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Original Article

Effects of a 12-week healthy-life exercise program on oxidized low-density lipoprotein cholesterol and carotid intima-media thickness in obese elderly women

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Abstract. [Purpose] This study examined the effects of a 12-week exercise program on plasma level of oxidized low-density lipoprotein cholesterol in obese elderly women, who are at increased risk of heart disease morbidity. [Subjects and Methods] Twenty participants were assigned into either a control (n = 10) or a supervised exercise program (n = 10) group. The 12-week exercise intervention was performed 3 days per week and involved combined aerobic exercise, resistance exercise, and traditional Korean dance. [Results] Two-factor analysis of variance revealed significant group × time interactions for body mass, diastolic blood pressure, appendicular muscle mass. For high-density lipoprotein cholesterol, oxidized low-density lipoprotein cholesterol, and the ratio of oxidized low-/high-density lipoprotein cholesterol, two-factor analysis of variance revealed significant interactions (group × time), indicating responses differed significantly between the control and exercise groups after 12 weeks. [Conclusion] A 12-week low- to moderate-intensity exercise program appears to be beneficial for obese elderly women by improving risk factors for cardiovascular disease.
Key words: Exercise, Obesity, Oxidized LDL

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INTRODUCTION

Macrophage uptake of oxidized low-density lipoprotein cholesterol (LDL) induces the migration and proliferation of smooth muscle cells, resulting in foam cell formation, which develops into the fatty streaks characteristic of cardiovascular disease[1)]. In addition, oxidized LDL is associated with increased incidences of metabolic syndrome[2)] and obesity[3, 4)], and is considered a risk factor for cardiovascular disease[5)]. Likewise, oxidized LDL is closely involved in the pathogeneses of ischemic heart disease, atherogenesis, and other chronic diseases and also plays a key role in the aging process[6–8)].

A recent study reports a strong association between plasma oxidized LDL concentrations and habitual physical activity in older populations[9)]. Some recent cross-sectional and longitudinal studies recently report that plasma concentrations of circulating oxidized LDL are directly associated with body mass index (BMI), waist circumstance, obesity, weight loss, and physical fitness[10)]. Obesity has important functional implications in elderly persons because it exacerbates the age-related decline in physical function, which can lead to frailty and loss of independence[11)].

Meanwhile, carotid intima-media thickness (CIMT) is an independent predictor of atherosclerotic diseases including coronary artery disease as well as cardiovascular events; it also increases with age in sedentary adults. Lakatta et al. report CIMT increases two- to three-fold between the ages of 20 and 90 years, even in healthy sedentary adults[10)]. This increase in CIMT with aging may increase the risks of pathophysiological disease mechanisms interacting, eventually leading to peripheral occlusive vascular disease[12)].

Even though these results suggest good cardiovascular and muscular fitness alter this association by improving plasma oxidized LDL concentrations and/or CIMT, it remains unclear whether regular exercise in elderly adults positively affects circulating oxidized LDL levels or modulates CIMT. Identifying effective strategies for behavioral change to prevent the oxidative modification of LDL and cardiovascular disease in older adults may reduce cardiovascular disease risk, making this a key public health issue. In addition, exercise training is a necessary component of

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Table 1. Baseline physical characteristics

	Exercise group (n = 10)	Control group (n = 10)
Age (years)	70.7 ± 0.7	71.3 ± 0.6
Body mass (kg)	62.8 ± 1.6	64.9 ± 1.0
Height (m)	1.54 ± 1.9	1.58 ± 1.0
BMI (kg/m^2)	26.3 ± 0.3	26.0 ± 0.2
Body fat (%)	31.8 ± 0.6	32.7 ± 0.6
SBP (mmHg)	129 ± 4	130 ± 2
DBP (mmHg)	81 ± 2	77 ± 1

Variables are mean ± SEM. BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure. Inter-group differences were not significant (unpaired Student's t-tests).

lifestyle modification in obese postmenopausal women[13]. However, no studies have examined the effects of exercise on plasma level of oxidized LDL in obese elderly women even though they have increased risks of heart disease and arteriosclerosis.

SUBJECTS AND METHODS

Participants were arbitrary recruited from the general population of local communities. They were asked to complete questionnaires about their current lifestyle, including habitual physical activity, current medication, alcohol consumption, and cigarette smoking, before the intervention. Ten participants were excluded from data analysis because they were taking lipid and/or glucose-lowering medications ($n = 4$), could not start exercise programs due to their condition levels ($n = 3$), had a history of cardiovascular disease, a regular exercise habit, and a high body fat percentage < 30% ($n = 3$). As a result, 20 participants were assigned to the control ($n = 10$) or supervised exercise program ($n = 10$) group. The physical characteristics of the participants are shown in Table 1. In accordance with the ethical standards of the Declaration of Helsinki, informed consent was obtained from all participants after they were provided a detailed description of the experiment. Ethical approval was obtained from the ethics review boards of our universities.

Physical and anthropometric variables were measured at baseline and after 12 weeks in both groups. Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, using a Venus 5.5 body composition analyzer (Jawon Medical, Gyeongsan, Korea). BMI was calculated as weight (kg) divided by height squared (m^2).

Arterial blood pressure was measured by a mercury sphygmomanometer after the participants had been seated at rest for 10 minutes. Two measurements were taken at each time point, and the mean was calculated and used for analysis.

Leg and arm skeletal muscle mass represents the sum of both right and left extremities. Total limb appendicular muscle mass was calculated as the sum of arm and leg lean tissue mass. Appendicular muscle mass was determined by dual-energy X-ray absorptiometry (Lunar DPX, GE Healthcare Technologies Lunar, USA).

CIMT was measured by B-mode ultrasound and a 10-MHz probe (LOGIQ 3, GE Healthcare, WI, USA). The participants were examined in the supine position with the neck extended and the probe in the anterolateral position. All CIMT measurements were taken in the longitudinal plane at the artery proximal to the adventitia–media junction. After freezing the image, measurements were made by electronic calipers. The maximum thickness of the intima-media width was measured three times, and the mean value was used for statistical analysis[14].

At baseline and after 12 weeks, venous blood samples were collected from both groups from an antecubital vein the morning (0800 to 0900 h) after an overnight fast (10–12 h). To measure triacylglycerol as well as total, HDL, and LDL cholesterol levels, samples were collected into tubes containing clotting activators to isolate serum. Thereafter, samples were allowed to clot for 45 minutes at room temperature and subsequently centrifuged at 3,000 rpm for 10 minutes at 4 °C. After separation, serum was dispensed into plain microtubes and stored at −80 °C for later analysis. To measure plasma oxidized LDL, venous blood samples were collected into tubes containing disodium salt-fluoride-EDTA. Thereafter, samples were immediately centrifuged and treated as described above.

The plasma concentration of oxidized LDL (Mercodia AB, Uppsala, Sweden) was determined by enzyme-linked immunosorbent assay using commercially available kits. The concentrations of serum triacylglycerol and total, HDL, and LDL cholesterol were determined by standard laboratory methods.

The 12-week exercise program intervention consisted of 3 days per week (i.e., Monday, Wednesday and Friday) of combined aerobic exercise, resistance exercise, and traditional Korean dance; this program is modified version of a program in previous study on obese elderly women[15]. Each exercise was performed for 15 minutes for a total 45 minutes plus 10 minutes each of warm-up and cool-down. Aerobic exercise consisted of walking and arms raise; jump and swing arms; side walking; leg raise to forward back and side; jump and knee up; walking and leg raise; walking and jump. Resistance exercise consisted of arm folding and spreading; arm raises to the front and side shoulder turning; waist bending; waist bending to the side; trunk twisting; knee-ups; and stretching legs and raises to the back and side. Finally, traditional Korean dance consisted movements of the arms, legs, trunk, and whole body, including jumping up and to the side as well as balance exercises (e.g., one-legged standing and one-legged jumping)[15]. Participants performed each exercise for 15 minutes at 50–60% of the HRR from weeks 1–6. After week 6, emphasis was placed on reaching and maintaining an exercise intensity of approximately 60–70% of the HRR for 15 minutes (Polar Heart Monitor; RS400, Finland).

Data were analyzed by PASW version 18.0 for Windows (SPSS Inc., Chicago, IL, USA). The Student's t-test was used to assess differences in baseline variables. The Shapiro-Wilk test was used to check for the normality of distribution. After controlling for age and weight, partial correlation analyses were performed to determine the correlations between muscle mass and plasma oxidized LDL and CIMT and

Table 2. Changes in body composition at baseline and after 12 weeks

		Exercise group (n = 10)	Control group (n = 10)
Height (m)	Baseline	1.54 ± 1.9	1.58 ± 1.0
Body mass (kg)	Baseline	62.8 ± 1.6	64.9 ± 1.0
	12 weeks	61.2 ± 1.5*	64.8 ± 0.9†
BMI (kg/m^2)	Baseline	26.3 ± 0.3	26.0 ± 0.2
	12 weeks	25.6 ± 0.3	25.7 ± 0.2
Body fat (%)	Baseline	31.8 ± 0.6	32.7 ± 0.6
	12 weeks	31.1 ± 0.6	33.7 ± 1.4
SBP (mmHg)	Baseline	129 ± 4	130 ± 2
	12 weeks	125 ± 3	130 ± 2
DBP (mmHg)	Baseline	81 ± 2	77 ± 1
	12 weeks	78 ± 2*	78 ± 1†
Upper-limb muscle mass (kg)	Baseline	4.3 ± 0.1	3.8 ± 0.1
	12 weeks	4.5 ± 0.1*	3.7 ± 0.1†
Lower-limb muscle mass (kg)	Baseline	11.6 ± 0.2	9.8 ± 0.2
	12 weeks	11.8 ± 0.2*	9.7 ± 0.1†
Appendicular skeletal muscle mass (kg)	Baseline	15.9 ± 0.3	13.5 ± 0.2
	12 weeks	16.3 ± 0.3*	13.4 ± 0.2†

Variables are mean ± SEM. BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure.
† Significant interaction between group × time ($p < 0.05$).
*Significantly different from baseline in the same group ($p < 0.05$).

Table 3. Changes in blood parameters at baseline and after 12 weeks

		Exercise group (n = 10)	Control group(n = 10)
Triacylglycerol (mmol/L)	Baseline	1.35 ± 0.01	1.33 ± 0.05
	12 weeks	1.32 ± 0.01	1.31 ± 0.04
TC (mmol/L)	Baseline	4.79 ± 0.04	4.96 ± 0.09
	12 weeks	4.76 ± 0.04	5.02 ± 0.07
HDL (mmol/L)	Baseline	1.03 ± 0.01	1.07 ± 0.02
	12 weeks	1.05 ± 0.02*	1.06 ± 0.02†
LDL (mmol/L)	Baseline	2.71 ± 0.06	2.81 ± 0.11
	12 weeks	2.67 ± 0.05	2.86 ± 0.13
Oxidized LDL (U/L)	Baseline	73.5 ± 2.6	70.3 ± 2.4
	12 weeks	71.6 ± 2.3*	71.8 ± 2.7†
Oxidized LDL/ HDL	Baseline	71.4 ± 2.7	66.0 ± 2.8
	12 weeks	68.1 ± 2.5*	67.8 ± 3.0†
CIMT (mm)	Baseline	0.55 ± 0.01	0.58 ± 0.01
	12 weeks	0.54 ± 0.01*	0.59 ± 0.01†

Variables are mean ± SEM. TC: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; CIMT: carotid intima–media thickness.
†Significant interaction between group × time ($p < 0.05$).
*Significantly different from baseline in the same group ($p < 0.05$).

in all subjects. Two-factor analysis of variance (ANOVA) was used to determine interaction (i.e., group × time) effects for all outcome variables. When significant group × time interactions were identified, post hoc paired t-tests were performed to detect differences between time points. The level of significance was set at $p < 0.05$. All variables are presented as mean ± SEM.

RESULTS

The baseline physical characteristics are presented in Table 1. At baseline, there were no significant differences in the physical characteristics between the two groups.

Body composition and appendicular muscle mass measured at baseline and after 12 weeks are presented in Table 2. Two-factor ANOVA revealed significant group × time interactions for body mass ($p = 0.019$), diastolic blood pressure (DBP) ($p = 0.001$), upper-limb muscle mass ($p = 0.001$), lower-limb muscle mass ($p = 0.001$), and appendicular muscle mass ($p = 0.001$). Intra-group analysis showed that body mass ($p = 0.012$) and DBP ($p = 0.001$) were significantly lower than baseline values in the exercise group after 12 weeks. Meanwhile, upper-limb muscle mass ($p = 0.001$), lower-limb muscle mass ($p = 0.001$), and appendicular muscle mass ($p = 0.001$) were significantly higher than baseline values in the exercise group after 12 weeks. ANOVA indicated responses differed significantly between the control and exercise groups after 12 weeks. However, there were no significant differences in BMI ($p = 0.215$), % body fat ($p = 0.277$), or systolic blood pressure ($p = 0.054$).

Two-factor ANOVA revealed significant interactions (group × time) for HDL cholesterol ($p = 0.023$), oxidized LDL ($p = 0.003$), and the ratio of oxidized LDL to HDL cholesterol ($p = 0.002$), indicating responses differed between the control and exercise groups after 12 weeks. Intra-group analysis showed that HDL cholesterol was significantly higher than baseline in the exercise group after 12 weeks ($p = 0.013$). Furthermore, oxidized LDL and the ratio of oxidized LDL to HDL cholesterol were significantly lower than baseline in the exercise group after 12 weeks ($p = 0.009$, $p = 0.007$, respectively). A significant group × time interaction was observed for CIMT ($p = 0.001$). CIMT was significantly thinner than baseline in the exercise group after 12 weeks ($p = 0.007$) (Table 3).

There was a significant partial negative correlation between changes in oxidized LDL and appendicular muscle mass after adjusting for age and gender ($r = -0.513$, $p < 0.05$). In addition, a significant negative correlation was observed between changes in CIMT and appendicular muscle mass ($r = -0.545$, $p < 0.05$).

DISCUSSION

This study examined the effects of a 12-week exercise program on plasma oxidized LDL concentrations and CIMT in obese elderly women. The main findings of this study are that the 12-week of exercise program attenuated plasma oxidized LDL and the ratio of oxidized LDL to HDL cholesterol in obese elderly women. In addition, the program improved CIMT and increased appendicular muscle mass. Our findings may suggest physical activity has a protective role against the process leading to cardiovascular disease.

Several studies show plasma oxidized LDL concentrations are reduced in older men and women following a high-intensity exercise intervention[16]. Furthermore, aerobic exercise training has been reported to decrease oxidized LDL concentrations in middle-aged individuals with coronary artery disease[17]. In the present study, plasma oxidized LDL decreased in obese elderly women after a 12-week exercise program that included traditional Korean dance as well as aerobic moves and resistance exercise. These results may imply that even moderate-intensity exercise programs are effective for reducing resting oxidized LDL in obese elderly women. The ratio of oxidized LDL to HDL cholesterol is a useful marker of cardiovascular disease risk factors and is a better biomarker than standard lipid measurements for differentiating between patients with coronary artery disease and normal subjects[18]. In the present study, the ratio of oxidized LDL to HDL cholesterol decreased significantly after the 12-week exercise program. The negative relationship between oxidized LDL and HDL concentrations is concordant with evidence suggesting HDL molecules are atheroprotective in part because they inhibit LDL oxidation[1]. Moreover, a previous study corroborates the present finding that plasma oxidized LDL concentration is inversely correlated with HDL cholesterol level[19]; a low-volume walking program (90 minutes per week) reduced the ratio of oxidized LDL to HDL cholesterol in older adults. Thus, a small change in the ratio of oxidized LDL to HDL cholesterol induced by exercise could have important public health implications from the perspective of reducing the risk factor of cardiovascular disease.

After adjusting for age and body weight, changes in skeletal muscle mass of elderly people negatively correlated with changes in CIMT and oxidized LDL. In the present study, the relative changes in upper- and lower-limb muscle mass were differed significantly between groups after the intervention period, and muscle strength improved significantly in the exercise group. Muscle/joint complaints could affect physical functioning independent of vascular disease. Previous studies[20–22] demonstrate that sarcopenia is associated with an age-related reduction in physical activity, especially a lack of muscle overload. Therefore, older adults are encouraged to regularly engage in specific muscle strengthening exercises and/or higher-impact weight-bearing activities to maintain and importantly to restore muscle health. Alternatively, moderate to intense aerobic activity such as brisk walking may provide sufficient muscular exercise to retard the loss of muscle mass or it may serve to indicate which individuals are performing sufficient resistance activity to conserve their muscle mass. Accordingly, Park et al.[21] and Shephard et al.[22] report that the appendicular muscle mass of older adults measured by electrical impedance is associated with regular habitual physical activity and more closely with moderate-intensity exercise than volume. To our knowledge, the present study is the first intervention study to examine the relationships between exercise and measures of muscle mass of the limbs in obese elderly women. This study also reconfirmed the results of previous studies which found that the effect of exercise on cardiovascular risk factors in this population[23, 24].

This study had some limitations. Time spent performing outdoor activities was not measured, which could have potentially affected the results. In addition, differences in diet might be another confounding factor. Indeed, we did not control diets in either group throughout the study. Finally, the sample size was small, which limits our ability to determine the significance of the results. Therefore, additional studies with larger sample sizes are required to determine the effectiveness of regular physical activity.

In summary, this study demonstrates that a 12-week exercise program improves the plasma oxidized LDL concentrations as well as other cardiovascular risk factor such as CIMT and appendicular muscle mass measured by dual-energy X-ray absorptiometry in elderly obese women. The beneficial effects of low- to moderate-intensity exercise on outcomes in elderly obese adults appear to be related to sustained improvement in risk factors for cardiovascular disease that becomes evident after 12 weeks of exercise. Therefore, low- to moderate-intensity physical activity should be recommended in conjunction with pharmacological therapy for elderly patients with chronic heart failure and arteriosclerosis.

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