change from baseline.

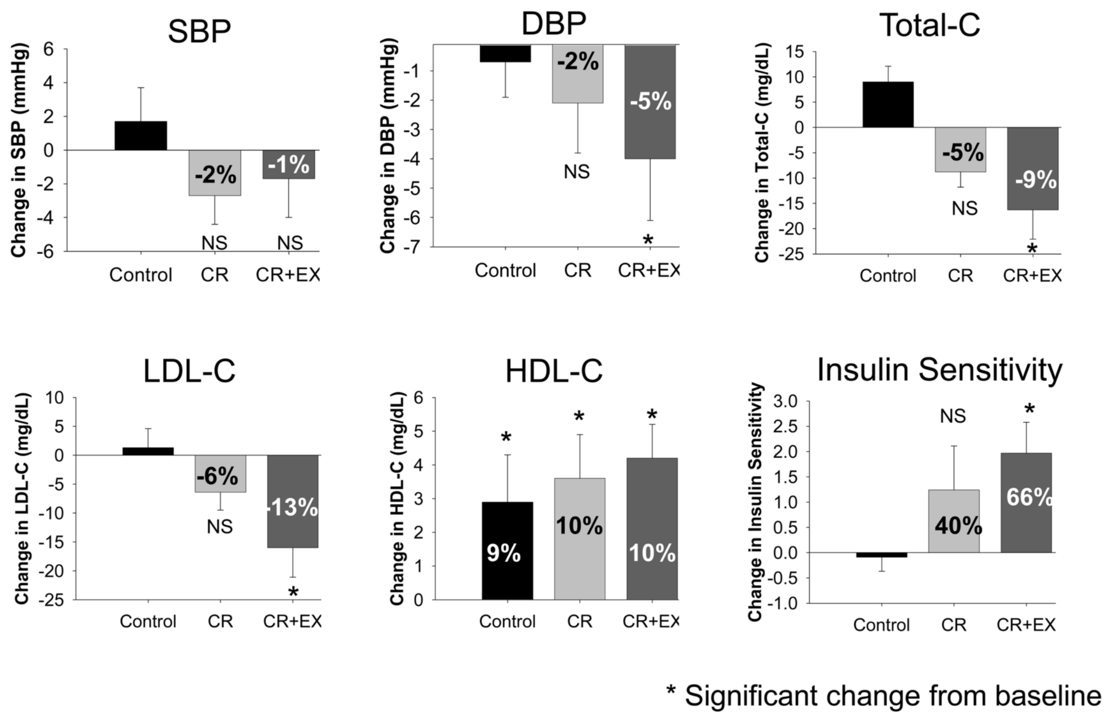

Figure 4.

Change in cardiometabolic risk factors after 6 months of treatment with control, caloric restriction (CR), and caloric restriction and increased structured exercise (CR+EX). Diastolic blood pressure, total cholesterol, LDL-cholesterol and insulin sensitivity were significantly improved vs. baseline in the CR+EX group but not in the CR or control groups. Systolic blood pressure was not changed by any of the treatments groups whereas HDL was significantly ($p<0.05$) increased in all treatment groups (including the control),. * Significant ($p<0.05$) change from baseline.