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Lower extremity muscle size and strength and aerobic capacity decrease with caloric restriction but not with exercise-induced weight loss

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Abstract

Caloric restriction (CR) results in fat loss; however, it may also result in loss of muscle and thereby reduce strength and aerobic capacity ($\dot{V}O_{2\max}$). These effects may not occur with exercise-induced weight loss (EX) because of the anabolic effects of exercise on heart and skeletal muscle. We tested the hypothesis that CR reduces muscle size and strength and $\dot{V}O_{2\max}$, whereas EX preserves or improves these parameters. Healthy 50- to 60-yr-old men and women (body mass index of 23.5–29.9 kg/m²) were studied before and after 12 mo of weight loss by CR ($n = 18$) or EX ($n = 16$). Lean mass was assessed by dual-energy X-ray absorptiometry, thigh muscle volume by MRI, isometric and isokinetic knee flexor strength by dynamometry, and treadmill $\dot{V}O_{2\max}$ by indirect calorimetry. Both interventions caused significant decreases in body weight (CR: $-10.7 \pm 1.4\%$, EX: $-9.5 \pm 1.5\%$) and lean mass (CR: $-3.5 \pm 0.7\%$, EX: $-2.2 \pm 0.8\%$), with no significant differences between groups. Significant decreases in thigh muscle volume ($-6.9 \pm 0.8\%$) and composite knee flexion strength ($-7.2 \pm 3\%$) occurred in the CR group only. Absolute $\dot{V}O_{2\max}$ decreased significantly in the CR group ($-6.8 \pm 2.3\%$), whereas the EX group had significant increases in both absolute ($+15.5 \pm 2.4\%$) and relative ($+28.3 \pm 3.0\%$) $\dot{V}O_{2\max}$. These data provide evidence that muscle mass and absolute physical work capacity decrease in response to 12 mo of CR but not in response to a similar weight loss induced by exercise. These findings suggest that, during EX, the body adapts to maintain or even enhance physical performance capacity.

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Keywords

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WEIGHT LOSS IN OVERWEIGHT and obese individuals is beneficial with respect to reducing the risk of developing cardiovascular disease, diabetes, and some cancers. Although caloric restriction (CR) is an effective means for achieving weight loss, the negative energy balance induced by CR may result not only in reductions in fat mass but also in catabolism of skeletal muscle and myocardium, thus affecting the capacity to perform physical work. Indeed, previous studies have demonstrated that CR-induced weight loss is associated with decreases in muscle size (6, 7, 13, 14) and strength (8, 10). Furthermore, because fat-free mass is a strong determinant of aerobic exercise capacity ($\dot{V}O_{2\max}$) (5), CR may also decrease $\dot{V}O_{2\max}$.

An increase in exercise energy expenditure, without a compensatory increase in food intake, is also an effective means for achieving weight loss (12, 14, 15). Negative energy balance occurs in humans and animals during catastrophic events, such as escaping from environmental disasters (floods, forest fires, earthquakes), avoiding predators (for example, when an animal's territory is invaded by another, more powerful species), or escaping from or participating in war. In this context, the ability to preserve or improve strength and $\dot{V}O_{2\max}$, despite a negative energy balance, might have been selected for during the course of evolution because it provided a survival advantage. Although the preservation of strength and $\dot{V}O_{2\max}$ may not be important in modern society for the purposes of avoiding predators, for example, decrements in strength and $\dot{V}O_{2\max}$ may be predisposing factors for physical frailty in late life (3, 4).

The purpose of the present study was to test the hypothesis that CR results in decreases in muscle size and strength and in $\dot{V}O_{2\max}$, whereas a similar energy deficit induced by increasing exercise energy expenditure without changing energy intake does not alter muscle size or strength and likely increases $\dot{V}O_{2\max}$. The data reported in this paper were obtained as part of a larger investigation of the feasibility of CR in healthy volunteers (CALERIE: Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy) (12).

METHODS

Participants

Fifty- to sixty-year-old men and women who had body mass index values in the high-normal to overweight range (i.e., 23.5–29.9 kg/m²) were recruited from the St. Louis, Missouri, metropolitan area. Candidates for the study were excluded if they had 1) a history of diabetes or a fasting blood glucose value ≥ 126 mg/dl, 2) a history or clinical evidence of coronary artery disease, stroke, or lung disease, 3) a resting blood pressure (BP) ≥ 170 mmHg systolic or 100 mmHg diastolic, or 4) a recent history or evidence of malignancy. Furthermore, all candidates had to be nonsmokers and sedentary (defined as exercising < 20 min per day twice per week during the 6 mo before baseline testing). Women had to be postmenopausal. All participants gave their informed, written consent to participate in the

study, which was approved by the Human Studies Committee and the General Clinical Research Center Advisory Committee at Washington University School of Medicine.

The participants were randomly assigned, with stratification for sex, to the CR, EX, or a control group in a 2:2:1 ratio. Among the 19 subjects in the CR and EX groups who started the intervention, 1 from each group dropped out of the study and 18 in each group completed the study. For reasons that included technical problems during testing, participant refusal to perform tests, and failure to achieve maximal exercise during the treadmill exercise test, data from some subjects were not included in the present analyses. Furthermore, because of the reasons described above, complete outcome data were only available on 4 of the 10 participants who were randomized to the control group; therefore, the control group data were not included in the analyses for the present report. In total, data from 34 subjects (CR: $n = 18$; EX: $n = 16$) are included in the present report. However, sample sizes for some outcomes are smaller because of missing data; specific sample size information for each outcome is as indicated.

CR intervention

The objective of the CR intervention was to decrease energy intake by 16% during the first 3 mo and by 20% during the remaining 9 mo. Study dietitians met with participants on a weekly basis to weigh them and teach them strategies for reducing portion sizes, replacing high-energy-dense foods with food of lower energy density, and daily self-monitoring of dietary intake with the use of either 7-day food diaries or personal digital assistant diet-tracking software. The CR group participants attended ~85% of the weekly meetings with the dietitians (12). Subjects with little or no weight loss were asked to frequently maintain food diaries, which the dietitians used to develop personalized dietary recommendations. Additional details about the CR intervention, including data to reflect adherence, have been reported previously (12, 20). However, in brief, average energy intake during the CR intervention was ~12% lower than baseline as determined by doubly labeled water, and physical activity levels remained unchanged according to physical activity recall questionnaires (12).

Exercise intervention

The goal of the EX intervention was to induce the same energy deficit as was induced by the CR intervention by increasing exercise energy expenditure by 16% of baseline total daily energy expenditure for the first 3 mo and by 20% for the subsequent 9 mo without changing energy intake. On a weekly basis, the participants met with exercise trainers for body weight measurements and to receive updated gross exercise energy expenditure goals. The participants attended ~85% of the weekly meetings with the trainers (12). The energy expenditure goals were based on 16 or 20% of total daily energy expenditure plus an estimate of how much energy would have been expended in the absence of exercise; further details have been described previously (20). The participants exercised either in our facility or on their own while wearing heart rate monitors (S610, Polar Electro, Kempele, Finland). These monitors gave the subjects feedback regarding their daily and weekly gross exercise energy expenditure. Although the participants were advised that frequent vigorous endurance exercise would be the most time-efficient way to meet their exercise energy

expenditure goals, specific information about exercise frequency, duration, and intensity were not prescribed. For participants who showed little or no weight loss during the intervention, the heart rate monitor data were first examined to assess compliance with the exercise recommendations, and individualized exercise plans were then developed as needed to improve compliance. If exercise compliance was acceptable, individuals with little or no weight loss were asked to record food diaries to determine whether energy intake had increased; as necessary, individualized diet plans were provided to encourage the participants to maintain energy intake at baseline levels. As reported previously (12, 20), the participants exercised ~6 days/wk for ~60 min per session at ~70% of maximal heart rate (HR_{max}), and this resulted in ~320 kcal/day gross exercise energy expenditure (or ~230 kcal/day net exercise energy expenditure). Walking, elliptical machine exercise, cycling, and running were the most commonly used exercise modes, and none of the subjects used strength training as a means for achieving their exercise energy expenditure goals. According to doubly labeled water-based estimates, average energy intake during the EX intervention did not change from baseline (12, 20).

Protein intake

Protein intake was assessed by use of 7-day food diaries and computerized nutrient analysis (Nutrition Data System for Research, versions 4.05, 4.06, and 5.0; Nutrition Coordination Center, University of Minnesota, Minneapolis, MN) as described previously (12, 20). Dietary data were collected before and during the intervention (i.e., at baseline and at 1, 3, 6, 9, and 12 mo), and data collected during the intervention were averaged for each individual to reflect year-long average protein intake.

Body weight and lean body mass

Body weight was measured in duplicate in the morning, after an overnight fast, while the participant was wearing only underwear and a hospital gown. Baseline and final body weights were calculated as the mean of multiple weekly weights (up to 5 at baseline and up to 3 at 12 mo), except when used for the calculation of relative VO_{2max} (i.e., $ml \cdot kg^{-1} \cdot min^{-1}$), for which body weight was measured immediately before the exercise test. Lean body mass (i.e., whole body mass minus fat mass and bone mineral mass) was measured by dual-energy X-ray absorptiometry (Delphi W, Hologic, Waltham, MA; software version 11.2). Lean mass for each subject was calculated as the mean of up to three assessments at baseline and one or two assessments at 12 mo.

Thigh muscle volume and average cross-sectional area

MRIs of both thighs were obtained at baseline and at the end of the intervention. Ten transverse images, 10 mm thick, were acquired just superior to the patella with no intersection gap between slices with a 1.5-T superconducting MRI instrument (Siemens, Iselin, NJ) and a T1-weighted pulse sequence. Muscle volume and cross-sectional area (CSA) were quantified in each slice by Analyze Direct software (version 5.0; Mayo Clinic, Rochester, MN), which distinguishes muscle from other tissues based on pixel brightness. Volume data for the 10 slices were summed to represent muscle volume in the 10-cm longitudinal region of interest. Average CSA was based on the CSA values from all slices in the region of interest. Muscle size data are reported as the sum of values from the right and

left thighs. When muscle volume data were used to normalize strength data (as described below), only data from the right thigh were used.

Muscle strength

Tests for concentric isokinetic and isometric knee flexor and knee extensor strength were performed at baseline and at the end of the intervention with a Cybex dynamometer (Ronkonkoma, NY). Many of the subjects were limited by patellar dysfunction during the knee extension test. Therefore, only knee flexion data are reported. The subjects were seated with the back supported and hips flexed at 120° and were secured to the seat of the dynamometer with thigh and pelvis straps. All tests were performed on the right leg. The isokinetic tests were performed at an angular velocity of 60°/s. The isometric tests were performed with the knee flexed at 45°. The best of three maximal voluntary efforts for each test component (i.e., isokinetic knee flexion and isometric knee flexion) was used as the measure of absolute strength. Strength data were also reported relative to body weight and relative to right thigh muscle volume as a measure of muscle-specific force. A composite strength score was calculated as the sum of the isometric and isokinetic knee flexion tests.

Physiological responses to maximal treadmill exercise

We previously reported $\dot{V}O_{2\text{ max}}$ data as an index of adherence to the EX intervention (12, 20). For the present study, however, because $\dot{V}O_{2\text{ max}}$ is reported as a physiological outcome, only data from subjects whose baseline and final tests met the criteria for “true” $\dot{V}O_{2\text{ max}}$, as described below, were included. Metabolic responses to treadmill exercise were measured by indirect calorimetry (True Max 2400, ParvoMedics, Salt Lake City, UT) during a graded treadmill exercise test. The incremental test started at a speed determined, during a warm-up period, to elicit ~70% of age-predicted HR_{max} and remained constant throughout the test, and grade was increased by 1–2% every 1–2 min. The test continued until the subject could no longer exercise because of exhaustion or until other conditions, such as ECG changes or development of symptoms, made it unsafe to continue. Metabolic data were generated every 15 s, and the highest average oxygen consumption ($\dot{V}O_2$) value from two consecutive 15-s data points was designated peak $\dot{V}O_2$. Peak $\dot{V}O_2$ was considered to be “true” $\dot{V}O_{2\text{ max}}$ if two of the following three conditions were met: 1) peak respiratory exchange ratio (RER) was ≥ 1.10 , 2) measured HR_{max} was \geq predicted HR_{max} minus 10 [where predicted $HR_{\text{max}} = 208 - 0.7 \times \text{age (19)}$], and 3) $\dot{V}O_2$ increase was ≥ 150 ml/min between the last two stages of the test. BP, measured by auscultation, and 12-lead ECG were monitored throughout the test. HR_{max} was determined from the maximal exercise ECG and was based on ≥ 5 R-R normal sinus cardiac cycles. Maximal exercise rate pressure product (RPP) was calculated as the product of HR_{max} and maximal exercise systolic BP. Maximal exercise oxygen pulse was calculated as $\dot{V}O_{2\text{ max}}$ divided by HR_{max} .

Statistical analyses

Between-group comparisons of the changes in the outcome variables were performed by analyses of covariance with the baseline to 12-mo change as the dependent variable (absolute change and percent change from baseline), treatment group as the independent variable, and baseline value as a covariate. Furthermore, percent change in body weight was

included as a covariate in analyses of all outcome data (except body weight) so the results can be evaluated as if the weight changes in the two groups were exactly equal. Age and sex were not included as covariates in these models because the sex distribution was not different between the groups and because small variations in age, within the relatively narrow 50- to 60-yr age range, would not be expected to affect the physiological responses to CR or EX. Significance of the within-group changes were based on the least squares means from the analyses of covariance. Associations between changes in selected variables were assessed by Pearson correlations. Analyses were performed with SAS software, version 9.1.3 of the SAS System for Linux (SAS Institute, Cary, NC). All statistical tests were two-tailed, and significance was accepted at $P = 0.05$. Data are presented as least squares means \pm SE, unless noted otherwise.

RESULTS

Participants

The male and female distribution was similar in the CR (7 men, 11 women) and EX (6 men, 10 women) groups. Mean age (\pm SD) for both groups was in the middle to upper end of the targeted age range for the study (CR: 55.2 ± 3.4 yr; EX: 59.4 ± 1.0 yr). Baseline body mass index (mean \pm SD) was 27.1 ± 2.5 kg/m² in the CR group and 27.0 ± 1.8 kg/m² in the EX group, reflecting the fact that most of the participants were overweight.

Protein intake

Absolute protein consumption (g/day) decreased significantly in the CR group but not in the EX group (Table 1). When expressed relative to body weight, protein consumption did not change in the CR group but increased significantly in the EX group (Table 1). The between-group comparisons of changes in absolute and relative protein consumption were both marginally significant.

Body weight and lean body mass

As reported previously by our group for a slightly larger sample (12, 20), body weight decreased significantly in both the CR (-8.1 ± 1.1 kg, $-10.7 \pm 1.4\%$) and EX (-7.7 ± 1.2 kg, $-9.5 \pm 1.5\%$) groups, and these changes were not different between groups whether expressed in absolute terms ($P = 0.80$) or as a percentage ($P = 0.58$). Likewise, lean body mass decreased significantly in both groups, and these changes were not different between groups (Table 1).

Thigh muscle volume

Thigh muscle volume and average thigh muscle CSA decreased significantly in the CR group but not in the EX group, and these changes were significantly different between groups (Table 1). In the CR group, the decrease in thigh muscle volume correlated with the magnitude of change in body weight, whereas in the EX group there was no evidence for such a relationship (Fig. 1). The comparison of correlation coefficients between groups did not achieve statistical significance.

Muscle strength

Isokinetic knee flexion torque decreased significantly in the CR group and remained unchanged in the EX group (Table 2 and Fig. 2). The between-group comparison of these changes was significant when expressed as a percentage. Isometric knee flexion did not change significantly in either the CR or EX groups (Table 2 and Fig. 2). Composite knee flexion strength decreased significantly in the CR group and remained unchanged in the EX group; these changes were statistically different between groups whether expressed in absolute terms or as a percentage (Table 2 and Fig. 2).

All indexes of knee flexor strength relative to body weight remained unchanged from baseline in the CR group and increased significantly in the EX group (Table 2 and Fig. 2). The changes in isokinetic flexion strength and composite knee flexion strength were significantly different between groups. The changes in isometric flexion torque were not significantly different between groups; however, it is noteworthy that the mean values for these changes were similar to those seen for isokinetic knee flexion. When strength data were reported relative to muscle volume, no changes from baseline were evident in either study group, and none of the between group differences was significant (Table 3 and Fig. 2).

Physiological responses to maximal treadmill exercise

CR resulted in a decrease in absolute $\dot{V}O_{2\max}$; however, when expressed per unit body weight or lean mass, no change in $\dot{V}O_{2\max}$ was evident (Table 4). $\dot{V}O_{2\max}$ increased in the EX group regardless of whether it was expressed in absolute terms or relative to body weight or lean mass. All of the changes in $\dot{V}O_{2\max}$, regardless of how it was expressed, were significantly different between the CR and EX groups.

The high values for maximal exercise RER and minute ventilation ($\dot{V}E$)/ $\dot{V}O_2$ observed during the treadmill tests (Table 4) indicate that the subjects achieved $\dot{V}O_{2\max}$. Both RER and $\dot{V}E/\dot{V}O_2$ during maximal exercise increased in response to the CR intervention, and the increase in maximal exercise RER was significantly different from that in the EX group. Although there was a tendency for the change in maximal exercise $\dot{V}E/\dot{V}O_2$ in the CR group to be different from that in the EX group, this comparison did not achieve significance. HR_{\max} did not change in either group, and there were no between-group differences (Table 4).

Oxygen pulse decreased significantly in the CR group and increased significantly in the EX group, and these changes were significantly different between groups (Table 5). Systolic BP during maximal exercise was significantly lower after the 1-yr intervention in the EX group only, whereas diastolic BP during maximal exercise was significantly lower during the final test in the CR group only (Table 5). The changes in maximal exercise systolic and diastolic BP were not different between groups. RPP during maximal exercise did not change in either group, and there were no differences between groups (Table 5).

Seven subjects (1 CR, 6 EX) were taking BP medications for hypertension during the study. Although the medications and dosages for these subjects did not change during the study, it is possible that the inclusion of these subjects might have affected the results of the hemodynamic outcomes. Therefore, we performed several subanalyses after excluding these

subjects. Exclusion of the one subject who was taking a beta-blocker (EX group) did not affect the HR_{max} or oxygen pulse results. Exclusion of all seven subjects who were taking any BP medication did not alter the results for maximal exercise RPP or maximal exercise diastolic BP; however, the significant decrease in maximal exercise systolic BP for the EX group became nonsignificant ($P = 0.26$).

DISCUSSION

Results from the present study indicate that 12 mo of CR results in significant reductions in absolute thigh muscle mass, knee flexor strength, and $\dot{V}O_{2max}$, whereas a similar 1-yr energy deficit induced by exercise completely preserves thigh muscle mass and strength and improves $\dot{V}O_{2max}$. When strength and $\dot{V}O_{2max}$ are expressed relative to body weight, there are no decreases in response to CR. However, in response to EX, there were increases in body weight-related strength (17–24%) and $\dot{V}O_{2max}$ (28%), despite the fact that the exercise regimens were designed primarily for expending energy and not necessarily for aerobic training or strengthening per se.

Previous studies have demonstrated that a negative energy balance induced by CR results not only in loss of fat but also in loss of muscle (6, 7, 13, 14). Although we did not measure total muscle mass in the present study, it is likely that both CR and EX resulted in net loss of skeletal muscle because lean mass measured by dual-energy X-ray absorptiometry (i.e., total body mass minus fat and bone mass) decreased significantly in both groups. We measured thigh muscle size as a representative region of muscle that is involved in most modes of endurance exercise, including those that were commonly used in the present study. Thigh muscle size decreased in the CR group and was completely preserved in the EX group. It is likely that the changes in the CR group were due to loss of contractile protein, as opposed to noncontractile components of muscle such as lipid and connective tissue, because the decreases in size were paralleled by decreases in strength. As a result, there were no changes in muscle-specific torque (i.e., torque per unit muscle volume). Together, these findings suggest that endurance exercise protects against the energy deficit-induced loss of skeletal muscle size and strength, although it is likely that this is only true for muscles that are active during exercise.

Dietary protein consumption may affect the amount of lean or muscle mass that is lost during CR-induced weight loss (2, 9). As a consequence of the reduced food consumption in the CR group, there was a marginally significant decrease in absolute daily protein consumption. In contrast, absolute daily protein consumption in the EX group remained unchanged. However, as a result of the decreases in body weight in both groups, protein consumption relative to body weight was unchanged in the CR group and increased in the EX group. It is possible that the differences in protein consumption between the CR and EX groups might have been partly responsible for the differential effects of the weight loss interventions on muscle size and strength.

Absolute $\dot{V}O_{2max}$ decreased in response to CR in the present study. Because $\dot{V}O_{2max}$ is the product of HR_{max} , maximal exercise stroke volume (SV_{max}), and maximal exercise arterio-venous oxygen content difference $[(a-v)O_{2max}]$ and because HR_{max} did not change during

the intervention, the decrease in $\dot{V}O_{2\max}$ was due to decreases in SV_{\max} and/or $(a-v)O_{2\max}$. In contrast to what was observed in the CR group, the energy deficit induced by exercise resulted in increases in $\dot{V}O_{2\max}$ and oxygen pulse. Previous studies have shown that $\dot{V}O_{2\max}$ increases in response to exercise training through increases in SV_{\max} and $(a-v)O_{2\max}$ (17, 18). To a large extent, the increases in SV_{\max} are because of physiological hypertrophy of the myocardium (11, 16) and the increases in $(a-v)O_{2\max}$ are because of increases in the capillary density and mitochondrial content in skeletal muscle (1). Therefore, despite the presence of a whole body catabolic state (i.e., weight loss), exercise may have had adaptive effects on skeletal muscle mitochondria and the myocardium. However, we do not have direct evidence to support this notion.

Interpretation of the body weight-independent data from the present study would suggest that CR has adverse effects on strength and cardiovascular fitness and that this might decrease the capacity for physical performance. It is important to note, however, that because CR resulted in substantial weight loss, the absolute work requirement for many (but not all) common activities, such as climbing stairs, also decreased. Therefore, from this perspective, the decreases in strength and $\dot{V}O_{2\max}$ are proportional to the reduction in body weight, and the capacity for weight-bearing exercise (i.e., walking, running, climbing) would not likely be impaired. In the same context, however, it should also be recognized that weight loss induced by exercise coincided with a preservation of absolute strength and an increase in absolute $\dot{V}O_{2\max}$ and therefore likely increased the capacity for physical performance.

The present study has strengths and limitations. One of the strengths is our measurement methods; we used a strict treadmill protocol to assess “true” $\dot{V}O_{2\max}$, and we used volumetric MRI-based measurements for thigh muscle size. Another strength is that we did not exclude data from subjects who were noncompliant with the intervention protocols; the data, therefore, reflect the average responses of overweight, middle-aged men and women to these interventions, rather than the best-case scenario for fully compliant individuals. A weakness of our study is that our strength assessments were limited to the knee flexor muscles; therefore, we cannot conclude about the effects of these interventions on strength in other regions of the body. Furthermore, because the muscle-specific torque data were based on all muscles in the thigh, rather than the knee flexors alone, and because we did not consider the biomechanical aspects of knee flexor force transfer, our data are only an index of muscle-specific torque and not a direct measure of force generation per unit of muscle tissue. Another limitation is that this was a fairly intensive intervention that required the participants to visit our facility on a weekly basis for weight checks and consultation. Therefore, data from the present study cannot be used to deduce the benefits of less supervised CR and EX interventions. Finally, because we did not include a combined CR and EX intervention, which might be more practical to perform, we cannot determine whether the beneficial effects of exercise override the effects of CR on absolute $\dot{V}O_{2\max}$, muscle size, and muscle strength.

In summary, data from the present study provide evidence that CR results in reductions in muscle size and strength and in $\dot{V}O_{2\max}$, although these changes are proportional to the reduction in body weight. In contrast, similar weight loss induced by increasing exercise

energy expenditure without changes in energy intake prevents the loss of muscle size and strength, at least in the exercised muscles, and increases $\dot{V}O_{2\max}$. Data from the EX group in the present study suggest that, in the presence of an overall negative energy balance, the body is capable of selectively preserving and/or synthesizing skeletal muscle and perhaps other tissues that are involved in oxygen uptake and thus maintaining the capacity for the performance of physical activity.

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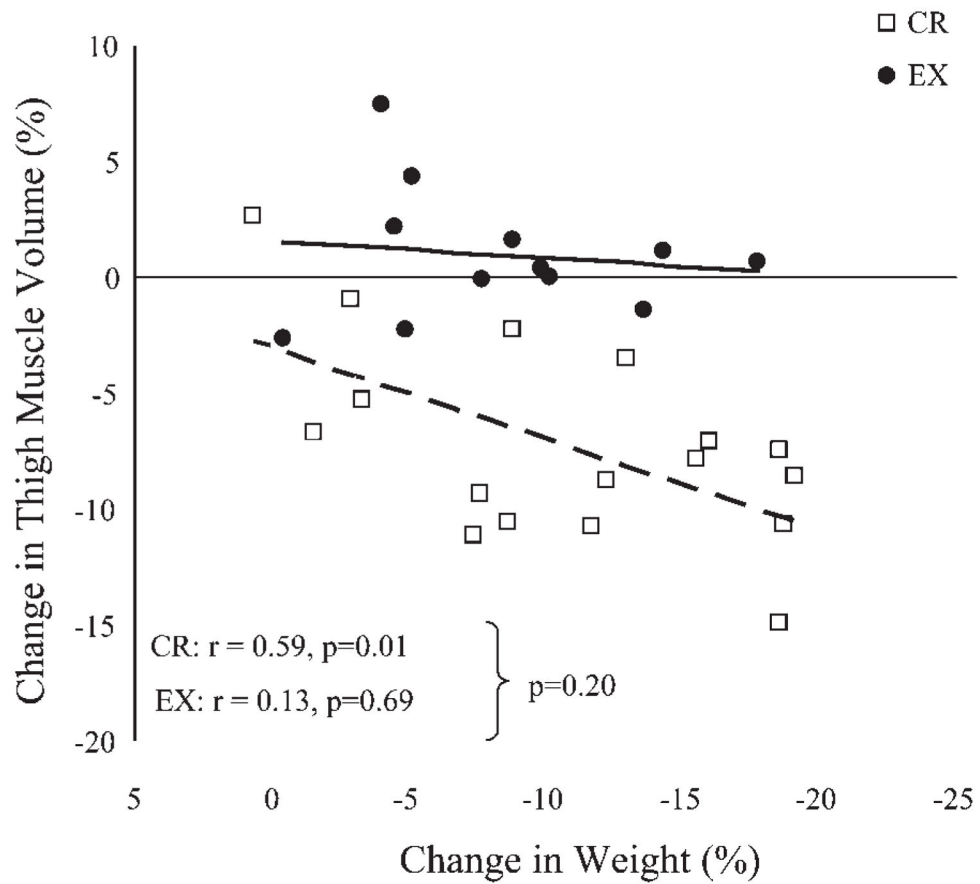


Fig. 1. Relationship (Pearson correlations) between the magnitude of weight loss and the magnitude of change in thigh muscle volume (sum of right and left thighs) in the caloric restriction group (CR) and the exercise group (EX).

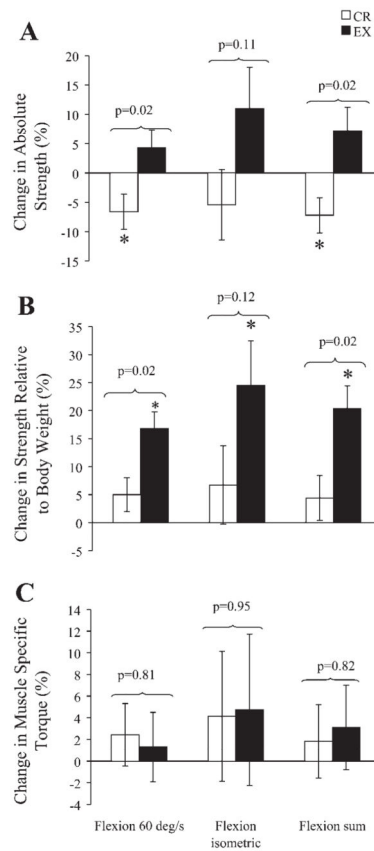


Fig. 2.

Changes in absolute muscle strength (A), strength relative to body weight (B), and muscle-specific torque (C) for the knee flexor muscles. Data are least-squares means \pm SE after adjustment for baseline values and percent change in body weight. Muscle-specific torque was calculated as absolute torque divided by muscle volume and was based on strength and muscle volume data from the right leg only. * $P < 0.05$ within group by ANCOVA with Tukey's adjustment for multiple comparisons.

Table 1

Protein consumption, lean mass, and thigh muscle size

	CR (n = 18)	EX (n = 16)	Between Group P Value
Protein consumption			
Baseline, g/day	88±6	83±5	
Average during intervention, g/day	80±4	87±6	
Change, g/day	-7.3±3*	3.1±3	0.03
Change, %	-5.9±4	4.7±4	0.06
Protein consumption			
Baseline, g·kg ⁻¹ ·day ⁻¹	1.11±0.05	1.09±0.04	
Average during intervention, g·kg ⁻¹ ·day ⁻¹	1.11±0.06	1.23±0.07	
Change, g·kg ⁻¹ ·day ⁻¹	0.003±0.04	0.14±0.05*	0.05
Change, %	1.7±4	13.1±4*	0.06
Lean mass			
Baseline, kg	49.1±2.4	47.9±2.8	
Final, kg	47.4±2.4	46.8±2.6	
Change, kg	-1.6±0.3*	-1.2±0.3*	0.41
Change, %	-3.4±0.7*	-2.3±0.7*	0.31
Thigh muscle volume			
Baseline, cm ³	1529±80	1516±81	
Final, cm ³	1413±67	1532±86	
Change, cm ³	-110±15*	7.95±17	<0.0001
Change, %	-6.9±0.8*	0.49±1.0	<0.0001
Thigh muscle CSA			
Baseline, cm ²	191±10	190±10	
Final, cm ²	177±8.4	192±11	
Change, cm ²	-13.8±1.8*	0.99±2.2	<0.0001
Change, %	-6.9±0.8*	0.49±1.0	<0.0001

Values are means ± SE except for change data, which are least squares means ± SE from the analysis of covariance (ANCOVA) with baseline value and percent change in weight as covariates. For protein consumption data, “average during intervention” reflects the mean of data collected at 1, 3, 6, 9, and 12 mo during the intervention and sample sizes in the exercise-induced weight loss (EX) group are 1 less than listed in table header. Thigh muscle size data represent the sum of the right and left thighs, and sample sizes for the caloric restriction (CR) and EX groups are 1 and 4 less than listed in table header, respectively. CSA, cross-sectional area.

* *P* 0.05 vs. zero by ANCOVA with Tukey’s adjustment for multiple comparisons.

Table 2

Isokinetic and isometric knee flexor strength

	CR (n = 15)	EX (n = 12)	Between Group P Value
<i>Torque (raw)</i>			
Peak torque at 60°/s			
Baseline, N·m	98±6	80±8	
Final, N·m	91±6	83±7	
Change, N·m	-6.1±3*	1.2±3	0.11
Change, %	-6.6±3*	4.3±3	0.02
Peak torque at 0°/s			
Baseline, N·m	95±8	73±7	
Final, N·m	88±7	79±7	
Change, N·m	-5.9±4	4.7±5	0.16
Change, %	-5.4±6	11.0±7	0.11
Sum of 0 and 60°/s peak torques			
Baseline, N·m	193±14	152±14	
Final, N·m	178±13	162±14	
Change, N·m	-13.3±6*	7.5±7	0.04
Change, %	-7.2±3*	7.2±4	0.02
<i>Torque relative to body weight</i>			
Peak torque at 60°/s			
Baseline, N·m ⁻¹ ·kg ⁻¹	1.24±0.06	1.06±0.08	
Final, N·m ⁻¹ ·kg ⁻¹	1.29±0.06	1.23±0.08	
Change, N·m ⁻¹ ·kg ⁻¹	0.05±0.04	0.16±0.04*	0.06
Change, %	5.0±3	16.8±3*	0.02
Peak torque at 0°/s			
Baseline, N·m ⁻¹ ·kg ⁻¹	1.19±0.08	0.97±0.07	
Final, N·m ⁻¹ ·kg ⁻¹	1.24±0.08	1.17±0.09	
Change, N·m ⁻¹ ·kg ⁻¹	0.05±0.06	0.20±0.07*	0.16
Change, %	6.7±7	24.5±8*	0.12
Sum of 0 and 60°/s peak torques			
Baseline, N·m ⁻¹ ·kg ⁻¹	2.43±0.13	2.03±0.14	
Final, N·m ⁻¹ ·kg ⁻¹	2.53±0.13	2.40±0.17	
Change, N·m ⁻¹ ·kg ⁻¹	0.08±0.08	0.40±0.09*	0.02
Change, %	4.4±4	20.4±4*	0.02

Values are means ± SE except for change data, which are least squares means ± SE from the ANCOVA with baseline value and percent change in weight as covariates.

* P = 0.05 within group by ANCOVA with Tukey's adjustment for multiple comparisons.

Table 3

Isokinetic and isometric muscle specific torque (torque ÷ thigh muscle volume)

	CR (n = 14)	EX (n = 11)	Between Group P Value
Peak torque at 60°/s			
Baseline, N·m ⁻¹ ·cm ⁻³	0.128±0.007	0.106±0.008	
Final, N·m ⁻¹ ·cm ⁻³	0.127±0.006	0.109±0.007	
Change, N·m ⁻¹ ·cm ⁻³	0.002±0.003	-0.001±0.004	0.60
Change, %	2.43±2.8	1.30±3.2	0.81
Peak torque at 0°/s			
Baseline, N·m ⁻¹ ·cm ⁻³	0.121±0.008	0.098±0.007	
Final, N·m ⁻¹ ·cm ⁻³	0.122±0.008	0.103±0.008	
Change, N·m ⁻¹ ·cm ⁻³	0.003±0.006	0.002±0.007	0.92
Change, %	4.13±6.0	4.74±7.0	0.95
Sum of 0 and 60°/s peak torques			
Baseline, N·m ⁻¹ ·cm ⁻³	0.249±0.014	0.204±0.014	
Final, N·m ⁻¹ ·cm ⁻³	0.248±0.013	0.212±0.014	
Change, N·m ⁻¹ ·cm ⁻³	0.003±0.008	0.004±0.009	0.96
Change, %	1.82±3.4	3.11±3.9	0.82

Values are means ± SE except for change data, which are least squares means ± SE from the ANCOVA with baseline value and percent change in weight as covariates. Data were calculated using right leg data for both strength and muscle volume.

* *P* 0.05 within group by ANCOVA with Tukey's adjustment for multiple comparisons.

Table 4Physiological responses to maximal treadmill exercise: $\dot{V}O_{2\max}$ RER, VE/ $\dot{V}O_2$, and heart rate

	CR (n = 15)	EX (n = 14)	Between Group P Value
Absolute $\dot{V}O_{2\max}$			
Baseline, ml/min	2075±139	1965±158	
Final, ml/min	1949±148	2250±175	
Change, ml/min	-133±46*	293±47*	<0.0001
Change, %	-6.8±2.3*	15.5±2.4*	<0.0001
$\dot{V}O_{2\max}$ relative to body weight			
Baseline, ml·kg ⁻¹ ·min ⁻¹	26.3±1.2	25.5±1.4	
Final, ml·kg ⁻¹ ·min ⁻¹	27.4±1.3	32.3±1.9	
Change, ml·kg ⁻¹ ·min ⁻¹	0.9±0.7	7.0±0.7*	<0.0001
Change, %	3.9±2.9	28.3±3.0*	<0.0001
$\dot{V}O_{2\max}$ relative to lean mass			
Baseline, ml·kg lean ⁻¹ ·min ⁻¹	43.5±1.2	40.5±1.2	
Final, ml·kg lean ⁻¹ ·min ⁻¹	42.0±1.3	47.7±1.5	
Change, ml·kg lean ⁻¹ ·min ⁻¹	-1.5±0.9	7.2±0.9*	<0.0001
Change, %	-3.3±2.1	17.8±2.2*	<0.0001
RER at maximal exercise			
Baseline	1.19±0.01	1.16±0.02	
Final	1.32±0.03	1.19±0.02	
Change	0.14±0.02*	0.03±0.02	0.001
Change, %	11.7±1.8*	2.49±1.8	0.002
VE/ $\dot{V}O_2$ at maximal exercise			
Baseline	30.1±1.1	29.9±1.1	
Final	33.0±1.5	30.0±0.9	
Change	2.9±0.95*	0.17±0.99	0.06
Change, %	9.37±3.3*	2.09±3.4	0.13
HR _{max}			
Baseline, beats/min	170±2	173±3	
Final, beats/min	170±2	173±2	
Change, beats/min	0.34±1.5	0.92±1.5	0.79
Change, %	0.24±0.9	0.64±0.9	0.76

Values are means ± SE except for change data, which are least squares means ± SE from the ANCOVA with baseline value and percent change in weight as covariates. $\dot{V}O_{2\max}$, maximal oxygen uptake; HR_{max}, maximal heart rate; RER, respiratory exchange ratio; VE/ $\dot{V}O_2$, ventilatory equivalent for oxygen uptake.

* *P* < 0.05 within group by ANCOVA with Tukey's adjustment for multiple comparisons.

Table 5

Physiological responses to maximal treadmill exercise: oxygen pulse, blood pressure, and rate pressure product

	CR (n = 15)	EX (n = 14)	Between Group P Value
Oxygen pulse at maximal exercise			
Baseline, ml/beat	12.2±0.8	11.3±0.9	
Final, ml/beat	11.5±0.9	13.0±1.0	
Change, ml/beat	-0.82±0.3*	1.7±0.3*	<0.0001
Change, %	-7.2±2.5*	15.3±2.6*	<0.0001
Systolic BP at maximal exercise [†]			
Baseline, mmHg	192±8.1	204±6.9	
Final, mmHg	186±5.7	188±6.4	
Change, mmHg	-10.6±5.4	-12.2±5.4*	0.84
Change, %	-4.44±2.4	-4.97±2.4*	0.88
Diastolic BP at maximal exercise [†]			
Baseline, mmHg	92±2.6	93±2.9	
Final, mmHg	85±3.6	89±2.0	
Change, mmHg	-7.04±2.9*	-3.74±2.9	0.44
Change, %	-6.46±3.4	-3.43±3.4	0.53
RPP at maximal exercise [†]			
Baseline, beats·min ⁻¹ ·mmHg	32740±1497	35243±1104	
Final, beats·min ⁻¹ ·mmHg	31692±1063	32620±1187	
Change, beats·min ⁻¹ ·mmHg	-1749±974	-1922±974	0.90
Change, %	-4.10±2.6	-4.65±2.6	0.88

Values are means ± SE except for change data, which are least squares means ± SE from the ANCOVA with baseline value and percent change in weight as covariates.

[†] Because of missing maximal exercise blood pressure (BP) data, CR group samples sizes for maximal systolic BP, diastolic BP, and RPP are 1 less than that listed in table header. RPP, rate pressure product.

* *P* < 0.05 within group by ANCOVA with Tukey's adjustment for multiple comparisons.