Scand J Med Sci Sports 2003: 13: 284–292
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 · ISSN 0905-7188
SCANDINAVIAN JOURNAL OF MEDICINE & SCIENCE IN SPORTS

Walking trials in postmenopausal women: effect of low doses of exercise and exercise fractionization on coronary risk factors

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Accepted for publication 17 March 2003

We studied the fractionization of walking training and searched for the minimum dose to affect coronary risk factors in two randomized controlled trials. Altogether 134 (Study I) and 121 (Study II) healthy, sedentary postmenopausal women started the trials, and 130 (Study I) and 116 (Study II) completed them. In Study I the exercise intensity was 65% of the maximal aerobic power (VO_{2max}) and a total of 300 kcal was expended in one (Group W1) or two (Group W2) daily walking bouts. In Study II the exercise was continuous, and the exercise intensity (% of VO_{2max}) and energy expenditure (kcal session^{-1}) were 55% and 300 kcal (Group W3), 45% and 300 kcal (Group W4), 55% and 200 kcal (Group W5) and 45% and 200 kcal (Group W6). All the subjects walked 5 days a week. The outcome measures were blood pressure, serum lipoproteins and blood glucose and plasma insulin in fasting state and also during 2-h oral glucose tolerance test in Study I. There was no change in diastolic pressure in the original study groups, but in the combined exercise group (W1+W2) in Study I, the mean diastolic pressure declined by −3.0 mmHg (95% confidence interval (CI) −5.5 to −0.4) ($P = 0.025$) in comparison with that of the controls. The mean blood glucose declined by −0.21 mmol L^{-1} (CI −0.33 to −0.09) in Group W1 and −0.13 mmol L^{-1} (CI −0.25 to −0.01) in Group W2 compared to controls ($P = 0.03$). Also the 2-h glucose concentration decreased in Groups W1 and W2 compared to controls. Systolic blood pressure, serum lipoproteins and insulin levels did not change in Study I or Study II. We conclude that our training program with the greatest exercise dose, exercise intensity 65% of VO_{2max} and weekly expenditure of 1500 kcal had a minimal, positive effect on diastolic pressure and blood glucose, and the effect was similar in one or two daily exercise session groups. This exercise dose is probably close to the minimum to affect coronary risk factors in healthy postmenopausal women. To get a more pronounced and clinically relevant effect, a greater exercise dose is needed.

Coronary heart disease (CHD) is the leading cause of death among postmenopausal women in the western world (Goodman & Kirwan, 2001). Abdominal obesity, postmenopausal estrogen deficiency and physical inactivity are associated with reduced insulin sensitivity and impaired glucose homeostasis, which leads to the entity of "menopausal metabolic syndrome". In turn, metabolic syndrome is associated with CHD and type 2 diabetes. Weight loss, especially loss of abdominal adipose tissue and increased physical activity, and also hormone replacement therapy (HRT) can reverse this syndrome (Spencer, 1997). The American Heart Association has given preventive guidelines for women (Mosca et al., 1999) with exercise recommendations supporting the physical activity recommendation for health (Pate et al., 1995). The statement suggests that every adult accumulate 30 min or more of moderate-intensity physical activity on most, but preferably, all days of the week. This corresponds to an exercise volume of approximately 200 kcal day^{-1} and 1000–1400 kcal week^{-1}.

Epidemiological studies indicate a linear dose–response relationship between physical activity and all-cause mortality, consisting mostly of CHD (see Kesäniemi et al., 2001). The energy expenditure of physical activity, needed to induce a 30% reduction in mortality for sedentary subjects, is around 1000 kcal week^{-1}. The minimum effective amount of exercise for health effects is not known, but it is estimated to be lower. Even exercise doses as low as 500 kcal week^{-1} are claimed to have some beneficial effect on all-cause mortality (Kohl, 2001; Lee & Skerret, 2001). In their follow-up study of almost 40 000 women, aged 45 years or over, Lee et al. (2001) found that the time spent in walking was more important than exercise intensity, and at least 1 h of light to moderate activity weekly decreased the CHD risk. This amount is less than the recent recommendation of physical activity for health suggests (Pate

et al., 1995). More studies are needed to clarify the matter especially on women, because most studies have been conducted on men (Lee & Skerret, 2001; Wilmore, 2001).

Epidemiological evidence suggests that activities performed on a regular basis, even in several sessions a day, will influence health outcomes if the total energy expended is sufficient (Paffenbarger et al., 1986; Haapanen et al., 1996; Hardman, 2001). To our knowledge only four randomized, controlled studies have been carried out to compare the effects of fractionated exercise vs. continuous exercise on CHD risk factors – two on lipids (Ebisu, 1985; Woolf-May et al., 1999) and two on blood pressure (Jakicic et al., 1995; Murphy & Hardman, 1998) and only one of these included postmenopausal women (Woolf-May et al., 1999).

We conducted two randomized, controlled studies, the first to compare the effects of equivolume brisk walking, once or twice a day, and the second to compare the effects of four low-dose walking programs on selected CHD risk factors in postmenopausal women. We have previously reported that all of these programs increased maximal aerobic power, and some of them also positively affected body composition (Asikainen et al., 2002a, b). In our present report, our hypothesis was that equivolume exercise would improve coronary risk factors equally in exercise groups with one or two sessions a day. In addition, low-dose walking programs would show small improvements in risk factors, and the minimum effective dose would be approached.

Materials and methods

Design

Study I was a randomized, controlled trial with three parallel groups: exercise with one or two daily walking sessions and a control group (Asikainen et al., 2002b). Study II was a randomized, controlled trial with five parallel groups, four low-dose exercise groups and a control group (Asikainen et al., 2002a). The exercise in Study I started in September 1995 and continued for 15 weeks. The exercise in Study II started in November 1996 and continued for 24 weeks. The outcome measures were blood pressure, fasting serum lipoproteins, and blood glucose and plasma insulin in fasting state, and in Study I, also during a 2-h oral glucose tolerance test. The study plan was approved by the independent Research Ethics Committee of the UKK Institute for Health Promotion Research. All the subjects gave their written informed consent.

Subjects

The subjects were recruited through announcements in the local newspapers. The recruitment processess have been described in detail previously (Asikainen et al., 2002a, b). The eligibility criteria were (1) female, (2) 2–10 years past the onset of menopause, (3) 48–63 years of age, (4) no chronic diseases or regular medication except for possible HRT, (5) nonsmoker, (6) body mass index (BMI) $<32\,kg\,m^{-2}$, (7) systolic pressure <160 mmHg and diastolic pressure <100 mmHg, and (8) not engaged in strenuous work or regular brisk leisure-time exercise more than once a week. An equal number of women with and without HRT were accepted.

Randomization

We randomly assigned the subjects to exercise or control groups. The HRT users and nonusers were randomized separately in order to get an approximately equal number of both in each group. The procedure yielded 46, 43 and 45 subjects in the two exercise groups and the control group, respectively, in Study I and 21, 21, 18, 21 and 40 subjects in the four exercise groups and the control group, respectively, in Study II. The randomization processes were computer based and have been described in detail previously (Asikainen et al., 2002a, b). The baseline characteristics of the subjects are shown in Table 1.

Exercise intervention

The exercise groups walked 5 days a week. In Study I the exercise intensity was 65% of the maximal aerobic power

Table 1. Baseline characteristics of the subjects in Study I and Study II*; means (SD)

Parameter	Study I			Study II				
	Group W1	Group W2	Group C1	Group W3	Group W4	Group W5	Group W6	Group C2
N	46	43	45	21	21	18	21	40
Age (years)	58 (4.4)	58 (4.2)	57 (4.2)	57 (3.8)	55 (3.7)	54 (3.5)	55 (4.2)	56 (3.8)
Body mass (kg)	67.6 (8.2)	67.9 (8.5)	67.0 (8.5)	67.9 (10.4)	68.7 (9.5)	67.5 (10.9)	66.1 (8.5)	70.8 (9.3)
VO_{2max} ($mL\,kg^{-1}\,min^{-1}$)	29.0 (3.8)	28.4 (3.6)	27.7 (3.5)	30.3 (5.0)	30.8 (4.2)	29.4 (4.1)	30.2 (4.1)	29.3 (3.6)
Systolic pressure (mmHg)	126.6 (14.7)	124.8 (12.3)	125.1 (17.1)	125.3 (14.6)	121.8 (15.1)	127.6 (16.7)	124.1 (14.6)	128.1 (15.8)
Diastolic pressure (mmHg)	80.5 (7.1)	80.1 (7.5)	82.3 (7.4)	80.3 (9.1)	79.6 (11.6)	80.4 (9.3)	75.9 (9.3)	81.1 (7.4)
Total cholesterol ($mmol\,L^{-1}$)	5.53 (1.00)	5.78 (0.99)	5.72 (0.98)	5.39 (0.63)	5.34 (1.02)	5.31 (0.97)	5.15 (0.79)	5.49 (0.94)
HDL-cholesterol ($mmol\,L^{-1}$)	1.56 (0.32)	1.54 (0.43)	1.56 (0.33)	1.68 (0.41)	1.60 (0.28)	1.55 (0.44)	1.62 (0.41)	1.57 (0.32)
LDL-cholesterol ($mmol\,L^{-1}$)	3.46 (0.95)	3.55 (0.94)	3.53 (0.88)	3.06 (0.53)	3.22 (1.02)	3.19 (0.98)	2.97 (0.72)	3.36 (0.84)
Triglycerides ($mmol\,L^{-1}$)	1.12 (0.34)	1.60 (1.63)	1.39 (0.57)	1.28 (0.53)	1.15 (0.29)	1.14 (0.45)	1.34 (0.42)	1.25 (0.41)
Glucose ($mmol\,L^{-1}$)	4.46 (0.30)	4.48 (0.32)	4.44 (0.32)	4.78 (0.33)	4.75 (0.26)	4.96 (0.44)	4.88 (0.30)	4.82 (0.35)
Insulin ($mU\,L^{-1}$)	6.3 (2.0)	6.9 (2.5)	6.9 (2.0)	7.1 (1.7)	7.1 (1.8)	8.2 (4.0)	7.4 (1.8)	7.9 (2.3)

*Study I: Groups W1 and W2 were the exercise groups and Group C1 was the control group.

Study II: Groups W3, W4, W5 and W6 were the exercise groups and Group C2 was the control group.

VO_{2max} = maximal aerobic power, HDL = high-density lipoprotein, LDL = low-density lipoprotein.

(VO_{2max}) and the estimated exercise energy expenditure was 300 kcal. Walking was performed in one (Group W1) or two daily sessions (Group W2). In Study II the exercise was carried out in one daily session, and different combinations of exercise intensity (% of VO_{2max}) and energy expenditure (kilocalories per session) were used: 55% and 300 kcal (Group W3), 45% and 300 kcal (Group W4), 55% and 200 kcal (Group W5) and 45% and 200 kcal (Group W6).

The target heart rate and duration of exercise were determined individually on the basis of a maximal exercise test (Asikainen et al., 2002a, b). Two weekly exercise sessions were supervised and conducted on an inside track, and other sessions were performed outdoors. The supervised exercise sessions of Groups W1 and W2 started with a light dynamic muscle workout for the main muscle groups. A few minutes of stretching was recommended before and after the exercise sessions for all the exercisers. Heart rate monitors (Polar Edge, Polar Electro, Kempele, Finland), step counters (Fitty 3, Kasper & Richter, Uttenreuth, Germany) and exercise diaries were used. The dietary and exercise habits and HRT use of all the subjects were checked with a questionnaire, followed by an interview, at the beginning and end of the intervention. Groups W3, W4, W5 and W6 also completed 3-day food diaries at the beginning and end of the intervention.

Measurements

All the measurements were conducted before and after the training period. Blood pressure was measured twice with a random zero sphygmomanometer (Hawksley & Son Ltd., England) as the subject sat after 5 min rest. The lowest of the two measurements with a 2-min interval was used.

Venous blood samples were obtained at 7 to 9 AM after a 12-h overnight fast, after a 15-min rest, while the subject was supine. The preceding exercise was approximately 48 h before the sampling. Fasting blood samples were taken for serum lipoproteins, baseline glucose and insulin determinations. In Study I an oral glucose tolerance test (OGTT) was carried out with a glucose dose of 75 g. Blood was sampled at 30, 60 and 120 min during OGTT for glucose and insulin measurements. In Study II the fasting blood samples were taken twice with a 1- week interval. The mean of the two measurements was used.

In both studies all analyses except glucose were made from frozen ($-70\,^{\circ}C$ to $-20\,^{\circ}C$) samples, and all samples from each subject were analyzed within a single batch to minimize analytical variations. Total serum cholesterol and triglyceride concentrations were measured using routine enzymatic methods. High-density lipoprotein cholesterol (HDL-cholesterol) was determined by dextran sulfate precipitation. Low-density lipoprotein cholesterol (LDL-cholesterol) was calculated by the equation of Friedewald et al. (1972). Blood glucose was assessed by the glucose dehydrogenase method. Plasma insulin determinations were carried out by radioimmunoassay (Phadeseph Insulin RIA, Pharmacia, Sweden).

The analytic variations (interassay CV) calculated from human serum-based quality control materials were 0.8–1.1% for total cholesterol, 1.9–1.1% for HDL-cholesterol at the concentration level 1.4–1.6 mmol L^{-1}, 4.2–4.6% at a very low HDL-cholesterol level 0.50 mmol L^{-1}, 1.1–3.8% for triglycerides, 0.8–3.4% for glucose and 2.1–5.0% for insulin.

Sample size and statistical analyses

The sample size calculations were originally performed for VO_{2max}, which was the main outcome of the study. Power calculations and statistical analyses have been described in detail previously (Asikainen et al., 2002a, b). On the basis of the widths of calculated confidence intervals of group differences, it can be concluded that sample size was adequate also in order to sufficiently find group differences of the risk factors. The intention-to-treat principle was used, and all the subjects were asked to participate in the end measurements, in spite of adherence to the exercise program or change in HRT use.

The results are given as means and standard deviations (SD). An analysis of covariance (ANCOVA) with the baseline measurements as the covariates was used to analyze the training effects, which were determined as net differences, i.e., mean differences between the changes in each walking group and the control group adjusted for baseline values. We also calculated the 95% confidence intervals (CI) for the mean net changes. In addition, the possible modifying effect of the HRT use was analyzed by an ANCOVA with the exercise groups and HRT group as factor variables. Additional ANCOVA analyses were performed in Study II with the groups combined according to exercise intensity or energy expenditure, with the baseline measurements as covariates.

Results

Compliance

All the subjects attended 88–95% of the prescribed exercise sessions in both studies. There were few injuries or other complications. Three of the 88 exercising subjects discontinued the exercise program in Study I, and three of 81 did so in Study II. There were four dropouts from the end measurements in Study I and eight in Study II. No changes in diet were reported in the questionnaire. For food diaries in Study II, four persons were missing, and seven were disqualified because of recording inaccuracies. The results showed no statistically significant quantitative or qualitative changes in the diet of the study groups. The mean estimated daily energy intake was 7.5 (1.5) MJ in the exercise groups and 7.6 (1.3) MJ in the control groups before the training and 7.5 (1.4) MJ and 7.3 (1.4) MJ after the training. Six subjects changed their use of HRT in Study I, and none did so in Study II.

Maximal aerobic power and body mass

In both studies, maximal aerobic power of the exercise groups improved statistically significantly ($P < 0.001$) when compared with that of the controls. Mean net changes in VO_{2max} were 2.5 mL min^{-1} kg^{-1} (CI 1.5–3.5), 2.5 mL min^{-1} kg^{-1} (CI 1.5–3.5), 2.9 mL min^{-1} kg^{-1} (CI 1.5–4.2), 2.6 mL min^{-1} kg^{-1} (CI 1.3–4.0), 2.4 mL min^{-1} kg^{-1} (CI 0.9–3.8) and 2.2 mL min^{-1} kg^{-1} (CI 0.8–3.5) in Groups W1, W2, W3, W4, W5 and W6, respectively. The mean body mass decreased when compared with that of the controls ($P = 0.001$) in Study I, -1.2 kg (CI -1.8 to -0.5) in Group W1 and -1.1 kg (CI -1.8 to -0.4) in Group W2, but in Study II there were no statistically

significant body mass changes (Asikainen et al., 2002a, b).

In Study I the VO_{2max} and body mass changes were similar in the one-session (W1) and two-session (W2) walking groups (Fig. 1). In Study II, combining the exercise groups according to exercise intensity (Group W3+Group W5 and Group W4+Group W6) or exercise energy expenditure (Group W3+ Group W4 and Group W5+Group W6) showed similar results in combined groups (Fig. 1). The subgroup analysis of the HRT users and nonusers showed similar results for VO_{2max} and body mass in both subgroups.

Changes in CHD risk factors

There were no statistically significant changes in blood pressure, total cholesterol, HDL-cholesterol, LDL-cholesterol or the triglycerides in any of the exercise groups compared to controls (Table 2).

When we combined the exercise groups W1 and W2 in Study I and exercise groups W1, W4, W5 and W6 in Study II, we found a statistically significant reduction of diastolic blood pressure of -3.0 (-5.5 to -0.4) mmHg ($P = 0.025$) in Study I, but not in Study II.

The mean fasting blood glucose declined by $-0.21\,\mathrm{mmol\,L^{-1}}$ (CI -0.33 to -0.09) in Group W1 and $-0.13\,\mathrm{mmol\,L^{-1}}$ (CI -0.25 to -0.01) in Group W2 when compared with that of the controls in Study I ($P = 0.003$). In Study I the mean 2-h glucose in the glucose tolerance test declined by $-0.48\,\mathrm{mmol\,L^{-1}}$ (95% CI -0.89 to -0.08) in Group W1 and $-0.43\,\mathrm{mmol\,L^{-1}}$ (95% CI -0.83 to -0.02) in Group W2 when compared with that of the controls ($P = 0.039$). No statistically significant changes occurred in the fasting plasma insulin in either of the studies or in the 2-h insulin in the glucose tolerance test in Study I.

In Study I the changes in the CHD risk factors in one-session (W1) and two-session (W2) walking groups compared to controls were quite similar (Fig. 1). The similarity of the groups can be concluded from the overlap of confidence intervals and estimated means. In Study II the results of combined exercise groups according to exercise intensity or energy expenditure, both compared to controls, also showed similarity between combined groups (Fig. 2). The subgroup analysis of the HRT users and non-users did not show any differences in any of the results for the CHD risk factors.

Discussion

We have previously reported that maximal aerobic power improved in all of our exercise groups of healthy, sedentary postmenopausal women, and in Study I also body mass declined (Asikainen et al., 2002a, b). In Study I we found that maximal aerobic power and body mass were equally affected by fractionated exercise. In Study II we found that even the lowest exercise dose improved maximal aerobic power, but it was not enough to decrease body mass. The main purpose of our present report was to focus on the effects of these exercise programs on CHD risk factors, to test the effect of fractionated exercise and to search for the minimum effective dose on blood pressure, blood lipids, glucose and insulin in our study subjects.

A recent meta-analysis of 54 randomized, controlled trials of 2419 adults, mostly men, concluded that systolic and diastolic blood pressure can be lowered by approximately 4 and 2 mmHg in normotensive subjects and approximately by 5 and 4 mmHg in hypertensive subjects, respectively, with dynamic physical training (Whelton, 2002). Kelley & Sharpe Kelley (1999) suggested, on the basis of a meta-analysis of 21 randomized and nonrandomized, controlled studies on women, that the training effect would be smaller for women, approximately 2 mmHg in systolic and 1 mmHg in diastolic blood pressure. The studies in the above meta-analyses used training regimens of 2–5 days per week, 15-60 min per session, with an intensity of 40–80% of VO_{2max}. The optimal exercise intensity remained unclear, but low intensities gave positive results in the studies and higher intensity did not improve the result.

Jakicic et al. (1995) compared the effects of 20–40-min brisk walking in one continuous session or multiple 10-min bouts combined with a reducing diet in a 20-week trial on 56 obese (mean BMI approximately $34\,\mathrm{kg\,m^{-2}}$) 35–46-year-old women. The multiple-bout group had better adherence and exercised more than the continuous exercise group. There was a mean decrease of 2.6 and 5.6 mmHg in systolic and diastolic pressure, respectively, in multiple-bout exercise group, and the corresponding values for the continuous exercise were 3.9 and 4.1 mmHg, while the data for the control groups were not shown. Murphy & Hardman (1998) studied 47 women, aged 44.4 (SD 6.1) years, during 10 weeks of brisk walking at an intensity of 70–80% of the maximal heart rate, 5 days a week, in one 30-min session vs. three 10-min sessions, and found no statistically significant changes in blood pressure. Staffileno et al. (2001) studied the effects of intermittent, moderate exercise with intensity of 50–60% of of VO_{2max}, 3 times 10 min a day, 5 days per week for 8 weeks in 18 hypertensive, postmenopausal women, and found that systolic pressure was reduced by 8 mmHg and diastolic by 5 mmHg in exercise group compared to controls. Staffileno et al. (2001) did not have a continuous exercise group.

Table 2. Coronary risk factors before and after training, means (SD) and the net change (95% CI) between the exercise and control groups in Study I and Study II*[a]

Risk factor	N	Before	After	Net change (95% CI)	P[b]
Systolic pressure (mmHg)					
Group W1	44	126.3 (14.7)	131.5 (14.0)	1.2 (–3.9 to 6.3)	
Group W2	43	124.8 (12.3)	130.2 (13.8)	0.8 (–4.4 to 5.9)	
Group C1	43	124.5 (16.8)	129.3 (16.7)		0.90
Group W3	20	125.3 (14.6)	126.6 (17.0)	4.4 (–1.3 to 10.2)	
Group W4	21	121.8 (15.1)	124.1 (11.9)	4.0 (–1.7 to 9.7)	
Group W5	15	127.5 (17.3)	124.8 (13.0)	1.3 (–5.0 to 7.7)	
Group W6	20	124.1 (14.6)	127.8 (14.0)	6.4 (0.6–12.1)	
Group C2	37	128.9 (15.6)	124.3 (13.3)		0.21
Diastolic pressure (mmHg)					
Group W1	44	80.5 (7.2)	79.6 (6.6)	–2.6 (–5.5 to 0.4)	
Group W2	43	80.1 (7.5)	78.6 (7.3)	–3.3 (–6.3 to –0.4)	
Group C1	43	82.1 (7.5)	83.3 (11.5)		0.071
Group W3	20	80.3 (9.1)	76.8 (7.6)	–2.7 (–6.0 to 0.6)	
Group W4	21	79.6 (11.6)	81.0 (7.8)	1.8 (–1.4 to 5.1)	
Group W5	15	80.8 (9.4)	79.7 (7.6)	–0.6 (–3.7 to 3.6)	
Group W6	20	75.9 (9.3)	76.6 (9.4)	–0.4 (–3.7 to 3.0)	
Group C2	37	81.4 (7.5)	80.1 (7.4)		0.20
Total cholesterol (mmol L^{-1})					
Group W1	46	5.53 (1.00)	5.47 (0.98)	0.13 (–0.09 to 0.34)	
Group W2	42	5.72 (0.94)	5.67 (1.00)	0.16 (–0.05 to 0.38)	
Group C1	44	5.72 (0.98)	5.50 (0.88)		0.30
Group W3	20	5.32 (0.54)	5.20 (0.47)	0.11 (–0.16 to 0.38)	
Group W4	21	5.34 (1.02)	5.22 (0.82)	0.11 (–0.16 to 0.37)	
Group W5	15	5.13 (0.94)	5.03 (0.91)	0.08 (–0.22 to 0.39)	
Group W6	19	5.21 (0.77)	5.13 (0.82)	0.12 (–0.15 to 0.40)	
Group C2	39	5.49 (0.95)	5.23 (1.00)		0.87
HDL-cholesterol (mmol L^{-1})					
Group W1	46	1.56 (0.32)	1.55 (0.35)	0.00 (–0.08 to 0.07)	
Group W2	42	1.56 (0.42)	1.57 (0.45)	0.01 (–0.07 to 0.09)	
Group C1	44	1.56 (0.33)	1.56 (0.33)	0.92	
Group W3	20	1.72 (0.39)	1.73 (0.28)	0.01 (–0.09 to 0.10)	
Group W4	21	1.60 (0.28)	1.70 (0.30)	0.08 (–0.01 to 0.17)	
Group W5	15	1.56 (0.45)	1.59 (0.50)	0.01 (–0.09 to 0.11)	
Group W6	19	1.63 (0.42)	1.65 (0.44)	0.00 (–0.09 to 0.10)	
Group C2	39	1.57 (0.33)	1.59 (0.38)		0.51
LDL-cholesterol (mmol L^{-1})					
Group W1	46	3.46 (0.95)	3.41 (0.90)	0.10 (–0.10 to 0.30)	
Group W2	41	3.56 (0.94)	3.51 (0.96)	0.12 (–0.09 to 0.33)	
Group C1	44	3.53 (0.88)	3.38 (0.94)	0.48	
Group W3	20	3.06 (0.53)	2.95 (0.52)	0.07 (–0.17 to 0.30)	
Group W4	21	3.22 (1.02)	2.98 (0.83)	–0.03 (–0.26 to 0.21)	
Group W5	15	3.06 (0.84)	2.96 (0.76)	0.08 (–0.19 to 0.34)	
Group W6	19	2.97 (0.72)	2.92 (0.75)	0.11 (–0.13 to 0.35)	
Group C2	39	3.36 (0.84)	3.12 (0.82)		0.84
Triglycerides (mmol L^{-1})					
Group W1	46	1.12 (0.34)	1.12 (0.41)	0.03 (–0.11 to 0.16)	
Group W2	41	1.30 (0.52)	1.23 (0.42)	0.03 (–0.11 to 0.16)	
Group C1	44	1.39 (0.57)	1.25 (0.47)		0.90
Group W3	20	1.21 (0.43)	1.16 (0.41)	0.02 (–0.12 to 0.16)	
Group W4	21	1.15 (0.29)	1.19 (0.42)	0.10 (–0.04 to 0.25)	
Group W5	15	1.13 (0.46)	1.05 (0.43)	–0.02 (–0.18 to 0.14)	
Group W6	19	1.36 (0.42)	1.24 (0.40)	–0.02 (–0.16 to 0.13)	
Group C2	39	1.24 (0.42)	1.16 (0.44)		0.55
Fasting glucose (mmol L^{-1})					
Group W1	46	4.46 (0.30)	4.41 (0.33)	–0.21 (–0.33 to – 0.09)	
Group W2	43	4.48 (0.32)	4.51 (0.32)	–0.13 (–0.25 to –0.01)	
Group C1	44	4.44 (0.32)	4.62 (0.36)	0.003	
Group W3	20	4.76 (0.33)	4.60 (0.31)	–0.16 (–0.29 to –0.02)	
Group W4	21	4.75 (0.26)	4.62 (0.24)	–0.13 (–0.27 to 0.00)	
Group W5	15	4.93 (0.40)	4.75 (0.41)	–0.13 (–0.28 to 0.01)	
Group W6	19	4.89 (0.30)	4.78 (0.27)	–0.08 (–0.21 to 0.06)	
Group C2	39	4.83 (0.35)	4.81 (0.38)		0.093
2-h glucose (mmol L^{-1})					
Group W1	44	4.76 (0.86)	4.88 (0.91)	–0.48 (–0.89 to –0.08)	
Group W2	41	5.01 (1.30)	5.08 (1.10)	–0.43 (–0.83 to –0.02)	
Group C1	41	4.98 (1.07)	5.49 (1.41)		0.039

Table 2. *(Continued)*

Risk factor	N	Before	After	Net change (95% CI)	P^b
Fasting insulin ($mU\,L^{-1}$)					
Group W1	46	6.34 (1.98)	6.01 (1.94)	–0.48 (–1.05 to 0.09)	
Group W2	43	6.92 (2.50)	6.59 (2.09)	–0.35 (–0.93 to 0.22)	
Group C1	44	6.91 (2.03)	6.93 (2.45)		0.23
Group W3	20	6.92 (1.62)	6.77 (1.46)	–0.61 (–1.40 to 0.17)	
Group W4	21	7.09 (1.79)	7.02 (2.03)	–0.48 (–1.25 to 0.29)	
Group W5	15	8.07 (4.36)	7.67 (2.93)	–0.55 (–1.40 to 0.31)	
Group W6	19	7.42 (1.85)	7.30 (1.83)	–0.44 (–1.23 to 0.34)	
Group C2	39	7.91 (2.37)	8.10 (2.60)		0.47
2-h insulin ($mU\,L^{-1}$)					
Group W1	44	30.30 (12.65)	30.08 (14.93)	–5.05 (–12.06 to 1.95)	
Group W2	42	33.36 (12.13)	33.52 (23.78)	–3.90 (–10.96 to 3.16)	
Group C1	41	33.42 (13.33)	37.46 (19.92)		0.33

*Study I: Groups W1 and W2 were the exercise groups and Group C1 was the control group.
Study II: Groups W3, W4, W5 and W6 were the exercise groups and Group C2 was the control group.
VO_{2max} = maximal aerobic power, HDL = high-density lipoprotein, LDL = low-density lipoprotein.
[a]Analysis of covariance with baseline measurements as covariates.
[b]Analysis of covariance.

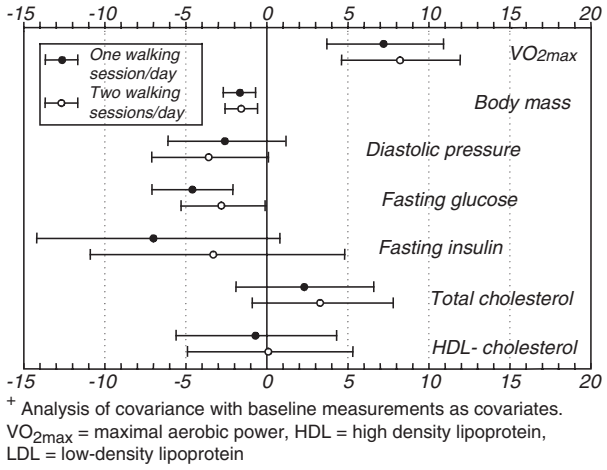

Fig. 1. Effect of continuous and fractionated walking on selected variables. Percent net difference (95% CI) during training in the exercise groups vs. the control group in Study I.

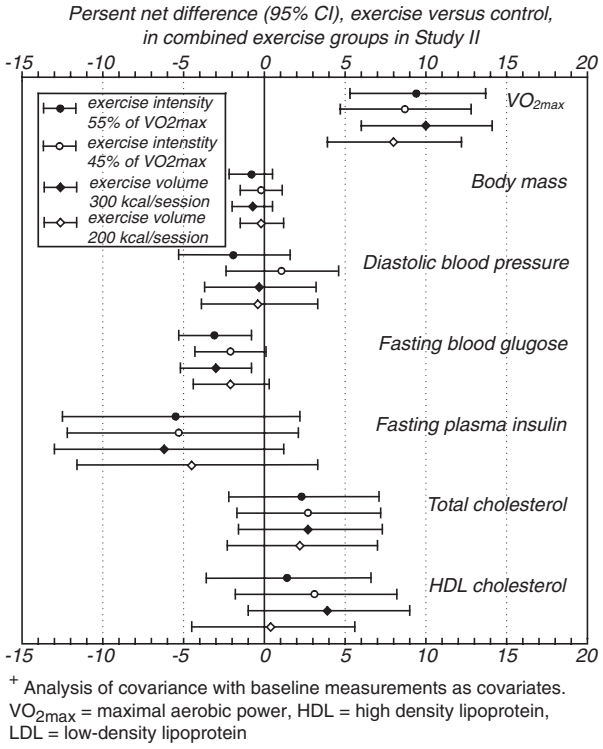

Fig. 2. Effect of exercise intensity and energy expenditure on selected variables in Study II. Percent net difference (95% CI) in the exercise groups vs. the control group. The exercise groups have been combined according to intensity or volume.

We found no statistically significant effects in blood pressure in our study groups. Combining the exercise groups showed a 3 mmHg reduction of diastolic pressure in Study I, but not in Study II. This could be due to the greater exercise dose of Study I. Our exercise doses were at the lowest border compared with the exercise doses of aforementioned meta-analyses. Approximately one-third of our study subjects had initially elevated blood pressure (130/85–160/100 mmHg). The amount of subjects with elevated diastolic pressure decreased during training in Study I, from 40 to 34 subjects at the end of intervention. Systolic blood pressure seemed to increase in Study I, although the increase was not statistically significant. Forty-four subjects had elevated systolic pressure at the baseline and 52 at the end of intervention. Seasonal variation could be

a possible explanation, since this was also seen in the controls. The end measurements were performed in December before Christmas in Study I and in June in Study II. In Study II no changes in blood pressure were found. The minimum dose needed to induce a minimal decrease in diastolic blood pressure in our mostly normotensive study group of sedentary postmenopausal women is probably close to the exercise dose of our Study I, 65% of VO_{2max}, 1500 kcal week^{-1}, and the exercise either continuous or fractionated into two daily bouts. A greater exercise dose is needed to also obtain an effect on systolic blood pressure.

We did not find any statistically significant changes in blood lipoproteins. According to a meta-analysis of 28 randomized, controlled studies mostly on men using endurance training (Leon & Sanchez, 2001), the response between individuals varies greatly for the same training stimulus. Also many confounding factors exist. We found much variability in the responses in our study in spite of good compliance and careful blood sampling. Leon & Sanchez (2001) showed that aerobic exercise increased HDL-cholesterol 4–5%. Most of the studies had an exercise frequency of 3–5 times a week and 30 min or more of exercise per session at moderate to strenuous intensity. There is limited evidence that a higher exercise intensity will give a greater HDL-cholesterol response than moderate or light intensity. The threshold to affect lipids during weekly training seems to be an exercise energy expenditure of 1200–1500 kcal and the minimum length of training should be 12 weeks (Leon et Sanchez 2001). A more recent finding in the 6 month study of 111 overweight men and women of Krauss (2002) suggests that energy expenditure is crucial and more important than exercise intensity, and the most marked effects were observed at an energy expenditure of 2000 kcal with strenuous intensity. The length of training period might also be very important especially in postmenopausal women. In the study of King et al. (1995), 1 year of moderate training in postmenopausal women was not enough, but 2 years showed statistically significant lipid improvements (King et al., 1995).

According to Leon & Sanchez (2001), baseline lipid levels strongly predict response: the lower the baseline HDL-cholesterol, the higher the response to exercise. Premenopausally, women have higher levels of HDL-cholesterol due to their hormonal status, but postmenopausally the levels decrease. HRT affects lipid levels in various ways (Haddock et al., 2000) which must be taken into account in exercise trials. The baseline lipid levels of our subjects were mostly in the normal range, e.g., 95% of the subjects had a baseline level of over 1.00 mmol L^{-1} for HDL-cholesterol. Our study design called for an equal number of subjects with or without HRT in each group.

There are only two randomized, controlled studies on the effect of fractionated exercise on blood lipids. Ebisu et al. (1985) studied the effects of jogging the same distance in one, two or three daily sessions at 80% of the maximal heart rate for 10 weeks in 53 male students. There was a significant increase in HDL-cholesterol only in the three-session exercise group. Ten weeks of exercise may have been too short to reveal a long-term effect on lipids. Woolf-May et al. (1999) conducted an 18-week study on 56 adults, aged 40–60 years, walking 20–40 min in one, two or three daily bouts. LDL-cholesterol decreased in the long (-0.29 mmol L^{-1}) and intermediate (-0.41 mmol L^{-1}) bout group, but not in the short bout group. However there were no HDL-cholesterol changes in any of the exercise groups.

The doses of exercise in our study were at the lower border of the aforesuggested minimum requirements for lipoprotein improvements. The minimum dose of exercise in healthy, sedentary, normolipemic postmenopausal women with or without HRT seems to be more than the greatest exercise dose of our study.

Manson et al. (1991) found a relationship between vigorous exercise and decreased risk of type 2 diabetes in an 8-year follow- up study of 87 252 women. In the Nurses Health Study, Hu et al. (1999) found that walking reduced the risk, but vigorous exercise reduced it more. We found a statistically significant, small reduction in the fasting and 2-h glucose concentrations in Study I but not in Study II, where the exercise intensity and exercise energy expenditure was smaller. The fasting glucose concentration in Group W2 and 2-h glucose concentration in Groups W1 and W2 improved only when compared to controls, and the absolute values did not improve. There could have been a seasonal variation that caused the rise in control groups fasting glucose just before Christmas, and exercise might have partly prevented this rise in exercise groups. The minimum dose of exercise needed to obtain a minimal effect on glucose in our study group of healthy, normoglycemic, sedentary postmenopausal women is probably very close to our largest exercise dose, 65% of VO_{2max}, 1500 kcal week^{-1}, in one or two daily exercise bouts. To achieve a more clinically relevant effect, more exercise is needed.

When the minimum dose of exercise to affect coronary risk factors is searched, small changes are to be expected, some of them statistically significant and some below the border of statistical significance, although showing a similar trend, but interpreted as no change, according to the dichotomous nature of statistical science. The interpretation of these results raises several questions. What are the smallest changes

that can be detected with our measurements? Are the changes caused by regression towards the mean of variables with high interindividual variation? Have the biological day-to-day and seasonal variations been taken into account? We tried to solve these problems in many ways. We estimated the smallest possible change that can be detected with our equipment and estimated that the number of subjects was sufficient for adequate statistical comparisons. We used a control group to minimize systemic errors, e.g., seasonal fluctuations. We used an analysis of covariance in order to be unaffected by possible minor baseline differences and the regression towards the mean. The randomized groups were comparable. The exercise dose was carefully controlled with personal supervision, heart rate monitors, exercise diaries, food diaries and pedometers. The program was closely followed by the participants and the dropouts were few. The measurements were carried out in strictly controlled, similar conditions, exercise group members and controls in mixed order. However, to some of these questions, there are no definite answers; therefore no exact values for minimum effective dose can be claimed based on our studies. To improve the design further, the intervention could have been longer to ensure that all potential effects, especially those on lipids, were detected.

Expending 1500 kcal weekly by walking at 65% of the VO_{2max} for 15 weeks in one or two daily bouts had a minimal positive effect on blood glucose and diastolic blood pressure. Expending 1000–1500 kcal weekly by walking at 45–55% of the VO_{2max} for 24 weeks did not cause any statistically significant improvements in CHD risk factors in spite of improvements in aerobic fitness. Expending 1500 kcal weekly by walking at 65% of the VO_{2max} in one or two daily exercise bouts is probably close to the minimum dose of exercise needed for minimal improvements in some of the CHD risk factors in healthy, sedentary, postmenopausal women, either with or without HRT. A larger exercise dose should be recommended to give greater and more clinically relevant improvements in blood pressure and blood glucose and also to affect lipoproteins.

Perspectives

Our findings support the US physical activity recommendation for public health (Pate et al., 1995). Regular brisk walking, also when fractionated into two daily bouts, can produce minimal positive effects on selected coronary risk factors in sedentary postmenopausal women. Contrary to earlier beliefs, our study shows that, at least in sedentary postmenopausal women, improving coronary risk factors requires a larger exercise dose than improving aerobic fitness.

The clinical short-term relevance of the minimal, but statistically significant, changes in maximal aerobic power, body mass and risk factors in our study is probably small. The exercise dose should be greater if clinically more relevant improvements in coronary risk factors are expected.

However, according to epidemiological studies, the most benefit for public health will come as sedentary subjects become active (Pate et al., 1995). The improvement in VO_{2max} in our study was enough to increase most of the subjects' level of fitness exceeding the VO_{2max} value of 31.5 mL min^{-1} kg^{-1} and therefore move the subjects into a low-risk category for all-cause mortality on the basis of the study of Blair et al. (1989), who followed up 3120 women for 8 years. The VO_{2max} value of 31.5 mL min^{-1} kg^{-1} represented the level of fitness at which the risk level for all-cause mortality fell clearly. In a more recent epidemiological study, Farrel et al. (2002) suggested an even lower VO_{2max} value of 28.0 mL min^{-1} kg^{-1} for 40–49-year old women to be classified as moderately fit and have low mortality. Thus the exercise we used in our study might, after all, have some long-term clinical significance for postmenopausal sedentary women, if exercise is continued. To achieve this, exercise has to be safe and feasible, as ours was, and easy to perform. The characteristics of this exercise regimen suggest that also a part of daily physical chores may meet the requirements of physical activity improving health.

Key words: exercise, dose–response, fractionization, postmenopause, lipoproteins, glucose, insulin, blood pressure, randomized controlled trial.

Acknowledgements

This study was supported in part by the Finnish Ministry of Education, the Juho Vainio Foundation, Finnish Foundation for Cardiovascular Research and Ulla Kauhanen Foundation. There are no conflicts of interest.

We thank Minna Aittasalo (MSc), Kati Rantamo (PT), Ulla Hakala (Medical Laboratory Technologist) and Kirsi Mansikkamäki (Medical Laboratory Technologist) for their assistance in data collection, Ulla Honkanen (Medical Laboratory Technologist) and Anne Rauhio (Medical Laboratory Technologist) for their technical assistance in biochemical analyses, Mr. Ismo Lapinleimu for assistance with the statistical analyses, and Ms Taru Malminen for secreterial work, all from UKK Institute.We are very grateful to Erkki Seppälä (MD, Head of Department of Clinical Chemistry, Tampere University Hospital) for valuable help in OGTT and we thank Steven N. Blair (PED) (Institute for Aerobics Reasearch, Dallas, Texas) for his valuable discussions during the study. We give warm thanks to our hard-working study subjects.

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