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Effect of exercise training on cardiometabolic risk markers among sedentary, but metabolically healthy overweight or obese post-menopausal women with elevated blood pressure

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ABSTRACT

Objective: To investigate the effect of exercise training on markers of the lipoprotein-lipid profile and inflammatory markers in post-menopausal overweight/obese women with a moderately elevated systolic blood pressure.
Methods: A total of 267 women [mean body mass index (BMI) = 32.0 ± 5.7 kg/m^2 and mean age = 57.3 ± 6.6 years] underwent a 6-month exercise intervention program. Exercise training was performed 3–4 times per week at a targeted heart rate corresponding to 50% of the maximal oxygen consumption.
Results: Compared to baseline values, mean change in relative VO_2 max (the primary endpoint) was of 1.18 ± 2.25 mL/min kg ($p < 0.0001$), mean weight loss was of 1.4 ± 3.3 kg ($p < 0.0001$), mean reduction in waist circumference was of 2.4 ± 6.9 cm ($p < 0.0001$) and systolic blood pressure did not change significantly (-1.2 ± 13.0 mmHg, NS). No changes were observed in markers of the lipoprotein-lipid profile. No changes were observed for plasma levels of C-reactive protein, interleukin-6, tumor-necrosis factor-α and adiponectin. Changes in VO_2 max were negatively associated with changes in body weight ($r = -0.26$, $p < 0.0001$) and waist circumference ($r = -0.16$, $p = 0.01$), but not with changes in cardiometabolic risk markers.
Conclusion: Although exercise training significantly increased cardiorespiratory fitness in these sedentary, but metabolically healthy obese/overweight women with a moderately elevated systolic blood pressure, no significant improvements were observed in their cardiometabolic risk profile.

1. Introduction

Obesity, and particularly its deleterious form, visceral obesity, is associated with insulin resistance and with a constellation of metabolic abnormalities which include the presence of an atherogenic dyslipidemia characterized by elevated apolipoprotein B and triglyceride levels, decreased apolipoprotein A1 and high-density lipoprotein (HDL) cholesterol levels and an increased preponderance of small, dense low-density lipoprotein (LDL) and HDL particles [1,2]. Other features of the visceral obesity include a pro-inflammatory profile characterized by increased levels of C-reactive protein (CRP), interleukin-6 (IL-6), tumor-necrosis factor-α (TNF-α) and reduced levels of adiponectin, a potentially anti-diabetic and anti-atherogenic adipokine [3,4]. Several prospective studies have shown that physically active individuals have increased levels of cardiorespiratory fitness and are therefore at lower risk of developing insulin resistance and cardiovascular disease (CVD)-related mortality [5,6]. Moreover, studies have also shown that increased cardiorespiratory fitness levels might reduce the CVD risk associated with either obesity or the metabolic syndrome [7]. Although studies have reported that exercise training had beneficial impact on cardiometabolic risk markers, few studies have investigated the effects of exercise training on car-

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diometabolic risk markers in overweight/obese post-menopausal women.

We therefore measured an expanded panel of cardiometabolic risk markers in overweight or obese post-menopausal women who participated to the Dose–Response to Exercise in post-menopausal Women (DREW) before and after a 6-month exercise-training program.

2. Materials and methods

2.1. Study design

A complete description of DREW design and methods has been previously described [8,9]. The study was a randomized, dose–response exercise trial with a no-exercise control group and 3 exercise groups with incrementally higher doses of energy expenditure (4, 8 or 12 kcal/kg/week [KKW]). The results of the primary endpoints of this protocol have been previously published [9]. They included changes in aerobic fitness, changes in anthropometric parameters such as body weight, body fat percentage and waist circumference and changes in basic plasma lipoprotein-lipid levels. The research protocol was reviewed and approved annually by the Cooper Institute's institutional review board, and written informed consent was obtained from all participants prior to their inclusion in the study.

2.2. Study participants

A total of 4545 telephone screening interviews between April 2001 and June 2005 were conducted and written informed consent was obtained from 464 eligible post-menopausal women aged 45–75 years. Women who were sedentary (not exercising >20 min on ≥3 d/week and taking <8000 steps/d assessed over the course of 1 week), overweight or obese [body mass index (BMI) of 25.0–43.0 kg/m^2], and who had a systolic blood pressure (SBP) ranging from 120.0 to 159.9 mmHg were randomly assigned to 1 of the 4 groups. Women in the no-exercise control group were asked to maintain their level of activity during the 6-month study period. Exclusion criteria included history of stroke, heart attack, or any serious medical condition that prevented participants from adhering to the protocol or exercising safely. Participants were recruited using a wide variety of techniques, including newspaper, radio, television, mailers, community events, and e-mail distributions.

2.3. Exercise training

Exercising women participated in three or four training sessions each week for 6 months with training intensity at the heart rate corresponding to 50% of each woman's peak VO_2. A computer-controlled exercise training management system allows for input of relevant data points on each woman (week of exercise, KKW dose according to group assignment, heart rate associated with 50% VO_2, training heart rate zone, body weight and number of visits per week). The computer then provides the appropriate power output for the cycle ergometer and the correct speed and grade for the treadmill that will elicit the programmed heart rate. Knowing the exact power output for the cycle ergometer and the treadmill, the total kilocalories expended each minute and the time needed to reach the target energy expenditure for the exercise session or for the week can then be calculated. The duration of each individual session depended on the number of visits required to reach the target KKW. During the first week, each group expended 4 KKW. Those assigned to that level continued to expend 4 KKW per week for 6 months. All the other groups increased their energy expenditure by 1 KKW a week until they reached level required for their group. All exercise sessions were performed under observation and supervision in an exercise laboratory with complete and strict monitoring of the amount of exercise completed in each session. Among women who completed the trial, those in the 4 KKW groups had a mean exercise time of 72.2 ± 12.3 min per week. Women in the 8 and 12 KKW groups have a mean exercise time of 135.8 ± 19.5 and 191.7 ± 33.7, respectively. Two exercise training facilities were used in this study: one in North Dallas and the other in Oak Cliff (South Dallas), TX. Participants were weighed each week and their weight was multiplied by their exercise dosage to determine the number of calories to be expended for the week. Women in the exercise groups alternated training sessions on semi-recumbent cycle ergometers and treadmills. Cardiorespiratory fitness was measured using a Lode Excalibur Sport cycle ergometer as previously described [9].

2.4. Participant retention and adherence

To reduce participant dropout and maintain adherence, several strategies were used including a 2-week prerandomization run-in period, behavioral contracts, and consistent support from staff members. Participants were reimbursed $150 ($75 each) for completion of baseline and follow-up assessments. Participants could earn another $350 in incentives based on adherence. For the control group, adherence was based on returning monthly step-count forms and medical symptom questionnaires. For each month missed, $50 was deducted from the $350 incentive. For the exercise groups, the $350 was reduced by $50 for each week of missed sessions beyond the 90% adherence target. Although this incentive is a substantial amount, it was considered appropriate because the study objective was to evaluate the dose–response effects of exercise. For this reason, excellent adherence to both intervention and measurement was necessary. If DREW was testing the effectiveness of an exercise intervention as a public health strategy, such a payment would not be appropriate. However, DREW was not testing whether financial incentives encourage individuals to exercise; rather, it was evaluating specific responses to various doses of exercise.

2.5. Measurement of cardiometabolic risk markers

Plasma levels of apolipoprotein B, apolipoprotein A1 and CRP were measured by a highly sensitive immunoassay that used monoclonal antibodies coated with polystyrene particles. The assay was performed with a Behring BN-100 nephelometer (Dade Behring) according to the methods described by the manufacturer [10]. LDL and HDL particle size were measured by nondenaturing polyacrylamide gradient gel electrophoresis (2–16% for LDL and 4–30% for HDL) as previously described [11,12]. Plasma glucose was measured enzymatically, whereas plasma insulin was measured by electrochemiluminescence [13]. ELISAs were used to measure plasma adiponectin (B-Bridge International, Inc., San Jose, CA), IL-6 and TNF-α (R&D Systems Inc., Mineapolis, MN).

2.6. Statistical analysis

Data are presented as mean ± SD. Spearman correlations were used to quantify associations between changes in anthropometric parameters and changes in cardiometabolic risk markers. Paired *t*-tests were performed to compare baseline and achieved levels of cardiometabolic risk markers and anthropometric parameters. Because the changes in the markers of the lipoprotein-lipid profile and in inflammatory markers were similar across the 3 intervention groups, women of the 3 intervention groups were pooled together. All statistical analyses were performed with the SAS package (SAS Institute, Cary, NC).