Effect of an Energy-Restrictive Diet, With or Without Exercise, on Lean Tissue Mass, Resting Metabolic Rate, Cardiovascular Risk Factors, and Bone in Overweight Postmenopausal Women

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PURPOSE: To study the effect of exercise added to an energy-restrictive diet in overweight postmenopausal women.

SUBJECTS AND METHODS: In a longitudinal clinical study, 121 healthy, overweight postmenopausal women (age 53.8 ± 2.5 years, body mass index: 29.7 ± 3.1 kg/m^2) were randomly assigned to 3 groups: controls, a 4,200 kJ/d diet, or a 4,200 kJ/d diet with combined aerobic and anaerobic exercise. Body composition (measured by dual-energy x-ray absorptiometry), fat distribution, resting metabolic rate, blood pressure, serum lipids and lipoproteins, bone mineral densities, and markers of collagen and bone turnover were measured before and after 12 weeks of intervention.

RESULTS: One hundred eighteen women completed the study. The mean loss of body weight (9.5 kg versus 10.3 kg, NS) was similar in the intervention groups, but compared with the diet-only group, the diet-plus-exercise group lost more fat (7.8 kg versus 9.6 kg, p <0.001) and no lean tissue mass (1.2 kg versus −0.0 kg, p <0.001). The resting metabolic rate (per kg wt) was increased in the diet-plus-exercise group compared with the control group (11% versus 4%, p <0.009). The levels of serum triglycerides, total cholesterol, low-density lipoprotein, and very-low-density lipoprotein decreased, and the ratio of high-density lipoprotein to low-density lipoprotein increased by 20% to 30% in both intervention groups compared with the control group (p <0.001). The systolic blood pressure dropped, and the waist-to-hip circumference ratio and abdominal-to-total body fat decreased in both intervention groups compared with the control group (10%, p <0.003, and 3.5%, p <0.0001). There were no consistent, major differences between the groups in terms of changes in total body, spinal, or forearm bone mineral densities, or in markers of collagen and bone turnover.

CONCLUSION: Overweight postmenopausal women benefit from addition of combined aerobic and anaerobic exercise to an energy-restrictive diet. The diet itself has a positive effect on cardiovascular risk factors.

Overweight, especially in women, has reached epidemic proportions in the industrialized world [1]. It is an independent predictor of cardiovascular disease (CVD), which is currently the leading cause of death and disability in Western societies [2–4]. At any given time, about 50% of American women are estimated to be on a diet in an attempt to reduce weight [1], and this may constitute a potential health threat [5]. Besides the loss of fat, the lean body mass and the resting metabolic rate may also be reduced. Addition of exercise to an energy-restrictive diet may promote the loss of body weight and fat, but the reported effects on lean body mass, resting metabolic rate, serum lipids and lipoproteins, and fat distribution are conflicting and may differ between the sexes [6–12]. Since all studies on this topic have been performed in men and premenopausal women, very little is known about the changes in overweight postmenopausal women. Postmenopausal women are at increased risk of CVD; estrogen deficiency, an atherogenic lipid and lipoprotein profile, and fat distribution all play a role [4,13,14]. Osteoporosis is another major cause of morbidity and mortality in postmenopausal women [15]. The consequences of weight reduction from dieting, with or without exercise, on bone in the osteoporosis-prone postmenopausal woman are unknown. Thus, our aim was to study the effects of an energy-restrictive diet, with or without exercise, on body composition, major cardiovascular risk fac-

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tors, and bone in overweight postmenopausal women.

SUBJECTS AND METHODS

Subjects

To ensure a representative population of overweight postmenopausal women, we examined questionnaires that had been sent out 3 years earlier to all women (n = 11,375) aged 45 to 54 years living in 8 municipalities of Copenhagen County in the catchment area of Glostrup hospital [16].

Those (n = 2,580) who were potentially eligible for this study (i.e., had an intact uterus and no past or present illnesses, operations, or current medication known to influence the variables to be studied) were sent a new questionnaire to elicit the latest information on the last menstrual bleeding, weight, height, past and present illnesses, operations, and current use of drugs. Two thousand two hundred forty-one questionnaires were answered. Since 213 questionnaires were returned due to address unknown, the response rate was 95%. A total of 260 women with a self-reported body mass index (BMI) greater than or equal to 25, last menstrual bleeding at least 6 months earlier, and no past or present illnesses, operations, and current medication known to influence the variables studied were invited to attend an information meeting. One hundred thirty-seven (53%) women gave their informed consent to participate in the study and underwent an initial medical screening. Exclusion criteria were menstrual bleeding within the preceding 6 months, hysterectomy, BMI less than 25, weight loss within the preceding 3 months, lack of motivation or ability to participate in the study, psychiatric illness, cardiovascular (diastolic blood pressure greater than 100 mm Hg, systolic blood pressure greater than 190 mm Hg), pulmonary, catabolic, renal, or hepatic disease, and medication known to influence body composition (i.e., psychopharmaceutics [neuroleptics, cyclic antidepressants, monoamine oxidase inhibitors, and lithium], antiepileptics [valproate and carbamazepine], hormones [sex hormones, glucocorticoids, and growth and thyroid hormones], antihistamines [flunarizine, cyproheptadine, methysergide, and pizotifen], and catabolic drugs. Sixteen of the 137 women were excluded after the initial medical screening due to hysterectomy (n = 1), menstrual bleeding within the preceding 6 months (n = 4), recent weight loss (n = 2), electrocardiographic abnormalities (n = 1), disease (n = 5), or the use of medication (n = 3) known to influence the variables studied.

The study was carried out in accordance with the Declaration of Helsinki II and with the approval of the ethical committee of Copenhagen County.

Study Design

After the baseline examinations, the women were randomly assigned to 3 groups, the size of which was calculated so as to detect a significantly different change between groups of about 1 kg lean tissue mass, given a type I error of 0.05 and a type II error of 0.10, and assuming a dropout rate of 10% [17] (diet only [n ≈ 50], diet plus exercise [n ≈ 50], and control [n ≈ 20]). The diet-only subjects were asked to continue their usual exercise pattern and the control subjects to maintain their usual diet and exercise patterns. The women were re-examined 12 weeks later.

The diet consisted of an obligatory basis of the formula diet NUPO (Oluf Mørk Biochemie A/S, Rødovre, Denmark) of 1.6 MJ daily, within which all international recommendations for proteins, essential amino and fatty acids, vitamins, minerals, and trace elements are met [18]. The formula diet (NUPO) supplied protein 65 g, carbohydrates 21 g, dietary fibers 30 g, fat 5 g, and calcium and phosphorus 800 mg each daily. To encourage compliance and adherence, an additional energy consumption of up to 2.6 MJ daily was permitted from food freely chosen, according to a "counter diet system," which is described in detail elsewhere [18]. Briefly, it is based on tables and figures that give and illustrate the portion or amount of any food that corresponds to 260 kJ. Thus, up to 10 260-kJ portions could be eaten daily. Some of the 10 260-kJ portions could be spared some of the days in the week and spent on others (celebrations, weekends). Intake of proteins and carbohydrates was encouraged. Thus, the diet included an obligatory dietary supplement (NUPO) plus food.

The women were weighed, and records of their energy intake (number of 260 kJ portions) during the preceding week were collected at a weekly session. On alternate weeks, each woman saw a physician (OLS) for consultation; on the other weeks, the women attended a 1-hour group consultation supervised by a clinical nutritionist. Each group consisted of 10 women receiving the same type of intervention.

The exercise sessions were performed 3 times weekly, and each session consisted of a combination of aerobic exercise and resistance weight training, increasing in intensity and duration (1 to 1.5 hours). The exercise program was specially designed for this study for the purpose of promoting loss of fat (aerobic exercise) and offsetting the loss of lean tissue mass by increasing the muscle mass (resistance weight training) [6,7]. Aerobics were performed as 30 minutes (increasing to 55 minutes) of bicycling, stair walking, or treadmill running with the subject's heart rate above that corresponding to

70% of the maximum oxygen uptake (assessed at a baseline bicycle ergometer test). In between the aerobics, two (increasing to three) periods were spent on resistance weight training, in which all major muscle groups were exercised. Each resistance weight-training period consisted of 8 (increasing to 10) exercises, with 7 to 15 repetitions in each. The resistance training was performed as dynamic muscle exercising with sequence training equipment (Ultra Rehab Aps, Odense, Denmark). The following machines (muscles) were used: leg press (knee and hip extensors), leg flexor (knee and hip flexors), calf (lower leg muscles), laying leg raise (back and hip extensors), back exerciser (back and hip extensors), pull down (back and upper torso), dips (chest and arm muscles), rowing (back, upper arm, and shoulder), aduktin (hip adductors), and abdominal (abdominal muscles). The exercise sessions ended with muscle stretching. The women exercised in groups of about 10, under the supervision and with the encouragement of an instructor. The resistance weight was calculated individually for each woman as about 65% of the maximum weight she could lift at any given time. The weight was regularly checked and adjusted by the instructor. All the women kept an exercise log that was signed by the instructor.

Measurements

ANTHROPOMETRY: With the women wearing light indoor clothes and no shoes, weight was measured to the nearest 0.1 kg and height to the nearest 0.5 cm. The right triceps, subscapular, paraumbilical, and supra-iliac skinfold thicknesses were measured with the same Harpenden skinfold calipers to the nearest 0.5 mm 4 seconds after application (coefficient of variation [CV%]: 8%). Waist and hip circumferences were measured to the nearest 0.5 cm at the smallest standing horizontal circumference below the ribs and at the largest standing horizontal circumference at the buttocks, respectively (CV%: 1.6%). Skinfold thicknesses and circumferences were measured twice, and the means were used in the calculations.

Body composition, total as well as abdominal (from L2-L4), was measured with a total-body dual-energy x-ray absorptiometry (DXA) scanner (DPX, Lunar Radiation Corporation, Madison, WI, software version 3.2) [19,20]. The total body bone mineral density (TBBD) (CV%: 0.9%), the fat tissue mass (FTM) (CV%: 4.7%), and the lean tissue mass (LTM) (CV%: 1.5%) were measured. The FTM is not solely adipose tissue but the sum of the fatty elements of all the soft tissue. Similarly, the LTM is not an anatomic entity but represents the sum of all chemical fat-free soft tissue elements.

Bone mineral density (BMD) of the lumbar spine (L2-L4) was measured with a DXA scanner (QDR-1000, Hologic Inc., Waltham, MA, software version 4.29) (CV%: 1.2%) [21], and BMD of the forearm, proximal to the site where the distance between the radius and ulna is 8 mm, was measured bilaterally (means were used in the calculation) by single-photon absorptiometry (CV%: 1.1%) [22] (DT-100, Osteometer A/S, Rødovre, Denmark, software version 2.1).

Resting metabolic rate and maximum oxygen uptake were measured by a Medgraphics CCM and a CPX system (Medical Graphics Corporation, Minneapolis, MN), respectively [23]. The resting metabolic rate was measured in the morning after a 12-hour overnight fast by indirect calorimetry with a ventilated canopy for 20 to 40 minutes (CV%: 3.7%) [23]. The maximum oxygen uptake was assessed by performance of an exercise test with an interfaced computer-controlled cycle ergometer (MedGraphics CPE 2000), where the work load was increased by 1 W every 3 seconds until exhaustion set in and profound lactate production was reached (respiratory exchange ratio greater than or equal to 1.1) (CV%: 6.9%). Measurements were performed breath by breath, and the mean was taken every 30 seconds for the calculations.

Seven-day food diaries were kept before the intervention and in week 12 of the intervention. The diaries were checked by a clinical nutritionist and, if inadequate or erroneous, discussed with the women. The consumption of nutrients was determined from computerized food-composition tables (Dan-Kost, software version 1.3b, Danish Food Administration, Søborg, Denmark).

Blood pressure and pulse rate were measured after 10 minutes of supine rest. The blood pressure was measured once with a digital blood pressure meter (A & D, Tokyo, Japan) to the nearest 5 or 10 mm Hg.

Blood samples were taken and urine samples collected in the morning after at least 12 hours of overnight fasting. All samples were stored at −20°C until analyzed.

High-density lipoprotein (HDL) was isolated by a phosphotungstic acid-$MgCl_2$ precipitation technique [24]. Levels of serum total cholesterol (intra-assay and interassay CV%: 2%/3%), triglyceride (interassay CV%: 3%), and HDL cholesterol (intra-assay and interassay CV%: 3%/6%) were determined enzymatically by Chem1 (CHOD-PAP method, Technicon Instruments, Tarrytown, NY). Very-low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) were calculated according to the formula of Friedewald *et al* [25].

BIOCHEMICAL MARKERS OF BONE AND COLLAGEN TURNOVER: Serum alkaline phosphatase was mea-

TABLE I

Baseline Values of Clinical Characteristics*

	Control (n = 21)	Diet Only (n = 51)	Diet + Exercise (n = 49)
Body weight (kg)	76.6 ± 8.8	78.1 ± 7.8	78.1 ± 10.3
Energy intake (kJ/d)	7,766 ± 1,610	7,858 ± 1,969	7,922 ± 2,401
Protein intake (g/d)	62 ± 11	62 ± 13	60 ± 18
Fat intake (g/d)	77 ± 23	83 ± 28	83 ± 30
Cholesterol intake (mg/d)	324 ± 110	302 ± 112	299 ± 112
Carbohydrate intake (g/d)	195 ± 58	189 ± 60	192 ± 68
Calcium intake (mg/d)	759 ± 219	761 ± 329	737 ± 306
VO_2 max (mL/kg/min)	21.1 ± 3.1	19.5 ± 3.7	20.6 ± 3.7
Resting pulse (beats/min)	76 ± 12	74 ± 11	73 ± 11
Resting metabolic rate (kJ/kg/d)	80.3 ± 10.0	77.0 ± 8.4	76.6 ± 9.6
Lean tissue mass (kg)	42.7 ± 3.5	42.1 ± 4.1	42.2 ± 3.1
Fat tissue mass (kg)	29.2 ± 6.0	32.1 ± 7.0	31.9 ± 6.2
Sum of SF (mm)	112 ± 21	120 ± 19	119 ± 22
Subscapular SF (mm)	28 ± 7	29 ± 7	29 ± 7
Abd/TB FTM (10^{-3})	98.9 ± 13.4	95.2 ± 11.2	88.8 ± 13.8
Waist-to-hip ratio	0.84 ± 0.09	0.84 ± 0.07	0.83 ± 0.08
Triglycerides (mmol/L)	1.21 ± 0.53	1.48 ± 0.91	1.20 ± 0.51
Cholesterol (mmol/L)			
Total	7.01 ± 1.11	6.98 ± 1.13	6.63 ± 1.14
HDL	1.68 ± 0.34	1.58 ± 0.37	1.65 ± 0.37
LDL	4.76 ± 1.11	4.70 ± 1.03	4.41 ± 1.13
HDL/LDL	0.38 ± 0.14	0.36 ± 0.12	0.41 ± 0.17
Blood pressure (mm Hg)			
Systolic	129 ± 19	129 ± 15	128 ± 18
Diastolic	80 ± 8	79 ± 9	79 ± 10

SF = skinfold thicknesses; Abd/TB FTM = abdominal-to-total body fat tissue mass; VO_2 max = maximal oxygen uptake; HDL = high-density lipoprotein; LDL = low-density lipoprotein.
*Mean ± SD. There were no differences between groups ($p > 0.05$, analysis of variance).

sured by routine procedures. Plasma bone Gla protein (osteocalcin) was determined by radioimmunoassay (intra-assay and interassay CV%: 3%/10%) [26]. Alkaline phosphatase and osteocalcin are believed to be noncollagenous markers of bone formation [26,27]. Serum carboxy-terminal propeptide of type I procollagen (PICP) (intra-assay and interassay CV%: 3%/7%) [28] and aminoterminal propeptide of type III procollagen (PIIINP) (intra-assay and interassay CV%: 3%/5%) [29] were measured by radioimmunoassay (Farmos Diagnostica, Turka, Finland). PICP is believed to be a marker of bone collagen formation, whereas PIIINP is believed to be a marker of nonbone collagen turnover [28–30]. Fasting urinary (FU) creatinine (cr) was measured on a SMA6/60 autoanalyzer (Technicon Instruments, Tarrytown, NY). Fasting urinary hydroxyproline (OHPr) was measured by a spectrophotometric method (intra-assay and interassay CV%: 15%/20%) [31], and fasting urinary pyridinoline (pyr) and deoxypyrdinoline (D-pyr) cross-links were measured by high-pressure liquid chromatography after CF1 partition column chromatography (intra-assay and interassay CV%: 5%/10%) [32]. FU creatinine, OHPr, pyr, and D-pyr were corrected for urinary creatinine excretion. Pyr and D-pyr are believed to be collagenous markers of bone resorption, whereas OHpr is believed to be a less specific collagenous marker of bone resorption [27,33].

The data collectors were "semi-blinded" to the treatment assignment, i.e., records and registration numbers were blinded, but the subjects were not, and they might have informed, directly or indirectly, the data collectors.

Calculations and Statistical Analysis

The waist-to-hip circumference ratio and the abdominal-to-total body fat tissue mass (by DXA)

TABLE II

Changes in Clinical Characteristics (mean ± SD) After 12 Weeks

	Control (n = 20)	Diet Only (n = 50)	Diet + Exercise (n = 48)	Analysis of Variance (p <)
Body weight (kg)	0.5 ± 1.7	−9.5 ± 2.8	−10.3 ± 3.0	0.001
Energy intake (kJ/d)	−59 ± 1,461	−3,287 ± 2,076	−3,526 ± 2,378	0.001
Protein intake (g/d)	−2 ± 12	33 ± 15	33 ± 18	0.001
Fat intake (g/d)	6 ± 17	−52 ± 29	−54 ± 29	0.001
Cholesterol intake (mg/d)	−30 ± 116	−174 ± 113	−193 ± 119	0.001
Carbohydrate intake (g/d)	−18 ± 17	−93 ± 61	−98 ± 69	0.001
Calcium intake (mg/d)	−9 ± 185	429 ± 344	439 ± 349	0.001
VO_2 max (mL/kg/min)	1.8 ± 10.4	2.3 ± 2.2	6.9 ± 9.6*	0.005
Resting pulse (beats/min)	−2 ± 7	−5 ± 10	−9 ± 11	0.014
Resting metabolic rate (kJ/kg/d)	2.9 ± 5.9	5.4 ± 6.7	8.8 ± 8.8	0.009
Lean tissue mass (kg)	0.6 ± 1.3	−1.2 ± 1.3	0.0 ± 1.7*	0.001
Fat tissue mass (kg)	0.5 ± 1.3	−7.8 ± 2.5	−9.6 ± 2.7*	0.001
Sum of SF (mm)	5 ± 11	−23 ± 13	−32 ± 15*	0.001
Subscapular SF (mm)	1 ± 6	−6 ± 4	−9 ± 5*	0.001
Abd/TB FTM (10^{-3})	−2.3 ± 4.6	−9.6 ± 8.4	−11.2 ± 6.8	0.001
Waist-to-hip ratio	0.01 ± 0.03	−0.03 ± 0.03	−0.03 ± 0.04	0.001
Triglycerides (mmol/L)	0.12 ± 0.32	−0.50 ± 0.69	−0.30 ± 0.46	0.001
Cholesterol (mmol/L)				
Total	−0.11 ± 0.46	−1.36 ± 0.84	−1.23 ± 0.67	0.001
HDL	−0.09 ± 0.22	−0.05 ± 0.31	−0.10 ± 0.23	0.42
LDL	−0.07 ± 0.50	−1.08 ± 0.70	−0.99 ± 0.68	0.001
HDL/LDL	−0.02 ± 0.06	0.10 ± 0.11	0.08 ± 0.11	0.001
Blood pressure (mm Hg)				
Systolic	−2 ± 11	−13 ± 12	−11 ± 11	0.003
Diastolic	−4 ± 7	−7 ± 8	−9 ± 8	0.059

Abbreviations as in Table I.
*p <0.05 different from diet only group.

were calculated as indicators of fat distribution. Differences in changes between groups were compared by one-way analysis of variance for continuous variables and by the χ^2 test of association for categorical variables. The significance level was 0.05, and Bonferroni adjustments were used for pair-wise comparisons between the intervention groups. Logarithms were used in the statistical analysis of the biochemical parameters. For simplicity, normal means and standard deviations are given in the results. The relation between measurements is expressed by Pearson's coefficient of correlation. The Statistical Analysis System (SAS Institute Inc., Cary, NC) was used for all analyses.

RESULTS

One hundred twenty-one women (age: 53.8 ± 2.5 year), with a postmenopausal age of 5.9 years (±3.9) (mean ± SD), were entered in the study and were allocated at random to the diet-only group (n = 51), the diet-plus-exercise group (n = 49), or the control group (n = 21). There were no statistically significant differences between the groups in the baseline values for any of the variables studied (**Table I**). Furthermore, there was no statistically significant difference between the groups in the time spent on exercise per week (1 h), number of smokers (23%), and number of cigarettes smoked daily, nor were there any changes in the number of smokers or cigarettes smoked daily at 12 weeks. Three women dropped out, one from the control group because of prolonged pneumonia, and one from each of the other two groups for personal reasons. Thus, 118 women (97.5%) completed the study.

Table II shows the changes in clinical characteristics at 12 weeks. The aerobic capacity increased in the diet-plus-exercise group (attendance at exercise sessions: 97%) compared with the diet-only and

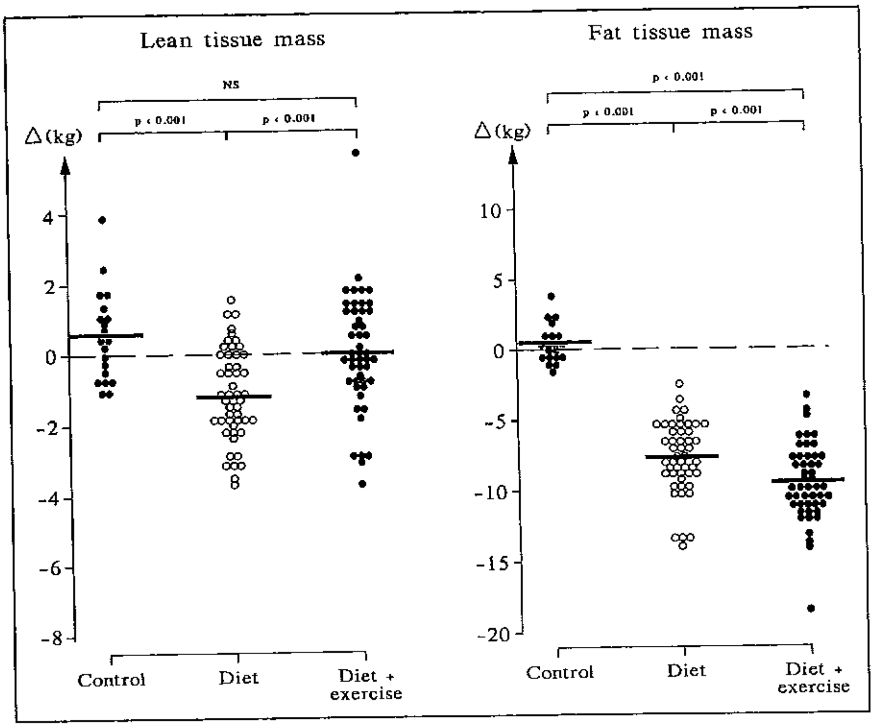

Figure 1. Changes in lean and fat tissue mass after 12 weeks in the control group (n = 20), diet-only group (n = 50), and diet-plus-exercise group (n = 48).

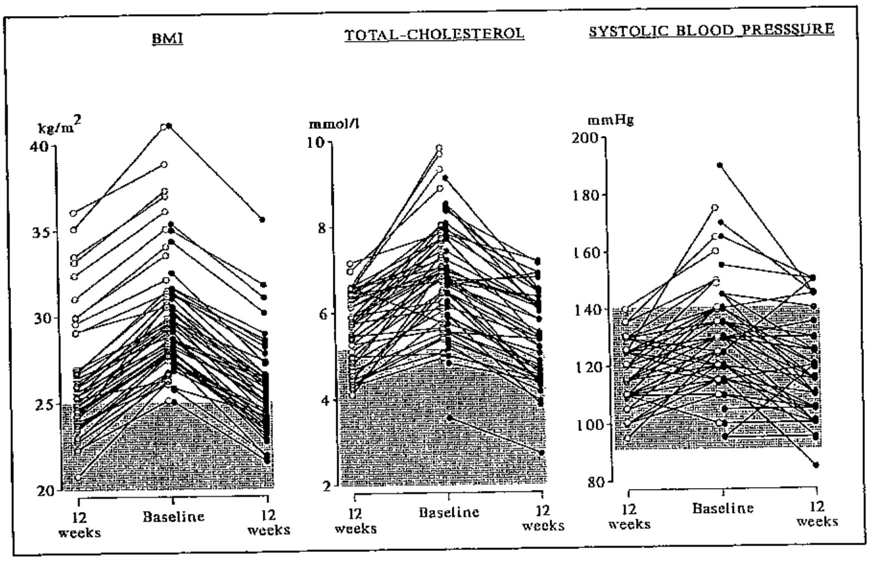

Figure 2. Individual changes after 12 weeks in body mass index, serum total cholesterol, and systolic blood pressure in the diet-only group (**open circles**, n = 50) and the diet-plus-exercise group (**closed circles**, n = 48). **Hatched regions** indicate recommended values [35–37].

control groups. The total energy intake decreased, the energy percent intake (percentage of total energy intake) from fat decreased (9 to 10 energy%), whereas the energy percent intake from protein (5 energy%) and carbohydrates (7 to 8 energy%) increased significantly in the intervention groups (compared with the control group), but with no significant difference between the diet-only and the diet-plus-exercise groups. Furthermore, there was no difference between the groups in the changes in the energy percent intake from ethanol ($p < 0.16$).

All women in the two intervention groups lost weight (range: 2.5 kg to 18.9 kg). The mean loss in weight was identical, but the composition of the loss was significantly different (**Figure 1**). In the diet-plus-exercise group, the loss of lean tissue mass was prevented and the loss of fat was increased compared with that in the diet-only and control groups. Furthermore, the resting metabolic rate (per kg wt) increased in the diet-plus-exercise group compared with that of the control group (Table II).

The waist-to-hip circumference ratio and the abdominal-to-total body fat tissue mass ratio decreased equally in the intervention groups compared with the control group, whereas the decrease in skinfold thicknesses was significantly higher in the diet-plus-exercise group than in the diet-only and control groups.

TABLE III

Baseline and Changes (in Percentage of Baseline) in Bone Mineral Density (BMD) and Noncollagenous Markers of Bone Turnover*

	Baseline (n = 121)	Changes (%) Control (n = 20)	Diet Only (n = 50)	Diet + Exercise (n = 48)	Analysis of Variance (p <)
BMD					
Total body (g/cm²)	1.13 ± 0.082	−1.2 ± 2.0	−1.9 ± 2.4	−1.9 ± 3.1	0.27
Lumbar spine (g/cm²)	0.99 ± 0.15	−0.4 ± 2.2	−1.6 ± 2.8	−2.4 ± 2.4	0.02
Forearm (g/cm²)	0.44 ± 0.061	0.1 ± 1.4	0.3 ± 2.2	0.2 ± 2.6	0.84
Osteocalcin (ng/mL)	7.2 ± 3.8	−11 ± 30	−29 ± 23	−22 ± 20	0.048
Alkaline phosphatase (U/L)	173 ± 47	4 ± 11	6 ± 36	−4 ± 37	0.45

*Values are mean ± SD.

TABLE IV

Baseline and Changes (in Percentage of Baseline) in Markers of Collagen Turnover*

	Baseline (n = 121)	Changes (%) Control (n = 20)	Diet Only (n = 50)	Diet + Exercise (n = 48)	Analysis of Variance (p <)
PIIINP (ng/mL)	3.6 ± 0.8	9.7 ± 9	−3.7 ± 18	2.2 ± 26	0.025
PICP (ng/mL)	130 ± 42	6 ± 11	12 ± 26	27 ± 30†	0.005
FU-OHPr/cr (mmol/mol)	10.1 ± 3.8	16 ± 62	14 ± 41	22 ± 53	0.78
FU-pyr/cr (μmol/mol)	61.3 ± 15.0	7 ± 19	22 ± 24	21 ± 27	0.07
FU-D-pyr/cr (μmol/mol)	9.5 ± 2.7	9 ± 22	32 ± 30	30 ± 33	0.011

*Values are mean ± SD. For abbreviations, see "Measurements" (Subjects and Methods).
†p <0.05 different from diet only group.

Serum triglycerides, total cholesterol, LDL, VLDL, and the systolic blood pressure decreased significantly, whereas the HDL to LDL ratio increased significantly (by 20% to 30%) and equally in both intervention groups compared with the control group. The reduction in the 12-year risk of cardiovascular disease, predicted by equations developed by Anderson *et al* [34], was similar (about 33%) in the intervention groups but different from that in the control group ($p < 0.001$).

Figure 2 illustrates the profound individual reductions in and drop to the recommended values [35–37] for three major independent CVD risk factors in the intervention groups. The losses in weight, fat tissue mass, and abdominal-to-total fat tissue mass were significantly correlated to the decrease in total cholesterol in the pooled ($r = 0.63$, 0.64, and 0.42, respectively, $p < 0.001$) as well as in the intervention groups alone (r about 0.28, $p < 0.01$). Similar findings were obtained for LDL. The changes in the waist-to-hip circumference ratio were significantly correlated only to the changes in total cholesterol and LDL in the pooled population ($r = 0.31$, $p < 0.001$).

Table III shows the changes in BMD, osteocalcin, and alkaline phosphatase. The measured BMD of the lumbar spine decreased statistically significantly in the diet-plus-exercise group, and, although not statistically significantly, the BMD of the total body tended to decrease in the intervention groups compared with the control group. BMD of the forearm did not change significantly in the intervention groups compared with the control group. Osteocalcin (noncollagenous marker at bone formation) tended to decrease in the intervention groups compared with the control group.

Table IV gives the changes in markers of collagen turnover. PICP (marker of bone collagen formation) had increased statistically significantly in the diet-plus-exercise group compared with the diet-only group. Fasting urinary pyr and d-pyr (collagenous markers of bone resorption) tended to increase in both intervention groups compared with the control group.

COMMENTS

The groups were well matched at baseline, and compliance and adherence to the study design were high, with a dropout rate of 2.5%. All the women in the intervention groups lost weight, and those on the diet-plus-exercise regimen increased their cardiopulmonary capacity. A permanent energy-restrictive, low-saturated-fat, low-cholesterol diet is recommended for the prevention of CVD and the treatment of overweight [1,36]. However, many persons are unsuccessful in maintaining a diet over a long period; thus, energy-restrictive diets of various kinds are widely used for short periods. At any time, about 50% of American women are dieting in an attempt to lose weight, and Americans spent an estimated $33 billion on diets and diet-related products and services in 1992 [1,38]. Fluctuation in body weight, i.e., repeated weight loss and gain, is strongly and independently associated with increased risk of CVD and mortality [5]. The loss of lean tissue might be associated with decreased functional status and survival of illness and aging [39].

Many studies have investigated the effect of exercise added to an energy-restrictive diet, but only three of these were properly controlled and randomized [8–10]. Aerobic exercise combined with an energy-restrictive diet did not prevent the loss of lean body mass in obese men and premenopausal women, whereas anaerobic training added to an energy-restrictive diet (with a protein supplement) preserved lean body mass and increased the muscle mass of obese premenopausal women [9]. We found that the addition of combined aerobic and anaerobic exercises to an energy-restrictive diet promoted the loss of fat and preserved the lean tissue mass in overweight postmenopausal women. A high protein intake seems to be necessary for a response to exercise, and, further, the effect on the composition of the weight lost may depend on the type, intensity, frequency, and duration of the exercise [7]. The difference in energy lost with changes in lean and fat tissue mass between the diet-only and the diet-plus-exercise groups corresponds to an estimated energy expenditure at each exercise session of 1.6 MJ. The resting metabolic rate (per kg wt) was also increased by the exercise. This suggests that exercise added to an energy-restrictive diet preserves, or even increases, the energy-expending lean tissue, like muscles, while decreasing the less energy-expending tissue. These results agree with those of previous reports [8,9], and, together, they suggest that anaerobic exercise may preserve lean tissue mass, whereas aerobic exercise may increase the loss of fat tissue mass when added to a diet with a high protein intake. However, further studies are needed to confirm this. Postmenopausal women who exercise as well as diet may benefit from a decreased risk of falls, fracture, and all-cause mortality due to improved physical fitness and lean tissue mass [15,40].

The effect on lipids and lipoproteins of combined aerobic and anaerobic exercises added to a diet in overweight postmenopausal women has not been described previously. In our sample of healthy, overweight postmenopausal women, there was a profound decrease in all risk factors for CVD, i.e., body mass index, lipids, and lipoproteins (except HDL), systolic blood pressure, and waist-to-hip circumference ratio, which was similar whether or not exercise was added to the diet.

To some extent, these results agree with findings in premenopausal women, in whom aerobic exercises and a 6,000-kJ, low-saturated-fat, low-cholesterol-fat diet for 1 year preserved HDL_2; otherwise, the decreases in lipids and lipoproteins were the same, whether or not exercise was added to the diet [10]. A 4,800-kJ diet, with or without aerobic exercise, did not produce changes in the lipids, lipoproteins, or blood pressure of premenopausal women [8]. On the other hand, the men in these two studies who exercised aerobically and dieted had significant decreases in body weight, fat, and various lipids and lipoproteins compared with those who only dieted and the controls.

Every 1% reduction in total cholesterol and LDL may reduce the risk of coronary heart disease by about 1.7% [41–43]. Thus, in this study of healthy, overweight postmenopausal women, the mean reduction in the estimated 12-year risk of CVD was 33%. However, if the reductions in body mass index, waist-to-hip circumference ratio, subscapular skinfold thickness, and systolic blood pressure, all of which are independent predictors of CVD [3,44–46], are taken into account, the reduction in the risk of CVD may even be larger. For instance, the relation of systolic blood pressure to the risk of CVD and all-cause mortality is strong, continuous, and graded, and the decline in systolic blood pressure of 12 mm Hg found in this study might reduce the number of annual deaths in middle-aged Americans by about 18% [46]. However, the estimated reductions in the risk of CVD and death imply that the present health status is maintained, without fluctuations in weight.

The "counter diet system" in this study is designed, unliked liquid very-low-calorie diets, to permit the subject to visualize and remember the energy (and fat) content of foods [18]. This knowledge might, at least theoretically, ensure adaption to an energy consumption required for maintaining weight after a weight loss. However, this needs to be addressed in a follow-up study.

The accuracy of bone mineral measurements may be slightly affected by the mass and the composition of the covering soft tissue [21]. Thus, the dramatic changes in soft tissue mass and composition in the present study could result in minor inaccuracies of the measured changes in the BMD, but major changes in BMD as a result of the intervention can be ruled out. There were no consistent, unequivocal effects on markers of noncollagenous bone turnover and collagen turnover, and the results are difficult to interpret. There might have been a slight increase in bone resorption. Major effects on bone turnover seem unlikely, but there might have been a 1% to 2% loss in BMD of the weight-bearing bones due to the intervention. This may be of no potential health hazard, unless the diet, with or without exercise, is continued. What happens to the bones after cessation of a diet, with or without exercise, is unknown. These issues need further investigation, and we are currently performing a follow-up study.

We conclude that, in overweight postmenopausal women, addition of combined aerobic and anaerobic exercise to a high-protein, energy-restrictive diet preserves lean tissue mass, promotes physical fitness, and increases the resting metabolic rate and loss of fat. The diet, with or without exercise, led to profound improvements in serum lipids and lipoproteins, blood pressure, and fat distribution. The weight loss induced by the diet, with or without exercise, does not seem to have any major detrimental effect on bone.

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