Effects of Aerobic Exercise on Lipid Profiles and High Molecular Weight Adiponectin in Japanese Workers

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Abstract

Background The metabolic syndrome is characterized by the accumulation of several metabolic risk factors. It is important to improve physical activity and dietary habits to reduce the risk of cardiovascular disease in humans.

Methods The study participants participated in a weekly aerobic exercise program that included a session composed of a brief meeting, warm-up exercises, and primary exercises (low and high impact, stretch, muscle training, and cooling down). To evaluate the effect of this intervention we measured body fat composition, holding power, and quality of life assessment. Blood tests were also carried out before and every 3 months during the study.

Results Of the 37 participants enrolled in the exercise group, 31 (83.8%) completed the 12-week program. The control group consisted of 42 subjects, 36 (85.7%) of whom were available for follow-up at the end of the 12-week study period. In the exercise group, weight, body fat percentage, waist circumference, the World Health Organization quality of life 26 (WHO-QOL 26) score, triglyceride, total cholesterol, high density lipoprotein cholesterol and low density lipoprotein cholesterol had improved significantly at the end of three months. The high molecular weight adiponectin concentration of the participants in the exercise group increased during the 9-month period of the study, although this change did not reach statistical significance compared with pre-exercise.

Conclusion Aerobic exercise led to an improvement in body composition and lipid profiles. High molecular weight adiponectin concentrations tended to improve compared with pre-aerobic exercise levels.

Key words: aerobic exercise, high molecular weight (HMW) adiponectin

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Introduction

The metabolic syndrome is characterized by the accumulation of several metabolic risk factors, such as abdominal obesity, dyslipidemia, hypertension, glucose intolerance, and prothrombotic and proinflammatory states (1-5). It is well known that patients with the metabolic syndrome have an increased risk of cardiovascular disease (6). Recently, the prevalence of patients with the metabolic syndrome has increased in Japanese workers. According to the International Diabetes Federation (IDF) and the National Cholesterol Education Program (NCEP) III criteria, the prevalence of the

metabolic syndrome in Japanese workers is reported to range from 25.8% to 33.0% (7).

It is important to improve physical activity and dietary habits to reduce the risk of cardiovascular disease in humans. Several earlier studies have shown that the beneficial effects of aerobic exercise on blood pressure, cholesterol levels, and insulin sensitivity occur regardless of whether weight loss is achieved or not (8, 9). In fact, the Pawtucket Heart Study group reported there is a close relationship between physical activity and the levels of high density lipoprotein (HDL) cholesterol (10). A study in 3,000 adult Japanese men also showed that the frequency of physical activity correlated positively with HDL cholesterol levels (11).

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The aims of the present study in Japanese workers were to assess the effects of long-term aerobic exercise on lipid profiles, glucose levels, and plasma high molecular weight (HMW) adiponectin, an anti-atherosclerotic adipokine.

Materials and Methods

Participants

Participants were enrolled in the study using newspaper and radio advertisements, and pamphlets. A total of 79 subjects aged 28-76 years (21 men and 58 women) were enrolled in the intervention group.

According to the Japanese diagnostic criteria, the metabolic syndrome is defined as a waist circumference of at least 85 cm in men, or 90 cm in women, plus at least two of the following characteristics: 1) triglycerides ≥ 1.69 mmol/L (150 mg/dL) or HDL cholesterol < 1.03 mmol/L (40 mg/dL), 2) systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg, and 3) fasting plasma glucose ≥ 6.11 mmol/L (110 mg/dL) (12). The exclusion criteria in this study were a history of cardiovascular diseases, other serious illnesses, and type 1 diabetes mellitus. After the participants were asked about their history of physical and psychiatric illnesses, a physical examination was carried out on each participant.

The consent forms explained the purpose of this study, confidentiality of data, the possibility of declining to participate, and the contact numbers of the researchers. Documents containing explanations and precautions, and consent forms were distributed to the participants to obtain their written permission before the survey. They obtained and approval the written informed consent from 79 subjects in total. The study protocol was submitted to and approved by the Institutional Review Board (IRB) of the Faculty of Medicine at Saga University.

Intervention

The exercise program was undertaken 1 day each week for 3 months or more up to a maximum of 18 months. The three-month course therefore consisted of a total of 12 sessions. Each session was of 1.5 hours duration and consisted of a brief meeting (10 minutes), warm-up exercises (5 minutes), primary exercises (30-35 minutes), stretch exercises (10 minutes), muscle training (25 minutes), and cooling down (5 minutes). Participants were assigned training ranges using a pre-established heart rate equivalent to 70% to 85% of their maximum heart rate (13).

Physical assessment

Physical assessment including weight, body mass index (BMI), body fat percentage (% body fat) was performed for each participant before the aerobic exercise program and 3 months later using the TANITA TBF-305 (Tanita, Tokyo, Japan) body fat/composition monitor. Waist circumference was measured at the navel with the subject in the erect position

after relaxed breathing. Duplicate measurements of holding power of the left and right hand were recorded using a grip dynamometer, and the average of the values recorded. During these measurements, the subjects were requested not to move the dynamometer.

QOL assessment

We evaluated the participants' quality of life using the World Health Organization Quality of Life scale (WHO-QOL) (14). The 26-item short form of the WHO-QOL is the brief version of the WHO-QOL 100, which was developed to assess subjects around the world, regardless of culture or local customs. It consists of 26 items classified into the following five domains: physical domain, psychological domain, social relationships, environmental domain, and general QOL. We evaluated the QOL assessment before the course and after three months of aerobic exercise.

Blood tests

The levels of triglyceride, total cholesterol, HDL cholesterol, low density lipoprotein (LDL) cholesterol, and fasting plasma glucose were measured during the study. Plasma HMW adiponectin level was measured using a sandwich ELISA kit (Fujirebio, Tokyo, Japan) that incorporated a monoclonal antibody to human HMW adiponectin, IH7 (15). A working standard of HMW adiponectin was prepared using human HMW adiponectin purified by passage through a Geratin-Cellulofine affinity column (Seikagaku Industrial Co., Tokyo Japan). The sensitivity and upper limit of the working range of HMW adiponectin levels were 0.18 to 22.05 $\mu\text{g/mL}$. The intra- and inter-assay variances were 2.4 to 3.0% and 4.2 to 5.1%, respectively.

Statistical analysis

The data were expressed as the mean $\pm$ standard error (SE). The Chi-square test and Mann-Whitney U test were used to compare the characteristics of the two groups. The Wilcoxon signed-rank test was used to compare the values before the program and after three months of aerobic exercise. A two-way repeated measures analysis of variance (ANOVA) (aerobic exercise duration $\times$ gender) was used to compare the values at 3, 6, 9, 12 and >12 months between the group performing exercises and pre-exercise. Pearson's correlation analysis and multiple regression analysis to examine the relationship between HMW adiponectin and the other factors and the Mann-Whitney U test was used to compare HMW adiponectin concentrations at 3, 6 and 9 months. The Statistical Package for the Social Sciences (SPSS, SPSS Japan Inc., Tokyo, Japan) software version 17 was used for the statistical analyses, with statistical significance being set at p values < 0.05 .

Results

Subjects

Thirty-seven subjects (10 men, 27 women, 73.0% women) who responded to the advertisement for participation in the present study were selected as the intervention group. We include 42 subjects as controls (11 men, 31 women, 73.8% women) who were matched to the subjects in the intervention group.

In the exercise group, 2 participants had a history of depression, 3 were dyslipidemia, and 3 had the metabolic syndrome. In the control group, 2 participants had a history of depression, 3 were dyslipidemia and 2 had the metabolic syndrome. The data were analyzed by the Chi-square test in order to confirm that the two groups were well matched and

that our hypotheses were tenable ($p=0.539$).

Adherence to aerobic exercise

Of the 37 participants in the exercise group, 31 (83.8%) completed the 12-week program (8 men, 23 women, mean age 45.5 ± 2.2 years, 74.2% women, mean BMI 23.5 ± 0.7 kg/m²), while 36 in the control group (85.7%) were available for follow-up at the end of the 12-week study period (10 men, 26 women, mean age 45.8 ± 1.2 years; 72.2% women, mean BMI 22.4 ± 0.4 kg/m²) (Table 1). The attendance rate for the aerobic exercise program ranged between 43% to 84% for each period.

Effect of exercise training on outcome variable

In the exercise group, weight, % body fat, waist circumference, WHO-QOL 26 score, triglyceride, total cholesterol, HDL cholesterol and LDL cholesterol had improved significantly by the end of the third month (Table 2). Of the 12 variables measured in the aerobic exercise group, (5 body composite variables, WHO-QOL 26 score, and 6 blood test variables), 4 variables improved significantly (Fig. 1). The aerobic exercise caused significant improvements in weight (men; $F=3.766$, $p=0.0152$, women; $F=3.834$, $p=0.0083$), waist circumference (men; $F=4.400$, $p=0.0075$, women; $F=2.830$, $p=0.0335$), WHO-QOL 26 score (men; $F=7.080$, $p=0.0005$, women; $F=6.120$, $p=0.0004$), and HDL cholesterol (men; $F=5.840$, $p=0.0017$, women; $F=3.732$, $p=0.0095$).

Correlation with HMW adiponectin

As shown in Table 3, there was a significant negative correlation between HMW adiponectin and body composition (BMI; $r=-0.509$, $p=0.037$), LDL cholesterol ($r=-0.578$, $p=0.015$), and fasting plasma glucose ($r=-0.559$, $p=0.020$). In

Table 1. Baseline Characteristics of Participants

Variables	Exercise group	Control group	p
n	31	36	
Men/Women	8/23	10/26	0.539 ^a
Age (year)	45.5 ± 2.2	45.8 ± 1.2	0.934 ^b
Height (cm)	161.9 ± 1.4	160.4 ± 0.9	0.368 ^b
BMI (kg/m ²)	23.5 ± 0.7	22.4 ± 0.4	0.189 ^b
% body fat (%)	26.0 ± 1.2	26.6 ± 1.1	0.708 ^b
Waist circumference (cm)	84.6 ± 2.0	80.6 ± 1.3	0.095 ^b
Weight (kg)	62.1 ± 2.2	58.5 ± 1.2	0.497 ^b

Values are expressed as means $\pm$ SE, a, using Chi-square test, b, using Mann-Whitney U test, BMI, body mass index, body fat percentage, % body fat.

Table 2. The Effects of Aerobic Exercise on the Exercise Group and Control Group during 3 Months

	Exercise group (n=31)			Control group (n=36)		
	Pre	3 months later	p	Pre	3 months later	p
Weight (kg)	62.1 ± 2.2	60.8 ± 2.1	0.001 *	58.5 ± 1.2	57.5 ± 1.1	0.381
BMI (kg/m ²)	23.5 ± 0.7	23.2 ± 0.7	0.249	22.4 ± 0.4	22.3 ± 0.5	0.825
% body fat (%)	26.0 ± 1.2	25.1 ± 1.2	0.008 *	31.3 ± 0.7	29.5 ± 1.0	0.169
Waist circumference (cm)	84.6 ± 2.0	80.1 ± 1.8	0.001 **	80.6 ± 1.3	81.1 ± 2.0	0.183
Left holding power (kg)	30.6 ± 1.9	31.3 ± 2.0	0.329	30.8 ± 1.7	31.0 ± 1.9	0.945
Right holding power (kg)	33.2 ± 1.9	33.5 ± 1.9	0.455	31.9 ± 1.7	32.1 ± 1.8	0.455
WHO-QOL 26 score	2.9 ± 0.1	3.1 ± 0.1	0.001 **	2.9 ± 0.1	2.9 ± 0.1	0.878
Triglyceride (mg/dL)	135.3 ± 14.5	121.5 ± 19.4	0.019 *	110.1 ± 8.7	107.7 ± 8.7	0.523
Total cholesterol (mg/dL)	210.8 ± 6.3	194.7 ± 5.5	0.002 **	217.1 ± 5.8	217.4 ± 5.9	0.600
HDL cholesterol (mg/dL)	61.0 ± 3.0	71.8 ± 2.9	0.001 **	70.0 ± 2.2	72.3 ± 2.4	0.080
LDL cholesterol (mg/dL)	119.7 ± 5.7	112.9 ± 4.9	0.037 *	122.1 ± 5.1	120.8 ± 5.0	0.768
Fasting plasma glucose (mg/mL)	97.1 ± 4.5	95.2 ± 2.4	0.931	96.9 ± 3.7	102.9 ± 3.7	0.073

Values are means $\pm$ SE. * $p<0.05$ ** $p<0.005$, using Wilcoxon signed-rank test. BMI, body mass index, body fat percentage, % body fat.

Figure 1. Changes in body composition and blood with the exercise group. Values are means $\pm$ SE. * $p < 0.05$, using two-way repeated measures analysis of variance (ANOVA). Numbers of men were as follows: pre, (n=8) 3 months, (n=8), 6 months, (n=8), 9 months, (n=7), 12 months or more, (n=5). Numbers of women: pre, (n=23), 3 months, (n=23), 6 months, (n=20), 9 months, (n=17), 12 months or more, (n=11).

Table 3. Pearson's Correlation Analysis and Multiple Regression Analysis of HMW Adiponectin and Other Factors

	Pearson's correlation analysis (n=17)		Multiple regression analysis (n=17)	
	Pearson's Y	p	β -values	p
BMI	-0.509	0.037 *	-0.174	0.018 *
% body fat	-0.031	0.907	-0.088	0.453
Waist circumference	-0.180	0.488	0.101	0.244
WHO-QOL26	0.207	0.426	0.040	0.213
Triglyceride	-0.093	0.722	0.024	0.361
Total cholesterol	-0.309	0.228	0.014	0.114
HDL cholesterol	0.665	0.004 **	0.389	0.002 **
LDL cholesterol	-0.578	0.015 *	-0.443	0.008 *
Fasting plasma glucose	-0.559	0.020 *	-0.306	0.010 *
R ²				0.761
Adjusted R ²				0.454

Values are means $\pm$ SE. * $p < 0.05$, ** $p < 0.005$, using pearson's correlation analysis and multiple regression analysis. R² = coefficient of determination. BMI, body mass index, body fat percentage, % body fat.

contrast, there was a significantly positive correlation between HMW adiponectin and HDL cholesterol ($r = 0.665$, $p = 0.004$). There was no relationship between HMW adiponectin and WHO-QOL 26 score, triglyceride, total cholesterol levels, % body fat, and waist.

Multiple regression analysis examined the relationship between HMW adiponectin and the other factors. There was a significant correlation between HMW adiponectin and body composition (BMI; $\beta = -0.174$, $p = 0.018$), HDL cholesterol ($\beta = 0.389$, $p = 0.002$), LDL cholesterol ($\beta = -0.443$, $p = 0.008$),

Figure 2. Changes in HMW adiponectin responses with the exercise group during the exercise and post exercise. Values are means $\pm$ SE. n.s., $p > 0.05$, using the Mann-Whitney U test. Numbers of participants were as follows: pre, (n=22), 3 months, (n=17), 6 months, (n=11), 9 months, (n=5).

and fasting plasma glucose ($\beta = -0.306$, $p = 0.010$, Coefficient of determination $R^2 = 0.761$, and adjusted $R^2 = 0.454$). There was still no relationship between HMW adiponectin and WHO-QOL 26 score, triglyceride, total cholesterol levels, % body fat, and waist.

Adiponectin responses

The concentration of HMW adiponectin increased in the exercise group, although the difference between pre- and post-exercise levels did not reach statistical significance (Fig. 2). The HMW adiponectin concentration was increased by 24% after 9 months of exercise compared with pre-exercise levels.

Discussion

Aerobic exercise improved body weight, waist circumference, WHO-QOL 26 score, and HDL cholesterol. The concentration of HMW adiponectin increased during the aerobic exercise program, with a significant negative correlation being observed between HMW adiponectin and body composition (BMI). HMW adiponectin also showed a significant positive correlation with HDL cholesterol and a significant negative correlation with LDL cholesterol. We found that the 31 (83.8%) participants who completed the exercise program had significant improvements in weight, % body fat, waist circumference, WHO-QOL 26 score, triglyceride, total cholesterol, HDL cholesterol and LDL cholesterol at the end

of the third month. These findings are in agreement with a previous study on endurance exercise training that reported positive changes in lipid and lipoprotein metabolism (16).

It is generally considered that aerobic exercising has several beneficial effects on health. For example, regular exercise may promote chronic positive effects such as an improvement in lipid profiles, insulin resistance, BMI, and % body fat, as well as basal metabolic state (17). As the metabolism of lipoproteins occurs mainly during the aerobic exercise (18), the positive changes in anthropometric variables observed in the present study indicate that periodical aerobic exercising has the potential to improve the lipid profile. The pathological changes in the lipid and glucose metabolism in metabolic syndrome are closely related to the state of insulin resistance, unfortunately we have no data of fasting insulin concentration (IRI); further studies are needed to rectify the relation between IRI and exercise.

A loss of body mass and fat has also been associated with decreases in total and LDL cholesterol and an increase in HDL cholesterol. The improvement in total cholesterol may result from the exchange of cholesterol esters between tissues and lipoproteins to HDL cholesterol. Furthermore, exercise training usually decreases the concentration of fasting plasma triglycerides. As a consequence, the levels of very low density lipoprotein (VLDL) decrease and HDL cholesterol levels tend to increase (19). It is considered beneficial to increase the clearance of VLDL and triglyceride, in order to decrease the mean residence time of these lipoproteins in

the circulation. The concentration of LDL cholesterol is regulated by the balance between synthesis in the liver and removal from the plasma by lipoprotein receptors, while HDL concentration is determined by both HDL cholesterol and apolipoprotein A-I (apoA-I) concentrations. HDL cholesterol concentration increases frequently in response to a decrease in triglyceride, although in this study exercise training did not change the triglyceride levels. Therefore, another possible mechanism for the exercise-induced rise in HDL cholesterol rise we observed may be induction of apoA-I synthesis. There is further evidence that lecithin and cholesterol acyltransferase (LCAT) activity are changed by exercise training, and may therefore also affect HDL cholesterol levels before and after exercise training (20-22).

In this study we showed that continued exercise training led to further improvements in weight, waist circumference, WHO-QOL 26 score and HDL cholesterol levels (Fig. 1) while the other variables remained stable. We also demonstrated that HMW adiponectin correlated positively with HDL cholesterol, and negatively with LDL cholesterol and fasting plasma glucose. It has been reported that HMW adiponectin is not only the more active form of the adipokine (23, 24), but is also related closely to insulin sensitivity in the metabolic syndrome (25, 26). The present study investigated the role of aerobic exercise and improvement in lipid profiles in relationship to changes in HMW adiponectin concentration. Blüher et al (27) found that HMW adiponectin concentration increased with exercise treatment even in subjects with normal glucose tolerance. In contrast, Bobbert et al (28) showed that HMW adiponectin concentration was similar before and after 6 weeks of marathon training without a reduction in body weight. In the present study, HMW adiponectin concentration increased in the exercise group, although this increase did not reach significance during the aerobic exercise program (Fig. 2). The effect of aerobic exercise on HMW adiponectin concentration therefore remains to be established conclusively. However, HMW adiponectin concentrations tended to be higher than in the pre-exercise period. Further studies are needed to determine whether HMW adiponectin concentration changes significantly during longer periods of aerobic exercise or with different intensity of exercises.

Conclusion

Aerobic exercise leads to an improvement in body composition and lipid profile. The concentration of HMW adiponectin also showed a tendency to improve with regular aerobic exercise compared with pre-exercise levels.

The authors state that they have no Conflict of Interest (COI).

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