Effect of Walking Exercise on Changes in Cardiorespiratory Fitness, Metabolic Syndrome Markers, and High-molecular-weight Adiponectin in Obese Middle-aged Women

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Abstract. [Purpose] The purpose of this study was to assess the effect of a 24-week exercise intervention on cardiorespiratory fitness, metabolic syndrome markers, and high-molecular-weight (HMW) adiponectin among obese middle-aged women. [Subjects] The subjects were 14 obese middle-aged women. [Methods] The exercise program involved walking at 50–60% of the maximum oxygen consumption, 3 times a week, for 24 weeks. Body composition analysis, blood pressure measurements, and blood analysis were performed before the exercise program and at weeks 6, 12, 18, and 24. [Results] The results showed that after 24 weeks in the exercise program, the obesity indices and metabolic risk factors, namely, weight, body fat, body mass index, waist circumference, systolic blood pressure, diastolic blood pressure, and triglycerides decreased significantly, whereas HDLC, a metabolic improvement factor, increased significantly. Additionally, VO2max increased significantly, together with the level of total and HMW adiponectins. Correlation analysis of the changes in measured variables (∆ score) during resulting from the 24-week exercise program showed that body fat had a significant negative correlation and VO2max had a significant positive correlation with HMW adiponectin. [Conclusion] Among obese middle-aged women, regular exercise increases cardiorespiratory fitness and HMW adiponectin expression and therefore can be effective in the prevention and treatment of obesity and metabolic syndrome.

Key words: Exercise, Cardiorespiratory fitness, Obesity

INTRODUCTION

The worldwide increase in the prevalence of obesity has prompted most countries to focus on its prevention and treatment to improve public health. Obesity is defined as an excessive accumulation of adipose tissue that leads to health problems and, in pathological terms, serves as the main risk factor for metabolic syndrome. Metabolic syndrome refers to a cluster of disorders consisting of obesity, insulin resistance, hypertension, and hyperlipidemia, which may increase the risk for the development of chronic disease.

Adipose tissues have been traditionally considered as the energy reservoir of the body. Recently, they have been recognized as an endocrine organ with various biological activities, including the synthesis of adipocytokines. Adiponectin is an adipocytokine that acts as an important mediator in insulin and glucose metabolism. The mechanism of adiponectin is currently a major focus in obesity and metabolic syndrome research. The name adiponectin was derived from the fusion of the terms adipocyte and protein, thus signifying a protein secreted by the adipose tissue. Its plasma concentration is within the range of 5–30 µg/ml, which is 1,000 times higher than the hormones leptin and cortisol and about 1 million times higher than the cytokines tumor necrosis factor (TNF)-α and interleukin (IL)-6. Specifically, high-molecular-weight (HMW) adiponectin is the biologically active form of adiponectin and is more functionally important than low-molecular-weight (LMW) and medium-molecular-weight (MMW) adiponectin.

The currently elucidated roles of adiponectin include promoting oxidation of fat in the liver and muscles to improve insulin sensitivity, anti-inflammatory effects by suppressing the secretion of cytokines from endothelial cells, and anti-atherosclerotic effects by suppressing the proliferation and migration of vascular smooth muscle cells promoted by the platelet-derived growth factor (PDGF). Additionally, the concentration of adiponectin plays an important role in insulin sensitivity and glucose homeostasis and is also closely associated with an increased risk for...
obesity and the components of metabolic syndrome such as type II diabetes, cardiovascular disease, hypertension, and dyslipidemia. Finding ways to increase the secretion of adiponectin or its activity has been suggested to be a potential factor in the treatment of obesity and metabolic disorders, and one of the most effective ways to achieve this condition is through regular exercise. Regular exercise decreases abdominal fat, increases high-density lipoprotein cholesterol (HDLC), decreases neutral fat, decreases blood pressure, and increases insulin sensitivity. Specifically, the increase in metabolic equivalents and cardiorespiratory fitness (CRF) due to exercise has been reported to decrease the risk for metabolic syndrome, increase insulin sensitivity, and prevent cardiovascular diseases.

In studies on the relationship between exercise and adiponectin, Esposito et al. applied dietary changes and aerobic exercise to obese middle-aged women and observed a decrease in body weight and a significant increase in adiponectin levels. Kriketos et al. reported an increase in adiponectin levels when overweight men engaged in walking exercises for 40 min a day, 4–5 times a week, for 10 weeks, at an intensity of 55–70% of maximum oxygen consumption (VO2max). Furthermore, Boudou et al. showed that middle-aged men and women who underwent a 16-week exercise program consisting of 30 min of aerobic exercise 5 times a week, at an intensity of 80–90% HRmax exhibited an increase in adiponectin levels. However, Polak et al. reported no changes in adiponectin among obese women who participated in a 12-week program consisting of aerobic exercise 5 times a week at an intensity of 50% VO2max. Giannopoulou et al. also did not observe any changes in adiponectin expression after 6 months of aerobic exercise, although a decrease in blood insulin concentrations and an increase in insulin sensitivity were reported. In a 6-month study on weight loss through dietary changes or treatment with medications that decrease insulin sensitivity, the total adiponectin levels did not change, although HMW adiponectin increased.

Various studies have reported the effect of exercise on adiponectin expression; however, they have reported conflicting findings. Furthermore, studies on the effect of long-term exercise intervention on adiponectin in middle-aged women, who generally undergo changes in body weight, are currently insufficient to generate robust conclusions. Additionally, we believe that assessing HMW adiponectin along with total adiponectin can more effectively determine the effect of exercise on this specific population. Therefore, the purpose of this study was to determine the effect of a 24-week exercise intervention on the cardiorespiratory fitness, metabolic syndrome indices, and HMW adiponectin in middle-aged women.

### SUBJECT AND METHODS

The study population included 14 middle-aged women who were 42 to 55 years of age and free of medical disorders. The subjects were selected after assessing age, physical activity level, changes in body weight in the past year, smoking, and current medication. Women who had both a waist circumference (WC) ≥ 80 cm and a body mass index (BMI) ≥ 25 kg/m2 and exercised less than twice a week were selected as subjects. Before conducting the experiment, the content and purpose of the experiment were fully explained to the subjects and they provided written consent. Kyungwoon university approved this study, which complies with the ethical standards of the Declaration of Helsinki. The general characteristics of the subjects are listed in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>BMI (kg/m²)</th>
<th>Body fat (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects (N = 14)</td>
<td>48.9 ± 4.4</td>
<td>156.9 ± 3.9</td>
<td>64.4 ± 3.7</td>
<td>26.2 ± 2.1</td>
<td>34.4 ± 2.8</td>
</tr>
</tbody>
</table>

Data are means ± SD

VO2max, as an index of CRF, was measured on a motor driven treadmill using the Bruce protocol as described in the American College of Sports Medicine (ACSM) guidelines. Specifically, the speed of the treadmill was initially set at a comfortable walking speed of 1.0–1.7 mph and at 10% grade. Speed and grade were then increased every 3 min until volitional exhaustion. VO2 was measured using standard breath-by-breath techniques of pulmonary gas exchange variables (Metabolic Gas Analyzer System; Quark b2, Cosmed Rome, Italy) and exercise heart rate was measured using 12-lead electrocardiography (Q4500, Quinton Instrument Company, Bothell, WA, USA). VO2max was considered as the highest oxygen consumption attained at the moment of exhaustion. During the incremental exercise test, the rate of perceived exertion (RPE, Borg scale) was measured. RPE was reported by the subjects at the end of each session based on the response to the question, “How hard did you work during this session?” The subjects rated their RPE while looking at a printed copy of the Borg scale. This self-reported scale has a score ranging from 6 to 20 and uses descriptive cues for each category of exertion within the scale, ranging from “very, very light” to “very, very heavy”.

The requirements to strictly define whether subjects reached their VO2max included meeting at least two of the following four criteria: (1) a respiratory exchange ratio of >1.15; (2) rate of perceived exertion >17 for the original category scale; (3) volitional exertion; and (4) achievement of age-predicted maximal heart rate. Study participants were verbally encouraged to exercise to exhaustion during the test.

The exercise program in this experiment consisted of walking at an intensity of 50–60% VO2max, 3 times a week, for 24 weeks. After a treadmill VO2max test, the individual’s regression line was calculated from the oxygen consumption per minute and heart rate. To determine whether the target calorie expenditure was achieved, the target heart rate of the subject during the walking exercise was assessed.
using an automatic heart rate monitor (Polar S610i heart rate monitor, Polar Electro, Kempele, Finland), from which energy expenditure was calculated. The energy expenditure per session was set at 400 kcal, 120 kcal per week (three sessions per week), and the duration of each session was set between 60 and 120 min, depending on individual performance.

Height and body mass were recorded using a stadiometer attached to a scale (DS-I02, Jenix, Seoul, Republic of Korea). WC measurements were made using a cloth tape measure at the level of the umbilicus. Percent body fat was assessed using an X-scan II bioelectrical body composition analyzer (Jawon Medical, Seoul, Republic of Korea), according to the procedures recommended by the ACSM\textsuperscript{180}. After a resting period of at least 5 min in a sitting position, resting BP was measured using an automated blood pressure cuff (FT-500R Automatic Blood Pressure Monitor, Jawon Medical, Seoul, Republic of Korea). WC measurements were made using a cloth tape meter attached to a scale (DS-102, Jenix, Seoul, Republic of Korea). All procedures were administrated by trained technicians who followed standardized protocols.

To minimize any possible effects of the last meal consumed before blood collection, the samples were collected after a 10–12 h overnight fast and in a sitting position. Blood samples were collected before the exercise program and at weeks 6, 12, 18, and 24 of the exercise program at the same time of the day and under the same conditions. The plasma was separated from the whole blood by centrifugation at 4 °C and plasma triglyceride levels were determined using a TG slide (Vitros TRIG DTD, Johnson & Johnson, New Brunswick, NJ, USA) and Vitros Chemistry DT60II HDLC slide (HDL cholesterol; Vitros HDLC DTD, Johnson & Johnson, New Brunswick, NJ, USA) and Vitros Chemistry DT60II HDLC slide (HDL cholesterol with magnesium chloride and dextran sulfate using an automated blood pressure cuff (FT-500R Automatic Blood Pressure Monitor, Jawon Medical, Seoul, Republic of Korea). All procedures were administrated by trained technicians who followed standardized protocols.

Table 2. Change in the obesity indices and metabolic risk factors after 24 weeks of exercise training

<table>
<thead>
<tr>
<th>Measured variable</th>
<th>Baseline</th>
<th>6 weeks</th>
<th>12 weeks</th>
<th>18 weeks</th>
<th>24 weeks</th>
<th>∆ score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>64.4 ± 3.7</td>
<td>62.4 ± 4.5**</td>
<td>61.4 ± 4.3***</td>
<td>60.6 ± 4.7***</td>
<td>59.9 ± 5.1***</td>
<td>−4.5 ± 3.2</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>34.4 ± 2.8</td>
<td>32.8 ± 3.4**</td>
<td>32.4 ± 3.3***</td>
<td>31.4 ± 3.5***</td>
<td>31.4 ± 3.7***</td>
<td>−3.0 ± 2.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.2 ± 2.1</td>
<td>25.4 ± 2.3**</td>
<td>25.0 ± 2.3***</td>
<td>24.5 ± 2.4***</td>
<td>24.2 ± 2.60***</td>
<td>−1.9 ± 1.3</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>89.8 ± 5.5</td>
<td>86.6 ± 4.8</td>
<td>86.1 ± 5.3**</td>
<td>86.9 ± 5.5**</td>
<td>86.6 ± 5.33**</td>
<td>−3.2 ± 3.8</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>120.4 ± 13.1</td>
<td>115.6 ± 16.2</td>
<td>112.2 ± 17.0*</td>
<td>111.4 ± 15.1**</td>
<td>113.7 ± 14.0**</td>
<td>−6.6 ± 9.7</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>80.3 ± 10.6</td>
<td>69.2 ± 8.3**</td>
<td>66.8 ± 9.6***</td>
<td>66.8 ± 9.0***</td>
<td>69.5 ± 6.6***</td>
<td>−10.7 ± 6.2</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>100.2 ± 14.5</td>
<td>90.1 ± 15.7***</td>
<td>93.5 ± 15.7*</td>
<td>91.8 ± 11.0**</td>
<td>97.0 ± 16.3</td>
<td>−5.3 ± 12.4</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>117.0 ± 52.1</td>
<td>111.6 ± 89.7</td>
<td>127.7 ± 82.8</td>
<td>97.2 ± 38.8</td>
<td>84.4 ± 35.0*</td>
<td>−32.6 ± 56.2</td>
</tr>
<tr>
<td>HDLC (mg/dL)</td>
<td>48.5 ± 15.6</td>
<td>46.5 ± 13.3</td>
<td>45.8 ± 13.4</td>
<td>45.4 ± 10.4</td>
<td>53.6 ± 14.3*</td>
<td>6.6 ± 9.3</td>
</tr>
</tbody>
</table>

Data are means ± SD. Significant differences are indicated by asterisks for comparisons with the values before the exercise program: *: p < 0.05; ** p < 0.01; *** p < 0.001. ∆ score = change in the score from baseline to 24 weeks; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; HDLC, high-density lipoprotein cholesterol.

RESULTS

Compared with the values before the exercise program, the obesity indices and metabolic risk factors of weight (p < 0.001), body fat (p < 0.001), BMI (p < 0.001), WC (p < 0.008), SBP (p < 0.023), DBP (p < 0.01), and TG (p < 0.049) decreased significantly, and HDLC, a metabolic improvement factor, increased significantly (p < 0.020) after 24 weeks of exercise training (Table 2).

Compared with the values before the exercise program, VO\textsubscript{2max} increased significantly (p < 0.001) and total (p < 0.006), and HMW adiponectin (p < 0.006 increased significantly after the 24 weeks of exercise training (Table 3).

Table 4 shows the correlation of the score changes score) of each measured variable. Body fat showed a significant negative correlation with total (r = −0.608) and HMW (r = −0.557) adiponectins; cardiorespiratory fitness (i.e., VO\textsubscript{2max}) showed a significant negative correlation with DBP (r = −0.677) and a significant positive correlation with HMW adiponectin (r = −0.753).
DISCUSSION

The ACSM recommends walking as a safe aerobic exercise to reduce obesity and increase CRF and have suggested 50–85% of VO_{2\text{max}} as an appropriate intensity. This study showed that a 24-week walking program at 50–60% of VO_{2\text{max}} improved the CRF of obese women. This is consistent with prior studies reporting CRF improvements as a result of regular walking exercise and we think the exercise was suitable for the purpose of this study.

The results of our study showed that a 24-week regular exercise program significantly improved obesity indices and metabolic risk factors of weight, percent body fat (%BF), BMI, WC, SBP, DBP, and TG. This is consistent with results of previous studies showing that regular exercise decreases obesity and metabolic risk factors; for example, it was shown to decrease abdominal obesity, improve blood pressure, decrease the neutral fat percentage, and increase HDL.

Venables and Jeukendrup suggested that exercise is effective in improving obesity because it leads to a decrease in body fat, an increase in fat-free mass, and an overall activation of body function, compared with other measures. Additionally, a decrease in waist circumference from exercise indicates a decrease in abdominal fat and this is effective in decreasing the risk for cardiovascular and metabolic diseases. Wessel et al. surveyed 906 women in terms of obesity, CRF, and death rate due to atherosclerosis and reported that low CRF is directly correlated with death rate. These results suggest that maintenance and improvements of CRF through regular exercise, along with obesity prevention, are important approaches in preventing and treating cardiovascular and metabolic diseases.

In this study, total and HMW adiponectin significantly increased after the 24-week exercise program, compared with the values before the program. Further, the correlation of the score changes of the measured variables before and after the program (Δ score) showed that body fat, which decreased as a result of exercise, is inversely correlated with HMW adiponectin, which increases as body fat decreases.

In previous studies on adiponectin expression in response to exercise, Gan et al. reported that the blood adiponectin concentration increased by up to 260% in 19 obese men who exercised for 10 weeks, 4–5 times a week, at 55–70% of the VO_{2\text{max}} intensity, compared with the non-exercise group, despite the lack of a change in body weight. Hulver et al. studied 11 healthy men and women and reported that after 6 months of an endurance exercise program, 4 times a week at 65–80% of the VO_{2\text{max}} intensity, the group that showed a decrease in body weight also showed a significant increase in adiponectin levels. However, the group that did not show a decrease in body weight showed no change in adiponectin levels. Yuji et al. studied 27 middle-aged women with an average age of 55 and reported that body fat and BMI decreased, whereas adiponectin levels significantly increased (by 20%) after a 12-week program consisting of walking exercise 5 times a week at 65–80% of the VO_{2\text{max}} intensity, which is similar to the results of our study.

The results of our study showed that the increase in VO_{2\text{max}} due to the exercise was positively correlated with HMW adiponectin, indicating that increases in the CRF from exercise can be an effective method of increasing MHW adiponectin. Church et al. divided their subjects into 4 groups according to obesity and CRF levels and compared their risks of early death. Compared with the group with the highest fitness levels, the groups with the second, third, and fourth highest fitness levels had 1.6, 2.8, and 4.5 times higher risks, respectively, of early death. If corrected for CRF, obesity did not significantly increase the risk of early death. Also, Church et al. conducted an additional 15 year longitudinal study and reported that a decrease in CRF led to a significant increase in risk of death. If CRF decreased by 1 MET, then the risk of death increased by 20%.

<table>
<thead>
<tr>
<th>Table 3. Change in the cardiopulmonary fitness and adiponectin levels according to 24 weeks exercise training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measured variable</td>
</tr>
<tr>
<td>VO_{2\text{max}} (mL·kg^{-1}·min^{-1})</td>
</tr>
<tr>
<td>Total adiponectin (µg/mL)</td>
</tr>
<tr>
<td>HMW adiponectin (ng/mL)</td>
</tr>
</tbody>
</table>

SD. Significant differences are indicated by asterisks for comparisons with the values before the exercise program: *: p < 0.05; ** p < 0.01; *** p < 0.001. Δ score = change in the score from before the exercise program to 24 weeks

<table>
<thead>
<tr>
<th>Table 4. Pearson correlations of variation after 24 weeks of exercise training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measured variable</td>
</tr>
<tr>
<td>Body fat</td>
</tr>
<tr>
<td>DBP</td>
</tr>
<tr>
<td>VO_{2\text{max}}</td>
</tr>
<tr>
<td>Total adiponectin</td>
</tr>
</tbody>
</table>
| HMW adiponectin | −0.5* | −0.6** | 0.7** | 1 | ** Correlation is significant at the 0.001 level (two-tailed) | ** Correlation is significant at the 0.01 level (two-tailed)

DBP, diastolic blood pressure; VO_{2\text{max}}, maximum oxygen consumption; HMW, high molecular weight
*Correlation is significant at the 0.05 level (two-tailed)
**Correlation is significant at the 0.01 level (two-tailed)
These results indicate that obese people with high CRF can have a relatively lower risk of metabolic disorders than obese people with low CRF. In this context, the decrease in body fat and improvements in VO2max from the exercise intervention program in this study can be a very important factor in increasing HMW adiponectin.

Currently, adiponectin is considered an important factor in obesity and metabolic syndrome and because people with abdominal obesity have an even lower concentration of adiponectin, their risk of degenerative diseases such as diabetes, chronic inflammation, atherosclerosis, and cancer is reported to be higher. Specifically, studies show that the HMW adiponectin distribution is more important than that of total adiponectin, highlighting the importance of the fraction of HMW adiponectin. The results of our study proved that regular exercise, by increasing CRF and decreasing body fat, could be an effective technique for increasing total and HMW adiponectin. In addition, obesity indices and metabolic risk factors are interrelated in a very complex manner and exercise can lead to a general improvement in metabolism, without side effects that certain medications can have. These results support the role of exercise in the treatment of obesity and chronic illnesses among women in middle age, which is when changes in body fat distribution and incidence rates of metabolic diseases precipitously increase.

REFERENCES