

Effect of walking exercise on abdominal fat, insulin resistance and serum cytokines in obese women

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Hye-Ryun Hong, Jin-Ok Jeong, Ji-Young Kong, Sang-Hee Lee, Seung-Hun Yang, Chang-Duk Ha and Hyun-Sik Kang. Effect of walking exercise on abdominal fat, insulin resistance and serum cytokines in obese women. *JENB.*, Vol. 18, No. 3, pp.277-285, 2014 **[Purpose]** The purpose of the study was to investigate the effect of 12-week walking exercise on abdominal fat, insulin resistance and serum cytokines in obese women. **[Methods]** Following baseline measurements, obese women (N=20) who met obesity criterion of BMI at 25 kg/m² or greater were randomly assigned to the control (n=10) or exercise groups (n=10). Women assigned to the exercise group participated in a walking exercise (with an intensity of 50-60% of predetermined VO₂max, a frequency of 3 days per week and duration of 50-70 minutes targeting 400 kcal of energy expenditure per session) for 12 weeks, while women assigned to the control group maintained their sedentary lifestyle. After the 12-week walking intervention, post-test measurements were conducted using the same procedure as the baseline measurement. Analyses of variance with repeated measures were used to evaluate any significant time by group interactions for the measured variables. **[Results]** With respect to body fat parameters, significant time-by-group interactions were found in the abdominal subcutaneous (p < 0.001) and visceral adipose tissues (p = 0.011). The exercise group had significant reductions in both subcutaneous and visceral adiposity, and the control group had no significant changes in those parameters. Similarly, there were significant time by group interactions in fasting glucose (p = 0.008), HOMA-IR (p = 0.029), serum TNF-α (p = 0.027), and IL-6 (p = 0.048) such that the exercise group had significant reductions in those parameters, with no such significant changes found in the control group. The exercise group also had a significant increase in serum adiponectin (p = 0.002), whereas the control group had no significant change in the parameter. **[Conclusion]** In summary, the current findings suggest that walking exercise can provide a safe and effective lifestyle strategy against abdominal obesity and serum insulin resistance markers in obese women. **[Key word]** Abdominal adiposity, insulin resistance index, serum cytokines.

INTRODUCTION

The metabolic syndrome is characterized by the clustering of metabolic risk factors, such as abdominal obesity, insulin resistance, hyperglycemia, hypertension and hyperlipidemia. The known leading causes of the metabolic complication include overeating, physical inactivity, insulin resistance, impaired whole body insulin sensitivity, and inflammation. Recent studies have showed that obesity-related inflammation is one of the main biological mechanism behind metabolic syndrome, and particularly, a series of attempts to reveal the role and function of adipocytokines specifically expressed in abdominal body fat tissue are in progress locally and abroad.

In other words, the excessive surplus energy stored in abdominal fat tissue secondary to overeating and physical inactivity produce cytokines, releasing them into the circulation. The fact that the released cytokines are transported through skeletal muscle and liver tissue by blood vessels, and primarily induce insulin resistance characterized by the dysfunction of carbohydrate metabolism, leading to a variety of chronic degenerative diseases such as Type 2 diabetes, hyperglycemia, hyper tension and cardiovascular disease has emerged from previous studies. Attempts to reveal the role and function of the adipocytokines specifically expressed in abdominal body fat tissue are in progress worldwide. Consequently, the adipocytokines have been one of the major

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topics in many recent studies. In this respect, fatty tissue is no longer evaluated only in the traditional sense where it plays a role in energy storage by simply storing excess energy. The role of fatty tissue as a major endocrine organ which creates and releases various proteins or cytokines that directly and indirectly control energy metabolism, edema response and immune function is receiving attention [1-3].

It has been reported that among the insulin resistant cytokines secreted due to the accumulation of excessive body fat, Tumor necrosis factor- α (TNF- α) is secreted by the stimulation of endotoxins such as lipopolysaccharide (LPS), and it has an effect on acute reactivity material as well as on the functions of lipid metabolism and fat cells [4]. It is known that increase in lipolysis occurs as a result of hormone sensitive lipase stimulus, inhibition of lipoprotein lipase, differentiation inhibition of fat cells, inducement of fat cell death, and insulin resistance. Previous studies have also reported that excessive increases in serum TNF- α level is not only associated with insulin resistance and endothelium dysfunction, but also that insulin resistance is caused by negative influences on the sign path and receptor of insulin. In particular, it is known that the expression of the mRNA of TNF- α is higher in visceral fat than in subcutaneous fat, and the expression level is increased in proportion to the weight of fat. It has also been reported that if an obese patient combines dietary restrictions and exercise training with the goal of weight loss, it causes positive results that significantly reduce TNF- α levels in the blood due to an increase of TNF- α receptors in tissue along with significant weight loss [5,6].

Serum Interleukin-6 (IL-6) concentration is significantly higher in insulin resistant and obese patients in comparison to normal people [7]. The additional IL-6 is derived from intra-abdominal fat, from where it is directly circulated to the liver, and consequently stimulates the secretion of neutral fats, damaging regeneration of insulin and leading to sugar damage in liver cells and insulin signaling from 3T3-L1 fat tissue [7]. The expression and secretion of IL-6 are estimated to be 2-3 times higher in visceral fatty tissue than in subcutaneous fatty tissue. Therefore, increased IL-6 cytokine level is closely associated with abdominal obesity, where adipose tissue is mainly distributed around the abdominal region.

It is known that insulin sensitive cytokines such as adiponectin not only play a role in inhibiting the secretion of TNF- α and IL-6, but also play an essential role in maintaining homeostasis in the human body. This includes maintenance of normal sugar and lipid metabolism, unlike the above-mentioned inflammatory or insulin resistant cytokines. The excessive accumulation of body fat in obesity

can significantly reduce serum adiponectin levels [8]. The cytokine increases insulin sensitivity by increasing fatty acid oxidation in muscles and reducing glucogenesis in the liver. It also increases the expression of genes involved in fatty acid oxidation in skeletal muscle. Consequently, it reduces insulin resistance by increasing fat-burning and energy dissipation.

On the other hand, previous studies showed that the obesity-induced imbalance between insulin resistance and insulin sensitive cytokines caused by obesity can be restored via regular exercise. The studies also reported that if an obese patient combines dietary restrictions with exercise training aimed at weight loss, the combination leads to weight loss and significant reductions in serum TNF- α levels due to an increase of TNF- α receptors in tissues [4-6]. The concentration of IL-6 in blood is influenced by exercise intensity. A single bout of high-intensity exercise at an intensity of $>VO_{2max}$ 85% resulted in increased IL-6 release in response to inflammatory immune reaction caused by muscle fatigue and local muscle damage from repetitive muscle contractions [9]. IL-6 is known to induce its own increased expression through a positive feedback loop, and expression of the adiponectin gene and protein, which have the opposite function, are reduced by pro-inflammatory adipocytokines [10]. Therefore, regular exercise significantly lowers the risk of chronic degenerative diseases such as diabetes and glycosuria by reducing IL-6 while increasing the level of adiponectin.

In some studies on the relationship between adiponectin and exercise with regard to insulin sensitivity, a close relationship between exercise and changes in serum adiponectin was identified. Specifically, serum adiponectin levels have been reported to increase, decrease or maintain a continuously increasing state based on the amount of exercise [11]. It has also been reported that the concentration of adiponectin in the blood of patients with cardiovascular or metabolic diseases increased after performing aerobic training [12,13]. Kondo *et al.* [14] stated that exercise training for 7 months with obese women as well as short time training for 4 weeks increased the serum adiponectin concentration along with the improvement of insulin resistance. Most studies agree that both short time exercise and long time exercise training increase serum adiponectin levels together with improvements in insulin resistance [15,16]. So far, previous studies have consistently showed an increase in adiponectin in response to acute exercise. However, there is a lack of consistency such as the increase, decrease or no change regarding the effect of exercise training. The reports generally indicate however, that regular exercise training significantly increases serum

adiponectin levels. It is expected that, the increase in serum adiponectin following exercise training will be higher in overweight or obese patients. Consequently, obtaining insights into the effect of exercise training on abdominal fat loss and the metabolic syndrome would certainly contribute to the development of new and improved options to treat the clinical conditions.

Therefore, the main objective of this study was to investigate the effect of a 12-week moderate aerobic walking exercise on abdominal fat, insulin resistance and serum cytokines in obese women.

METHODS

Research subjects

A total of 20 women volunteers were randomly assigned to either control (CON) (n = 10) or exercise (EX) group (n = 10). All the subjects were women aged 30-40 years who were obese based on body mass index ($> 25 \text{ kg/m}^2$). In addition, all the subjects in this study comprised of women who were not taking drugs that affect blood lipid, carbohydrate metabolism, blood pressure, or weight. The subjects received full explanation about the content and purpose of the study prior to the experiments, and were enrolled after signing an agreement of participation.

Measurement and analysis items

Body composition measurement

The weights of the subjects were measured using automatic measuring equipment (DS-102, Jenix Co., Korea) with the subjects wearing light clothing. Body fat percentage was measured using the X-Scan Body Composition Analyzer (Jawon Medical Co., Korea), an auto body composition analyzer that uses bioelectrical impedance, and was also calculated using the formula $\text{BMI} = [\text{weight (kg)}/\text{height (m)}^2]$. Waist circumference (WC) was measured to the closest 0.1cm unit from the midpoint of the lowest part of the rib and the top of the iliac crest with the subjects breathing lightly while in an upright posture. Care was taken not to press the skin with the tape measure. The average value of more than 2 measurements was used for all items recorded. The blood pressure was measured 2 times using an automatic sphygmomanometer after more than 10 minutes in a stable condition, and the results were averaged.

Computerized tomography(CT) measurement of abdominal fat

A computerized tomography (CT) scan for abdominal fat measurement was conducted at the Korea Association of Health Promotion in S-city before and after the exercise program. The CT scans measured the area with Hounsfield number $-190 \sim -30$ from a cross section at the umbilical level in the midpoint between the fourth lumbar and fifth lumbar. The scans were performed using the General Electric High Speed Advantage 9800 Scanner (SCT-7800TE, SHIMADZU, Japan) after 12 hours in the fasting state. Total abdominal fat area was then obtained using the built-in program in the CT equipment. That is, the inside of the boundary of the abdominal and dorsal peritoneum was calculated as the visceral adipose tissue (VAT) area, while the outside was calculated as the subcutaneous fat area containing subcutaneous adipose tissue (SAT).

Analysis of insulin resistance index

After 12 hours of fasting, 10 ml of blood was collected from the forearm veins of all subjects using heparin-treated blood tubes (plasma) and blood tubes without heparin (serum). The plasma was separated by centrifugation at 4°C immediately after collection and stored in a -80°C cryogenic freezer until analysis. The stored serum was used to analyze the blood sugar level using the Vitros Chemistry DT60 (Johnson & Johnson, NY, USA) with slides from the same company. The serum insulin level was analyzed using a commercial insulin analysis kit (Human insulin ELISA-kit, DSL, Texas, USA) according to the manufacturer's instructions. The blood sugar and insulin levels measured in the fasting state were used to calculate the Homeostasis Model Assessment Index ($\text{HOMA-IR} = [\text{fasting insulin } (\mu\text{U/ml}) \times \text{fasting glucose (mmol/l)}]/22.5$), following the insulin resistance index calculation proposed by Matthews *et al.* [17].

Analysis of inflammation-related serum cytokine

The concentrations of serum-related cytokines such as TNF- α (Human TNF- α ELISA kit, DSL, Texas, USA), IL-6 (Human IL-6 ELISA kit, DSL, Texas, USA), and adiponectin (Human Adiponectin ELISA kit, AdipoGen, Seoul, Korea) were analyzed using the stored serum from the cryogenic freezer (-80°C).

Walking exercise

Taking into account the recommendation from ACSM (2006) that 60% of the maximal oxygen uptake is the appropriate exercise intensity for burning fat tissue during exercise, a test of gradual exercise loading using the modified Bruce protocol was conducted prior to the study. A linear

regression equation between heart rate at the time of the exercise test and the oxygen uptake reaction per minute was calculated. The exercise time (50 to 70 minutes) needed to induce exercise energy consumption of 400 kcal per session at the heart rate corresponding to 50-60% of each individual's maximal oxygen uptake was determined using the resulting regression equation. Each subject wore a Polar Heart Rate Monitor while performing the walking exercise at home. The exercise was performed 3 times a week for a total of 12 weeks ($400\text{kcal} \times 3 \text{ times} \times 12\text{weeks} = 14,400 \text{ kcal}$) at the exercise intensity determined in advance (50-60% of maximum oxygen consumption). Whether the heart rate during the walking exercise reached the target heart rate and whether the correct momentum was reached was verified using the Polar heart Monitor (Polar S610i, Polar Electro, Finland). The exercise was also monitored using a Kenz Lifecorder Ex accelerometer (Suzuken Co, Ltd, Nagoyz, Japan). In this program, the health status of the subjects and whether the desired exercise intensity and target consumption energy were reached were managed by conducting continuous recommendations and follow-ups for each group. The control group was advised to avoid performing regular exercise during the study period, and to maintain their sedentary lifestyles. Compliance was checked two times a week.

Dietary intake

All subjects had to complete a diet diary developed by the research team. The diary was completed three times a week (twice on weekdays, once on the weekend) between the pre-test and the post-test periods. The average daily intake of calories, and the intake ratio of the main energy source (such as carbohydrates, fats and protein) were analyzed using the Can-Pro (version 2.0), which is a program for Korean nutrition analysis.

Data analysis

The mean and the standard deviation of all data were calculated using the SPSS-PC (version 18.0) statistical program. The level of verification of all hypotheses was $\alpha = .05$ level. The authors checked whether the collected data was distributed normally prior to analyzing the data. Data that was not in the normal distribution was converted to the normal distribution by applying a log₁₀ transformation. The difference verification for physical characteristics, abdominal fat, insulin resistance index, and serum cytokine of pre- and post-exercise between the groups was performed using Two-way ANOVA with repeated measure. If post-test was necessary, it was analyzed using LSD post-test.

RESULTS

Physical characteristics

Table 1 shows the results by group comparing the average body composition and blood pressure measured before and after 12 weeks of walking exercise. The mean value of the weight, body mass index (BMI), body fat, and waist circumference (WC) of the exercise groups showed a tendency to decrease post-exercise compared to pre-exercise. However, that difference was not statistically significant in comparison with the control group. In other words, the change in weight ($p = 0.076$), BMI ($p = 0.148$), body fat ($p = 0.439$), and waist circumference pre- and post-walking exercise did not show statistically significant differences between the measurement time and group. However, the weight ($p < 0.001$), BMI ($p < 0.001$), body fat ($p < 0.001$) and waist circumference ($p < 0.001$) were significantly decreased post-exercise compared to pre-exercise, regardless of the group.

Abdominal body fat

Table 2 shows the comparison results between the groups for changes in abdominal subcutaneous fat and visceral fat measured before and after the 12-week walking exercise. The table shows that the mean values of the abdominal subcutaneous and visceral fat ($p = 0.011$) measured by CT scans before and after the walking exercise had interaction

Table 1. Effect of 12 weeks of walking exercise on body fat and resting blood pressures

		CON (n = 10)	EX (n = 10)	P Value
Weight (kg)	Pre	65.4 ± 10.1	74.1 ± 14.9	a: < 0.001
	Post	64.3 ± 10.1	71.4 ± 15.1	b: 0.192 c: 0.076
BMI (kg/m ²)	Pre	26.9 ± 2.9	27.9 ± 4.8	a: < 0.001
	Post	26.4 ± 2.7	26.8 ± 4.7	b: 0.323 c: 0.148
Body fat (%)	Pre	35.0 ± 4.4	36.3 ± 4.6	a: < 0.001
	Post	34.0 ± 4.9	34.8 ± 4.4	b: 0.626 c: 0.439
WC (cm)	Pre	92.8 ± 9.1	95.2 ± 9.1	a: < 0.001
	Post	91.5 ± 10.2	92.4 ± 11.6	b: 0.226 c: 0.373
SBP (mmHg)	Pre	126.3 ± 11.5	128.3 ± 21.3	a: 0.025
	Post	123.8 ± 10.8	107.1 ± 13.8	b: 0.276 c: 0.037
DBP (mmHg)	Pre	71.3 ± 4.1	70.2 ± 3.3	a: 0.025
	Post	72.1 ± 4.3	65.8 ± 3.5	b: 0.735 c: 0.108

a = time; b = group; c = time×group; CON: control; EX: exercise; BMI: body mass index; WC: waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

Table 2. Effect of 12 weeks of walking exercise on abdominal adiposity

		CON (n = 10)	EX (n = 10)	P Value
SAT (mm ²)	Pre	22950 ± 8762	31477 ± 12341	a: < 0.001 b: 0.220
	Post	22010 ± 9063	25793 ± 11967	c: < 0.001
VAT (mm ²)	Pre	7620 ± 4510	9948 ± 5728	a: < 0.001 b: 0.549
	Post	7056 ± 3802	7339 ± 4750	c: 0.011

a = time; b = group; c = time×group, CON: control; EX: exercise; SAT: subcutaneous abdominal fat; VAT: visceral abdominal fat.

Table 3. Effect of 12 weeks of walking exercise on markers of insulin resistance

		CON (n = 10)	EX (n = 10)	P Value
Glucose (mg/dL)	Pre	108.9 ± 11.8	114.0 ± 12.9	a: < 0.001 b: 0.932
	Post	107.1 ± 14.0	102.9 ± 10.0	c: 0.008
Insulin (μU/mL)	Pre	23.9 ± 9.6	23.6 ± 7.0	a: 0.333 b: 0.561
	Post	25.0 ± 10.3	20.1 ± 11.6	c: 0.072
HOMA-IR	Pre	6.39 ± 2.66	6.78 ± 2.56	a: 0.112 b: 0.722
	Post	6.65 ± 3.04	5.31 ± 3.58	c: 0.029

a = time; b = group; c = time×group,; CON: control; EX: exercise.

effects between the time of measurement and group. Such interaction effects meant that the subcutaneous and visceral fat of the exercise group were significantly reduced in comparison to the control group. The subcutaneous and visceral fat of the control group before and after exercise did not change significantly.

Insulin resistance index

Table 3 shows the results of comparison between the groups for the insulin resistance index, including comparisons of blood glucose, insulin, and homa index measured before and after the 12-week walking exercise. The mean values of the blood glucose and homa index measured before and after the walking exercise showed a significant interaction effect between the measurement time and group. The interaction effect was interpreted to mean that the average blood glucose and homa index in the exercise group were significantly reduced post-exercise in comparison with pre-exercise values. In the control group however, the average values of these variables had no statistically significant changes. Insulin showed a non-significant tendency towards interaction ($p = 0.076$) between the measurement time and the group.

Serum cytokine

Table 4 shows the on insulin resistant and insulin sensitive cytokine levels measured before and after 12 weeks of

Table 4. Effect of 12 weeks of walking exercise on serum cytokines

		CON (n = 10)	EX (n = 10)	P Value
TNF-α (pg/ml)	Pre	5.71 ± 0.17	5.80 ± 0.12	a: 0.006 b: 0.005
	Post	5.82 ± 0.42	5.11 ± 0.29	c: 0.027
IL-6 (pg/ml)	Pre	5.52 ± 1.27	6.21 ± 1.80	a: 0.001 b: 0.001
	Post	5.01 ± 1.15	5.10 ± 1.42	c: 0.048
Adiponectin (ug/ml)	Pre	12.6 ± 2.65	13.2 ± 3.20	a: 0.008 b: 0.001
	Post	13.21 ± 2.27	16.11 ± 2.15	c: 0.002

a = time; b = group; c = time×group,; CON: control; EX: exercise

walking exercise. The average value of the serum cytokine TNF-α ($p = 0.027$), IL-6 ($p = 0.048$), and adiponectin ($p = 0.002$) showed that there was significant interaction effect between the measurement time and the group. The significant interaction was interpreted to mean that the TNF-α and IL-6 levels significantly as the adiponectin level significantly increased post-exercise compared to pre-exercise.

DISCUSSION

Physical characteristics, abdominal fat, and insulin resistance index

In this study, the purpose was to verify the influence of 12 weeks of walking exercise on the abdominal fat, insulin resistance index, and serum cytokine levels of middle-aged obese women. The results of this study support the existing data showing that walking exercise is not only a major muscle group exercise involving rhythmic and dynamic movement, but it is also a typical aerobic exercise [18,19] that is relatively stable and economic. Walking can be recommended to women with obesity or metabolic syndrome at relatively high clinical risk that do not have prior experience with exercise.

In addition, the differences between the insulin resistance index, including blood glucose, insulin and homa index of the two groups before and after the 12-week experimental treatment was verified. The blood glucose and homa index of the exercise group showed significantly reduced values post-experimental treatment compared to pre-experimental treatment. Generally, if body fat increases excessively in the body, the small peripheral fat cells will store the excess neutral fat in liver cells, skeletal muscle cells, abdominal fat cells, and peripheral large adipocytes. Since insulin resistance is initiated from the liver and muscles, increasing energy consumption through physical activity and exercise decreases body fat. Walking exercise is effective in primary prevention interventions [20] to maintain proper weight and is therefore

recommended as a major treatment for insulin resistance. The increased blood flow from skeletal muscle contractions can improve glucose inflow due to insulin, and therefore, the increase in blood flow causes the removal of excess glucose. Furthermore, the capillarization and Mean transit time of subjects who received aerobic training increased, indicating an increase of insulin and glucose exposure in the tissue [21]. Increasing exercise energy consumption by 500 kcal results in a 6% protective effect against the rate of diabetes. However, it has been reported that light physical activity such as walking up and down stairs, as well as walking for a long time, does not have the same effectiveness [22]. Above all, studies have shown that continuous aerobic exercise increases the utilization of glucose after exercise due to the resulting glucose synthesis [23].

The results of this study demonstrate that participation in 12 weeks of walking exercise is effective to improve insulin resistance in obese middle-aged women. These results are in agreement with previous studies reporting that regular exercise and enhancement of cardiorespiratory fitness induce positive effects such as lowering the prevalence and mortality of cardiovascular disorders and metabolic syndromes [24] such as obesity, insulin resistance, hyperlipidemia, and higher blood pressure.

Insulin resistance is clinically characterized as the clustering phenomenon of metabolic risk factors, such as abdominal obesity, hypertension, hyperlipidemia and hyperglycemia [25]. It has been reported that individuals who are diagnosed with insulin resistance have relatively high risk of transitioning to type 2 diabetes and cardiovascular disease in comparison with normal individuals [26]. In fact, epidemiological investigation showed that the transition to diabetes is 2-4 times higher, and the likelihood of cardiovascular disease is 4-11 times [27] higher than for a normal person. It has also been reported that the risk of coronary artery disease and sudden death are 3 times higher than for normal individuals [28].

Of all the lifestyle factors known as direct and indirect causes of insulin resistance, the increase of abdominal subcutaneous and visceral fat is known as an independent risk factor for cardiovascular disease and Type 2 diabetes [29]. Thus, abdominal obesity is the most important lifestyle-related factor that increases the risk of insulin resistance or metabolic syndrome where hypertension, hyperlipidemia and hyperglycemia form a cluster. Abdominal obesity is also a common risk factor that causes various forms of cardiovascular diseases [30].

Additional research is required to verify the effects of exercise prescription and develop various forms of interven-

tion programs that can more effectively, continuously and stably reduce abdominal fat. A complex mediation combining various forms of lifestyle modifications, such as controlled caloric intake along with physical activity and the improvement of physical strength should be developed for the future.

Serum cytokine

The adipocytokine synthesized in adipose tissue can be broadly classified into insulin-desensitizing adipocytokine and insulin-sensitizing adipocytokine. The degree of expression plays a role in the pathological link that causes obesity, inflammation, and insulin resistance [31]. Because exercise training is well known as a non-pharmacological means to increase insulin sensitivity in skeletal muscle along with reducing body fat, comparison of the results before and after 12 weeks of walking exercise was performed in this study.

The results showed that the exercise group that participated in walking exercise had significantly lower TNF- α and IL-6 concentrations, corresponding to the insulin resistance related cytokines, post-exercise in comparison to pre-exercise levels. In addition, the level of adiponectin, an insulin sensitivity cytokine, was significantly increased. It has also been reported in previous studies overseas that excessive accumulation of body fat plays a role in inflammation and insulin resistance by leading to an imbalance in insulin sensitive and insulin resistant cytokines expressed specifically in fat cells. The results of this study show that walking exercise significantly lowers the serum insulin resistant cytokine level, decreasing the insulin function as well as the insulin resistance index by reducing abdominal obesity. The increase in serum adiponectin level identified in the results of this study supports previous studies [14,16] reporting that short and long periods of exercise training also increase the serum adiponectin level in addition to improving insulin resistance [33]. reported that walking exercise of moderate intensity is effective in preventing the occurrence of Type 2 diabetes by maintaining insulin sensitivity.

Adiponectin has an important role in fatty acid and glucose metabolism by activating AMPK and PPAR- α , and by activating insulin sensitivity and energy oxidation [34]. According to previous studies related to exercise and adiponectin, aerobic exercise increases insulin sensitivity by increasing the expression of serum adiponectin and decreasing the expression of RBP4 [35]. It has been reported that short-term and long-term exercise training also increases serum adiponectin levels along with improving insulin resistance [15,16]. It is well known that the increase of serum adiponectin after exercise training reduces the level of TNF- α

while reducing arterial stiffness and inflammatory cytokines. The increased serum adiponectin also plays anti-obesity, anti-diabetic, and antiedemic roles such as inhibiting the regeneration of glucose by causing the increase of AMPK and PPAR- α , p38 expression.

The above results are in agreement with the previous study [36] showing that the levels of TNF- α and IL-6, known as insulin resistant cytokines, were closely associated with metabolic diseases including obesity and Type 2 diabetes. The results also support reports that the TNF- α and IL-6 levels of obese patients were significantly decreased by moderate walking exercise, as well as a previous study [37] reporting that adult males and females at more than 1.7x the relative risk for ischemic heart disease who performed 6 months of exercise training had a 58% reduction in edema-related cytokine production including serum IFN- γ , IL-6 and IL-1 β . For those individuals, production of antiedemic cytokines such as TGF- β and IL-10 was reduced by 36%. In addition, the results of this study can be interpreted in the same vein as the research results of [38] that physical activity or cardiorespiratory fitness level has a negative correlation with serum TNF- α and IL-6, whereas it has a positive correlation with serum IL-10 level. Besides, TNF- α is known to induce the death of fat cells and to cause insulin resistance and is a substance secreted by the stimulus of endotoxins such as lipopolysaccharide. Previous studies have shown that if an obese patient combines dietary restriction and exercise training aimed at weight loss, serum TNF- α levels decrease significantly due to the increase of TNF- α receptors along with significant weight loss [39,40]. Therefore, in this study, it was expected that serum TNF- α reduction in the exercise group will be related to the loss of abdominal fat. A succeeding study to reveal the biological mechanisms of the exercise effect by including gene and protein expression will be needed in the future.

The results of this study are in agreement with the research results of reporting that 9 weeks of exercise training in animal experiments significantly reduced the expression of leptin mRNA in adipose tissue [41]. The leptin mRNA reduction had significant correlation with the size reduction of fat cells. In addition, reported that in animal experiments, a complex treatment that combined exercise training and diet significantly decreased not only the weight [42] and the white adipose weight, but also the level of TNF- α and IL-1 β [43]. reported that 16 weeks of treadmill exercise by high-fat diet mice significantly decreased the expression of TNF- α mRNA and F4/80 mRNA in adipose tissue without loss of body fat. These results demonstrate that the significant reduction of abdominal fat due to exercise training can induce positive effects that

reduce the expression of edema or insulin resistance-related cytokines in adipose tissue. Abdominal obesity causes insulin resistance in end-organs, including the liver, skeletal muscles and pancreas. Ultimately, the known pathological mechanisms that cause Type 2 diabetes are as follows: ① the buffering role of adipose tissue that prevents the influx of serum lipid (ex. Free fatty acid, neutral fatty acid) is excessively increased through the hydrolysis of body fat and controlled hydrolysis of serum lipoproteins containing lipids [44]. ② The role of adipose tissue as the endocrine system that adjusts the expression and discharge of insulin sensitive and insulin resistant cytokines [45,46]. ③ The nutrition controlling cell growth and differentiation, as well as cell hypertrophy along with the maintenance of energy homeostasis in cells - the role of adipose tissue as a signal transfer system is involved [47, 48, 49]. Additional studies that reveal the biological relationship between exercise training, insulin resistance and abdominal obesity using overall approach methods such as microarray will be required in the future.

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