

Journal of Exercise Rehabilitation 2018;14(6):1032-1040

# Effects of exercise type on estrogen, tumor markers, immune function, antioxidant function, and physical fitness in postmenopausal obese women

Jae-Ryang Yoon<sup>1</sup>, Gi-Chul Ha<sup>1</sup>, Kwang-Jun Ko<sup>2</sup>, Seol-Jung Kang<sup>3,\*</sup>

This study aims to identify the effects of exercise type on estrogen, tumor markers, immune function, antioxidant function, and physical fitness in postmenopausal obese women. The subjects were 30 postmenopausal obese women with body fat percentage higher than 30%. Participants were divided into aerobic exercise group (n = 10; age,  $53.70 \pm 3.37$  years), resistance exercise group (n = 10; age,  $52.20 \pm 2.15$  years), and control group (n = 10; age,  $52.50 \pm 2.68$  years). Estrogen and growth hormone showed no significant difference in the aerobic exercise group, resistance exercise group, and control group. Tumor marker alpha-fetoprotein was increased in the aerobic exercise, resistance exercise, and control groups (P<0.01). The metabolic syndrome risk factor was decreased in the aerobic and resistance exercise groups, which was shown by the reduction of weight (P<0.001), body fat percentage (P<0.001), waist circumference (P<0.005), and increase of high density

lipoprotein-cholesterol (P<0.001). natural killer cell activity was increased in the aerobic exercise group, resistance exercise group, and control group (P<0.001). Oxidative stress was decreased in the aerobic exercise group, resistance exercise group, and control group (P<0.001). Maximum oxygen uptake was increased in the aerobic and resistance exercise groups, but aerobic exercise was more effective (P<0.05). Knee isokinetic extensor muscle was increased in both the aerobic and resistance exercise groups (P<0.001). Aerobic and resistance exercise of postmenopausal obese women can be considered an effective intervention program to prevent metabolic syndrome and improve physical fitness.

Keywords: Exercise type, Postmenopausal obese woman, Estrogen, Metabolic syndrome, Physical fitness

#### INTRODUCTION

Menopause is a type of aging process during which the secretion of the female hormone estrogen is decreased due to a decline of follicular function, and the quality of life and physical functions deteriorate due to menopausal symptoms (Nelson, 2008). In particular, postmenopausal women are known to have a higher chance of having cancer than premenopausal women (Rosano et al., 2007). With recent emphasis on the importance of early discovery of cancer, researches on tumor markers have been actively done. Tumor markers are used to selecting and tracking the early diagnosis of cancer and to predict the pre- and postoperative prognosis, but

due to low sensitivity and specificity for tumor diagnosis, they appear to be increased or get detected even when one does not have cancer (Perkins et al., 2003). In other words, most cancers are easy to track down but tumor markers for liver cancer and breast cancer, which often start around menopausal stage, have been reported to be diagnostically useful (Sturgeon, 2002).

Also, postmenopausal women have reduced production of estrogen, which serves a cardioprotective function; this event leads to a higher risk of developing cardiovascular disease (Knopp, 1988). In other words, estrogen deficiency due to menopause accelerates the accumulation of visceral fat, which increases the risk of metabolic syndrome, in which abdominal obesity and insulin resistance

\*Corresponding author: Seol-Jung Kang https://orcid.org/0000-0002-6258-2996 Department of Physical Education, Changwon National University, 20 Changwondaehak-ro, Uichang-gu, Changwon 51140, Korea Tel: +82-55-213-3520, Fax: +82-55-266-8467, E-mail: sjkang803@hanmail.net Received: September 10, 2018 / Accepted: November 2, 2018

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

<sup>&</sup>lt;sup>1</sup>Department of Physical Education, Korea National Sport University, Seoul, Korea

<sup>&</sup>lt;sup>2</sup>Department of Sports Medicine, National Fitness Center, Seoul, Korea

<sup>&</sup>lt;sup>3</sup>Department of Physical Education, Changwon National University, Changwon, Korea



play important roles (Carr, 2003). Moreover, estrogen plays an important role in lymphocyte activation, but menopause decreases the efficiency of cell-mediated and antibody-mediated responses by thymic atrophy (Pernis, 2007; Ryan et al., 2005).

On the other hand, the pathogenesis of cancer, cardiovascular disease, and impaired immune function can be attributed to the deterioration of cell damage and antioxidant activity by free radicals (Valko et al., 2007) and is significantly affected by physical inactivity (Hamilton et al., 2007). However, aerobic exercises suggested for menopause stage are known to be effective in the prevention of cancer and metabolic syndrome, improvement of immune system and antioxidant activity (Bruunsgaard and Pedersen, 2000; Friedenreich, 2001; Hartmann and Niess, 1988; Oliveria and Christos, 1997). In addition, since the skeletal muscles are decreased during menopausal period, resistance exercise is also important. Resistance exercise has been shown to be effective in improving myocardial function and preventing chronic diseases (Bemben et al., 2000; Hurley et al., 1988).

However, studies that have compared and analyzed changes in estrogen, tumor marker, metabolic syndrome indicator, immune function, antioxidant function and physical fitness between aerobics and exercises among obese postmenopausal women are highly limited. Therefore, the aim of this study is to compare and analyze the effect of 12-week-long aerobic and resistance exercises on estrogen, tumor marker, metabolic syndrome indicator, immune function, antioxidant function and physical fitness in postmenopausal obese women.

## MATERIALS AND METHODS

#### **Subjects**

For the subjects of this study, 30 obese postmenopausal women with a body fat percentage of 30% or higher were registered at Seoul regional sports center, and they were randomly distributed into aerobic exercise group (n = 10), resistance exercise group (n = 10), and control group (n = 10). Physical characteristics of the subjects are shown in Table 1. The exclusion criteria were those who were taking medication due to heart disease, those who have been taken sex hormonal drugs, those under estrogen replacement therapy, and those who have experienced chest pain, dyspnea, and arrhythmia during exercise. This study was approved by the Institutional Review Board of the Korea National Sport University's Bioethics Committee (approval number: 1263-201706-BR-005-04).

#### Measurement items and methods

Height and weight were measured using an automatic body meter (Jenix, Seoul, Korea). The body mass index (BMI) was calculated by dividing the measured body weight (kg) by the square (m<sup>2</sup>) of the height (cm). The waist circumference was measured up to 0.1 cm in the upright posture from the lower end of the rib and the midpoint of the upper iliac crests. The body fat percentage was measured using a body fat analyzer (X-Scan II, Jawon Medical, Gyeongsan, Korea) following the bioelectrical impedance method.

The blood pressure measurement was done by measuring systolic and diastolic blood pressures in the left brachial artery at the same height as the heart by using a mercury blood pressure meter after at least 10 min of resting.

Maximum oxygen uptake (VO<sub>2max</sub>) was measured to show cardiovascular strength by performing an exercise load test based on a modified version of Balke protocol using an automatic breathing gas analysis system (Q4500, Quinton, Bothell, WA, USA). The criteria for ending the exercise load test were when the oxygen consumption did not increase even when the exercise load was increased, when the exercise self-conscious level was 17 or higher, when the heart rate was  $\pm 5$  than the age-dependent predicted maximum heart rate by age, and when the respiratory exchange rate was higher than 1.15.

To measure the maximal strength, relative strength, and extensor motion range of the knee extensions and flexor muscles, the test was performed using isokinetic equipment (System 3 Pro, Biodex, Shirley, NY, USA). The measurement was done 3 times at the left

Table 1. Characteristics of subjects

Group	Age (yr)	Height (cm)	Weight (kg)	BMI (kg/m²)	Body fat (%)
Aerobic exercise (n = 10)	$53.70 \pm 3.37$	$157.30 \pm 6.46$	$59.70 \pm 5.52$	24.16±2.21	$31.65 \pm 1.86$
Resistance exercise (n = 10)	$52.20 \pm 2.15$	158.04±3.21	$60.79 \pm 5.41$	$24.31 \pm 1.65$	$32.48 \pm 1.37$
Control (n = 10)	$52.50 \pm 2.68$	$159.69 \pm 4.87$	61.11 ± 6.96	$23.94 \pm 2.18$	$31.60 \pm 0.98$
P-value	0.452	0.560	0.860	0.918	0.327

Values are presented as mean ± standard deviation.

BMI, body mass index.



and right at the speed of 60°/sec after matching the subject's knee motion axis and dynamometer axis and by fixating the trunk and thigh with Velcro to minimize the motion of other body parts.

Blood samples were collected from the vein after confirming the 10-hr fasting state. The collected blood was centrifuged at 3,000 rpm for 10 min and stored at -70°C. Blood analysis items and methods are as follows. Estrogen was analyzed via radioimmunoassay. Growth hormone was analyzed using chemiluminescence immunoassay. Tumor markers alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), cancer antigen 125 (CA 125), and CA 153 were analyzed by radioimmunoassay. The triglyceride, high-density lipoprotein cholesterol (HDL-C), and fasting state blood sugar were analyzed by enzymatic method, while low density lipoprotein cholesterol (LDL-C) was done by homogeneous enzymatic colorimetric assay. To assess the extent of insulin resistance, the formula of Matthews et al. (1985) was used: "HOMA- $IR = [fasting plasm insulin (\mu U/mL) \times fasting plasm glucose (mg/mu) \times fasting plasm glucose$ dL)]/405." Natural killer (NK) cells were analyzed by enzyme-linked immunosorbent assay, whereas immune-globulins (IgA, IgG, and IgM) were analyzed by turbidometry method. Total antioxidant status (TAS) and total oxidant status (TOS) were analyzed using a colorimetry method.

#### Exercise program

The aerobic and resistance exercise program of this study was conducted 3 times a week for 12 weeks after the subjects were given an education on exercise method and intensity setting, as well as an adjustment period. The heart rate reserve (HRR) was set using the Karvonen et al. (1957) formula for the aerobic exercise intensity. Resistance exercise intensity was set using the indirect measurement method of one repetition maximum or 1 RM (Fleck and Kramer, 1987). Exercise time included 10 min of preexercise, 40 min of main exercise, and 10 min of finishing exercise. The pre-exercise consisted of 5 min of walking and 5 min of stretching, while the finishing exercise included 10 min of stretching. The main exercise was as follows.

The aerobic exercise started with walking on a treadmill at dif-

ferent speeds and slopes at the HRR of 60%-80%. During the exercise, the subject wore a heart rate monitor (Polar, Kempele, Finland) to check whether the exercise intensity has been reached. Resistance exercise included bench press, lat-pull down, triceps push-down, dumbbell curl, sit-up, squat, leg extension, leg flexion, and leg press at 1RM of 60%. The exercises were repeated 8-12 times for 3 sets. The resting time between two exercise types was 1-min long.

#### **Data analyses**

The mean and standard deviation per measured item from this study's data were calculated using the IBM SPSS ver. 18.0 (IBM Co., Armonk, NY, USA). Two-way analysis of variance with repeated measures was performed to verify the mean difference. The significance level ( $\alpha$ ) of this study was set to P < 0.05.

# **RESULTS**

## Change in estrogen and growth hormone

Estrogen and growth hormone change due to aerobic exercise and resistance exercise is shown in Table 2. Value of estrogen and growth hormone did not have a significant difference between groups and measuring time points and there was no interaction effect.

#### Change in tumor markers

Tumor markers change due to aerobic exercise and resistance exercise is shown in Table 3. The value of AFP tended to increase in each of aerobic exercise group, resistance exercise group, and control group, while significant difference was shown between measuring time points (P < 0.05). There were no interaction effects. On the other hand, for CEA, CA 125, and CA 153, values did not have significant difference between groups and measuring time points. There were no interaction effects.

## Change in metabolic syndrome risk factors

Change in metabolic syndrome risk factors due to aerobic exer-

Table 2. Change of estrogen and growth hormone

Variable	Aerobic exercise		Resistance exercise		Control		<i>P</i> -value		
	Pre	Post	Pre	Post	Pre	Post	Group	Time	Interaction
Estrogen (pg/mL)	83.50±33.32	86.80 ± 21.62	85.20±30.58	94.90 ± 18.56	85.90 ± 26.93	88.80 ± 28.24	0.877	0.388	0.876
GH (ng/mL)	$2.25 \pm 1.67$	$1.40 \pm 1.23$	$0.89 \pm 0.70$	$1.09 \pm 1.20$	$1.83 \pm 1.71$	$1.12 \pm 0.89$	0.231	0.091	0.225

Values are presented as mean ± standard deviation.

GH, growth hormone.



**Table 3.** Change of tumor markers

Variable	Aerobic	Aerobic exercise		Resistance exercise		Control		<i>P</i> -value		
	Pre	Post	Pre	Post	Pre	Post	Group	Time	Interaction	
AFP (ng/mL)	2.94 ± 1.25	$3.03 \pm 0.71$	2.20±1.16	2.88 ± 1.09	$3.26 \pm 4.57$	4.07 ± 5.36	0.699	0.010	0.273	
CEA (ng/mL)	$1.41 \pm 0.57$	$1.30 \pm 0.78$	$1.69 \pm 0.96$	$1.54 \pm 0.99$	$1.94 \pm 0.83$	$2.16 \pm 0.76$	0.120	0.928	0.485	
CA 125 (U/mL)	$5.77 \pm 2.96$	$4.88 \pm 3.08$	$7.29 \pm 8.64$	$5.04 \pm 3.04$	$5.25 \pm 2.96$	$5.29 \pm 2.87$	0.832	0.265	0.592	
CA 153 (U/mL)	$9.96 \pm 3.03$	$7.55 \pm 5.49$	$12.67 \pm 3.90$	$9.83 \pm 7.71$	9.54±4.13	$10.38 \pm 3.60$	0.428	0.120	0.217	

Values are presented as mean ± standard deviation.

AFP, alpha-fetoprotein; CEA, carcinoembryonic antigen; CA, cancer antigen.

Table 4. Change of metabolic syndrome risk factors

Variable	Aerobic exercise		Resistanc	Resistance exercise		ntrol		<i>P</i> -value		
variable	Pre	Post	Pre	Post	Pre	Post	Group	Time	Interaction	
Weight (kg)	59.70 ± 5.52	58.85 ± 5.51	60.79±5.41	59.96 ± 5.43	61.11 ± 6.96	61.48±7.27	0.759	0.000	0.000	
BMI (kg/m²)	$24.16 \pm 2.21$	$23.79 \pm 1.96$	$24.31 \pm 1.65$	$24.02 \pm 1.76$	$23.94 \pm 2.18$	24.11 ± 2.22	0.976	0.010	0.001	
Body fat (%)	$31.65 \pm 1.86$	$31.41 \pm 1.90$	$32.48 \pm 1.37$	$32.28 \pm 1.37$	$31.60 \pm 0.98$	$31.50 \pm 0.98$	0.345	0.000	0.001	
WC (cm)	$81.60 \pm 5.65$	$80.70 \pm 5.62$	$82.50 \pm 4.42$	$80.30 \pm 3.89$	$79.95 \pm 4.07$	$79.70 \pm 4.19$	0.706	0.026	0.251	
SBP (mmHg)	$113.60 \pm 16.11$	$110.50 \pm 12.46$	116.10±1426	$115.10 \pm 14.74$	$113.90 \pm 18.05$	113.10 ± 18.38	0.844	0.578	0.938	
DBP (mmHg)	$70.60 \pm 8.24$	$70.20 \pm 7.29$	$72.00 \pm 7.92$	$71.60 \pm 5.13$	$71.10 \pm 15.52$	$71.40 \pm 10.99$	0.939	0.910	0.975	
TG (mg/dL)	$97.50 \pm 55.60$	$106.10 \pm 86.07$	111.20±75.79	$109.90 \pm 47.92$	$106.80 \pm 51.10$	$109.00 \pm 31.58$	0.936	0.738	0.909	
HDL-C (mg/dL)	$51.80 \pm 9.25$	$58.30 \pm 9.48$	$49.20 \pm 10.15$	57.70 ± 12.76	$57.60 \pm 11.60$	$58.50 \pm 10.89$	0.588	0.001	0.093	
LDL-C (mg/dL)	$117.70 \pm 32.38$	$113.30 \pm 39.47$	$115.70 \pm 23.96$	$120.90 \pm 40.54$	$112.90 \pm 29.47$	$113.60 \pm 33.90$	0.923	0.942	0.847	
FBG (mg/dL)	$88.20 \pm 6.76$	$91.10 \pm 6.26$	$104.40 \pm 29.28$	$108.30 \pm 19.79$	$100.40 \pm 18.88$	$100.90 \pm 12.46$	0.099	0.167	0.710	
Insulin (MU/mL)	$4.44 \pm 2.52$	$3.61 \pm 1.92$	$5.30 \pm 1.56$	$5.27 \pm 2.89$	$5.68 \pm 2.54$	$6.00 \pm 2.33$	0.131	0.684	0.567	
HOMA-IR	$0.99 \pm 0.64$	$0.84 \pm 0.50$	$1.40 \pm 0.64$	$1.39 \pm 0.74$	$1.43 \pm 0.73$	$1.50 \pm 0.64$	0.075	0.804	0.744	
CRP (mg/L)	$0.16 \pm 0.26$	$0.05 \pm 0.06$	$0.11 \pm 0.20$	$0.07 \pm 0.05$	$0.06 \pm 0.05$	$0.06 \pm 0.06$	0.628	0.147	0.360	

Values are presented as mean ± standard deviation.

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, high-density lipoprotein cholesterol; LDL poprotein cholesterol; TG, triglyceride; FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance index; CRP, C-reactive protein.

cise and resistance exercise is shown in Table 4. The value of weight tended to decrease in the aerobic exercise group and resistance exercise group, and there was significant difference between measuring time points (P < 0.001). There was also interaction effect (P < 0.001). The value of BMI tended to decrease in the aerobic exercise group and resistance exercise group, and there was significant difference between measuring time points (P < 0.01). There was also interaction effect (P < 0.01). The value of body fat tended to decrease in the aerobic exercise group and resistance exercise group, and there was significant difference between measuring time points (P < 0.05). There was no interaction effect. The value of waist circumference tended to decrease in the aerobic exercise group and resistance exercise group, and there was significant difference between measuring time points (P < 0.05). There was no interaction effect.

The value of systolic blood pressure and diastolic blood pressure did not have a significant difference between measuring time points.

There was no interaction effect. The value of triglyceride did not have significant difference between groups and measuring time points. There was no interaction effect. The value of HDL-C tended to increase in the aerobic exercise group and resistance exercise group, and there was significant difference between measuring time points (P < 0.01). There was no interaction effect. The value of LDL-C did not have a significant difference between groups and measuring time points. There were no interaction effects.

The value of fasting blood glucose, insulin, homeostasis model assessment of insulin resistance index (HOMA-IR), and C-reactive protein (CRP) did not have significant difference between groups and measuring time points. There were no interaction effects.

## Change in immune function

Change in immune function due to aerobic exercise and resistance exercise is shown in Table 5. The value of NK cell activity tended to increase in all aerobic exercise groups, in the resistance



Table 5. Change of immune function

Variable	Aerobic exercise		Resistance exercise		Cor	<i>P</i> -value			
	Pre	Post	Pre	Post	Pre	Post	Group	Time	Interaction
NK cell (pg/mL)	1,229.29 ± 435.20	1,691.64 ± 322.33	1,345.73 ± 507.70	1,574.10 ± 418.77	1,090.39 ± 338.81	1,558.49±444.78	0.537	0.001	0.550
IgA (mg/dL)	$247.20 \pm 85.50$	$239.30 \pm 77.33$	$282.10 \pm 114.76$	$277.80 \pm 108.71$	$234.80 \pm 102.95$	$238.40 \pm 99.01$	0.577	0.377	0.377
IgG (mg/dL)	$1,310.30 \pm 271.95$	$1,251.00 \pm 269.24$	$1,269.70 \pm 227.95$	$1,191.40 \pm 140.55$	$1,219.70 \pm 216.38$	$1,245.10 \pm 205.63$	0.850	0.026	0.030
IgM (mg/dL)	$109.70 \pm 40.68$	$99.00 \pm 36.04$	$123.20 \pm 77.04$	$114.40 \pm 75.61$	$85.80 \pm 49.96$	$82.90 \pm 47.63$	0.406	0.000	0.100

Values are presented as mean ± standard deviation.

NK cell, nature killer cell; IgA, immunoglobulin A; IgG, immunoglobulin G; IgG, immunoglobulin M.

Table 6. Change of antioxidant function

Variable –	Aerobic exercise		Resistance exercise		Control		<i>P</i> -value		
	Pre	Post	Pre	Post	Pre	Post	Group	Time	Interaction
TAS (mmol/L)	1.46 ± 0.07	1.83±0.55	$1.48 \pm 0.06$	2.35±1.96	1.47 ± 0.08	1.55±0.08	0.316	0.051	0.336
TOS (mmol/L)	$2.99 \pm 1.43$	$1.64 \pm 0.79$	$2.57 \pm 1.16$	$1.49 \pm 0.75$	$2.56 \pm 1.11$	$1.38 \pm 0.47$	0.516	0.000	0.901

Values are presented as mean ± standard deviation.

TAS, total antioxidant status; TOS, total oxidant status.

**Table 7.** Change of cardiorespiratory fitness and knee isokinetic function

Variable	Aerobic exercise		Resistance exercise		Cor	<i>P</i> -value			
	Pre	Post	Pre	Post	Pre	Post	Group	Time	Interaction
VO <sub>2max</sub> (mL/kg/min)	31.44±3.63	33.80 ± 4.29	31.74 ± 4.64	31.82±3.85	32.84 ± 2.63	$30.53 \pm 2.66$	0.785	0.944	0.016
Rt Knee EX TQ/BW (Nm)	142.49 ± 35.15	164.06 ± 31.33	141.44 ± 21.01	175.38 ± 22.05	140.21 ± 16.25	141.43 ± 24.53	0.205	0.001	0.036
Lt Knee EX TQ/BW (Nm)	$142.64 \pm 31.50$	$160.52 \pm 24.00$	140.15 ± 28.88	$168.06 \pm 28.06$	$135.23 \pm 27.05$	$136.58 \pm 22.41$	0.222	0.001	0.043
Rt Knee FX TQ/BW (Nm)	$75.05 \pm 20.62$	$78.70 \pm 11.48$	$76.88 \pm 15.02$	$78.73 \pm 14.33$	$72.51 \pm 18.35$	$72.04 \pm 14.21$	0.558	0.661	0.906
Lt Knee FX TQ/BW (Nm)	$71.99 \pm 22.36$	$73.60 \pm 12.28$	$69.40 \pm 19.66$	$69.20 \pm 16.95$	67.10±21.91	$69.42 \pm 19.07$	0.749	0.795	0.975

Values are presented as mean ± standard deviation.

Rt Knee EX TQ/BW, right knee-extensor peak torque/body weight; Lt knee EX TQ/BW, Left knee-extensor peak torque/body weight; Rt Knee FX TQ/BW, right knee-flexion peak torque/body weight; Lt Knee FX TQ/BW, Left knee-flexion peak torque/body weight.

exercise group, and in the control group. There was significant difference between measuring time points (P < 0.001). There was no interaction effect. The value of IgA did not have a significant difference between measuring time points. There was no interaction effect. The value of IgG tended to decrease in the aerobic exercise group and resistance exercise group but increase in the control group. There was significant difference between measuring time points (P < 0.05), and also interaction effect (P < 0.05). Value of IgM tended to decrease in the aerobic exercise group and resistance exercise group. There was significant difference between measuring time points (P < 0.001). There was no interaction effect.

## Change in antioxidant function

Change in antioxidant function due to aerobic exercise and resistance exercise is shown in Table 6. TAS, which is a measurement indicator for antioxidant capacity, did not show significant difference in value between groups and measuring time points. There was no interaction effect. The value of TOS, which is a measurement indicator for oxidative stress, tended to decrease in the aerobic exercise group, resistance group, and control group. There was significant difference between measuring timing points (P < 0.001). There was no interaction effect.

## Change in physical fitness

Change in cardiorespiratory fitness and isokinetic function of knee joint due to aerobic exercise and resistance exercise is shown in Table 7. The value of VO<sub>2max</sub> increased in the aerobic exercise group and decreased in the control group. There was no significant difference between measuring time points. There was interaction effect (P < 0.05).

The value of left knee joint isokinetic extensor tended to increase in the aerobic exercise group and resistance exercise group.



There was significant difference between measuring time points (P < 0.001). There was interaction effect (P < 0.05). The value of right knee joint isokinetic extensor tended to increase in the aerobic exercise group and resistance exercise group. There was significant difference between measuring time points (P < 0.001). There was interaction effect (P < 0.05). The value of left and right knee joint isokinetic flexors did not have a significant difference between groups and measuring time points, and there was no interaction effect.

## DISCUSSION

This study assessed the effects of exercise type on estrogen, tumor markers, immune function, antioxidant function and physical fitness in postmenopausal obese women. As a result, aerobic and resistance exercises did not affect changes in estrogen and growth hormone. The tumor marker AFP was increased, while IgG and IgM were decreased. On the other hand, the exercises appeared to be effective in the reduction of obesity indicators of metabolic syndrome, increase of HDL-C, NK cell activation, reduction of oxidative stress, and improvement of physical fitness. However, no variables except for VO<sub>2max</sub> showed significant changes between the aerobic and resistance exercises. Moreover, the control group of this study showed an increase of AFP and NK cell, as well as reduction of oxidative stress.

Menopause comes with various physiological changes due to the cease of menstruation from ovarian functional failure. During the menopausal state, the decrease of estrogen secretion is one representative symptom. On the other hand, if postmenopausal women are exposed to high estrogen level, it can induce breast cancer (Cauley et al., 1989). This study revealed that aerobic, resistance, and control exercise groups all showed an increase in estrogen level but with no significant differences. Similar to this study, Robles et al. (2012) also tested premenopausal and postmenopausal women by having them do aerobic exercises for 6 months but no changes were found in their estrogen level. According to Smith et al. (2013), a 16-week aerobic exercise did not affect the change in estrogen level in postmenopausal women, but it was effective in the prevention of breast cancer by inducing the increase of estrogen metabolites 2-hydroxyestrone and reduction of 16α-hydroxyestrone. Therefore, the study on the exercise type and estrogen metabolism in postmenopausal women needs to be studied in further detail. In this study, growth hormone was decreased in aerobic exercise and control group but increased in aerobic exercise group, and no significant differences were observed.

Both aerobic and resistance exercises showed to have similar effects on the stimulation of growth hormone secretion, but since the amount of exercise decided by the intensity and duration is a critical factor, future studies should be done by taking this into consideration (Wideman et al., 2002).

Obesity after menopause increases the risk of having cancer (Song et al., 2008). Tumor markers are useful diagnostic tools that can be used for the early detection of cancer, the determination of treatment efficacy, and the possibility of recurrence (Perkins et al., 2003). According to cohort studies on cancer development, exercise is protective against cancer (Friedenreich, 2001). The results from this study show that AFP, a tumor marker of liver cancer, was significantly increased in aerobic exercise, resistance exercise, and control group. On the other hand, CEA, cervical CA 125, and breast CA 153 were decreased but not significantly changed. Similar to this study, 8 weeks of aerobic exercise was shown to be ineffective in inducing changes in the CEA and CA 153 among breast cancer patients (Esfahbodi et al., 2018). However, tumor markers have a low specificity and, thus, play limited role in cancer screening. Furthermore, various physiological factors are known to affect tumor marker levels. In particular, the increase of AFP observed in this study may be elevated due to various liver diseases such as hepatitis, liver cirrhosis, and liver tumors (Christiansen et al., 2001). Therefore, future studies are needed to assess the exercise and tumor marker in obese menopausal women from multifaceted points of view.

The low prevalence of cardiovascular disease in premenopausal women is due to the protective effects of estrogen against cardiovascular disease (Gavin et al., 2009). However, menopausal estrogen deprivation results in abdominal fat accumulation and insulin resistance, which are major risk factors for the development of metabolic syndrome (Lobo, 2008). The results of this study showed that aerobic exercise and resistance exercise were effective in decreasing obesity indicators (weight, BMI, waist circumference, body fat percentage) and increasing HDL-C among metabolic syndrome risk factors. However, no significant changes were observed in blood pressure, triglyceride, insulin resistance level, and inflammatory marker CRP. These results are partially in line with studies that have shown that aerobic exercise in postmenopausal women fights against metabolic syndrome risk factors while reducing HOMA-IR (Earnest et al, 2013; Kim and Kim, 2012) and that metabolic syndrome z-score is decreased by resistance exercise (Conceição et al., 2013). In general, postmenopausal women have increased body fat and abdominal obesity due to the imbalance between nutritional intake and consumption, and a de-



crease in estrogen secretion promotes this process (Poehlman, 2005). In this study, aerobic and resistance exercise reduced weight and waist circumference without significant changes in the level of estrogen, which causes fat accumulation in postmenopausal obese women. This is due to that fact that calorie consumption-inducing exercise decomposes the triglyceride stored in adipocytes into free fatty acids which is to be used as energy source by muscles.

Exercise is effective in preventing cancer and infectious diseases by improving cell-mediated immune responses and adaptive immune responses (Karacabey et al., 2005). This study showed that NK cell activity was significantly increased in aerobic exercise, resistant exercise, and control group. On the other hand, IgA was not changed, but IgG and IgM were significantly decreased in aerobic exercise group and resistant exercise group. Campbell et al. (2008) reported that aerobic exercise increased NK cell, IgA, and IgG levels among postmenopausal women, but the changes were not significant. The increased NK cell activity shown in this study suggests that it may be effective in preventing cancer among postmenopausal women. However, the reason that NK cell activity was increased in both exercise and control groups may be due to external factors such as nutritional intake, stress level, and sleep status. In addition, IgG and IgM, which are known to be increased by exercise, were decreased. This may be due to immunoglobulin inhibition occurring through an increase in male hormone testosterone in the menopausal state (Giltay et al., 2000). Moreover, immunoglobulin is affected by exercise intensity, stress level, and nutritional status (Pedersen and Hoffman, 2000). Therefore, it is necessary to analyze the exercise and immunoglobulin promoting effect in postmenopausal obese women by considering these variables in the future.

Development of cancer, cardiovascular disease, and deterioration of immune function in postmenopausal women is suggested to be due to increased free radical production and decreased antioxidant function. Oxidative stress caused by free radicals results to oxidative damage of cellular proteins, lipids, and nucleic acids (Andriollo-Sanchez et al., 2005). This study showed that the TAS was increased in the aerobic exercise group, resistant exercise group, and control group, but there was no significant difference. It was found to be effective in reducing TOS, which is an oxidative stress indicator. In a previous study, it was reported that aerobic exercise increases antioxidant enzyme activity while decreasing oxidative stress (Attipoe et al., 2008; Jarrete et al., 2014). Similarly, aerobic and resistance exercise among postmenopausal women can be beneficial in reducing oxidative stress, which is used as a disease pathogenesis measure. However, in this study, the increase of antioxidant activity and increase of oxidative stress level were also observed in the control group. This may be due to the fact that the antioxidative role of various nutritional factors like vitamin C, vitamin E, albumin, and beta-carotene was not appropriately considered in this study. It seems necessary to identify the effect of exercise by considering this factor in the future.

On the other hand, low cardiorespiratory fitness and decreased muscle strength are risk factors for cardiovascular disease (García-Hermoso et al., 2018; Wessel et al., 2004). A number of studies reported that aerobic and resistance exercise are effective in increasing cardiorespiratory fitness and muscle strength among postmenopausal women (Karacan, 2010; Oliveira et al., 2015; Orsatti et al., 2008). This study showed that VO<sub>2max</sub> was increased in all exercise groups but more significantly in the aerobic exercise group. The isokinetic knee extensor muscles were increased in both the aerobic exercise group and resistance exercise group. Recently, Robinson et al. (2017) have shown that aerobic interval training exercise is effective in increasing VO<sub>2max</sub> and muscle strength, while resistance exercise does not affect VO<sub>2max</sub> enhancement. The difference in the cardiovascular fitness and muscular strength enhancement between aerobic and resistance exercises were also observed in this study, but it can suggest it as an effective method for increasing physical fitness, which is important for the prevention of cardiovascular disease in postmenopausal obese women.

The limitation of this study is that it is difficult to generalize the data because subjects were selected in postmenopausal obese women from one single region. Moreover, this study did not include the amount of physical activity, smoking, drinking, dietary habits, and stress level, indicating that the study did not take the effect of these factors on the measuring variables into consideration.

In conclusion, aerobic exercise and resistance exercise are not effective in inducing changes in the estrogen secretion in postmenopausal obese women but may be considered as a basis for intervention for the prevention of metabolic syndrome and improvement of physical fitness. In order to verify the effect of each variable, future studies are needed to be carried out by taking intensity, amount, and duration of aerobic and resistance exercise.

## **CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.



#### ACKNOWLEDGMENTS

This work was supported by the National Research Foundation of Korea (NRF) grantfunded by the Korea government (2017S1 A5A2A01026057).

## REFERENCES

- Andriollo-Sanchez M, Hininger-Favier I, Meunier N, Venneria E, O'Connor JM, Maiani G, Coudray C, Roussel AM. Age-related oxidative stress and antioxidant parameters in middle-aged and older European subjects: the ZENITH study. Eur J Clin Nutr 2005;59 Suppl 2:S58-62.
- Attipoe S, Park JY, Fenty N, Phares D, Brown M. Oxidative stress levels are reduced in postmenopausal women with exercise training regardless of hormone replacement therapy status. J Women Aging 2008;20: 31-45.
- Bemben DA, Fetters NL, Bemben MG, Nabavi N, Koh ET. Musculoskeletal responses to high- and low-intensity resistance training in early postmenopausal women. Med Sci Sports Exerc 2000;32:1949-1957.
- Bruunsgaard H, Pedersen BK. Special feature for the Olympics: effects of exercise on the immune system: effects of exercise on the immune system in the elderly population. Immunol Cell Biol 2000;78:523-531.
- Campbell PT, Wener MH, Sorensen B, Wood B, Chen-Levy Z, Potter JD, McTiernan A, Ulrich CM. Effect of exercise on in vitro immune function: a 12-month randomized, controlled trial among postmenopausal women. J Appl Physiol (1985) 2008;104:1648-1655.
- Carr MC. The emergence of the metabolic syndrome with menopause. J Clin Endocrinol Metab 2003;88:2404-2411.
- Cauley JA, Gutai JP, Kuller LH, LeDonne D, Powell JG. The epidemiology of serum sex hormones in postmenopausal women. Am J Epidemiol 1989;129:1120-1131.
- Christiansen M, Høgdall CK, Andersen JR, Nørgaard-Pedersen B. Alphafetoprotein in plasma and serum of healthy adults: preanalytical, analytical and biological sources of variation and construction of age-dependent reference intervals. Scand J Clin Lab Invest 2001;61:205-215.
- Conceição MS, Bonganha V, Vechin FC, Berton RP, Lixandrão ME, Nogueira FR, de Souza GV, Chacon-Mikahil MP, Libardi CA. Sixteen weeks of resistance training can decrease the risk of metabolic syndrome in healthy postmenopausal women. Clin Interv Aging 2013;8:1221-1228.
- Earnest CP, Johannsen NM, Swift DL, Lavie CJ, Blair SN, Church TS. Dose effect of cardiorespiratory exercise on metabolic syndrome in postmenopausal women. Am J Cardiol 2013;111:1805-1811.
- Esfahbodi A, Fathi M, Rahimi GR. Changes of CEA and CA15-3 biomarkers in the breast cancer patients following eight weeks of aerobic exercise. Basic Clin Cancer Res J 2018;9:4-12.

- Fleck SJ, Kramer WL. Designing resistant training program. Champaign (IL): Human Kinetics; 1987.
- Friedenreich CM. Physical activity and cancer prevention: from observational to intervention research. Cancer Epidemiol Biomarkers Prev 2001;10:287-301.
- García-Hermoso A, Cavero-Redondo I, Ramírez-Vélez R, Ruiz JR, Ortega FB, Lee DC, Martínez-Vizcaíno V. Muscular strength as a predictor of all-cause mortality in an apparently healthy population: a systematic review and meta-analysis of data from approximately 2 million men and women. Arch Phys Med Rehabil 2018;99:2100-2113.e5.
- Gavin KM, Seals DR, Silver AE, Moreau KL. Vascular endothelial estrogen receptor alpha is modulated by estrogen status and related to endothelial function and endothelial nitric oxide synthase in healthy women. J Clin Endocrinol Metab 2009;94:3513-3520.
- Giltay EJ, Fonk JC, von Blomberg BM, Drexhage HA, Schalkwijk C, Gooren LJ. In vivo effects of sex steroids on lymphocyte responsiveness and immunoglobulin levels in humans. J Clin Endocrinol Metab 2000;85: 1648-1657.
- Hamilton MT, Hamilton DG, Zderic TW. Role of low energy expenditure and sitting in obesity, metabolic syndrome, type 2 diabetes, and cardiovascular disease. Diabetes 2007;56:2655-2667.
- Hartmann A, Niess AM. Oxidative DNA damage in exercise. Pathophysiology 1988;5:112.
- Hurley BF, Hagberg JM, Goldberg AP, Seals DR, Ehsani AA, Brennan RE, Holloszy JO. Resistive training can reduce coronary risk factors without altering VO2max or percent body fat. Med Sci Sports Exerc 1988; 20:150-154.
- Jarrete AP, Novais IP, Nunes HA, Puga GM, Delbin MA, Zanesco A. Influence of aerobic exercise training on cardiovascular and endocrineinflammatory biomarkers in hypertensive postmenopausal women. J Clin Transl Endocrinol 2014;1:108-114.
- Karacabey K, Saygin O, Ozmerdivenli R, Zorba E, Godekmerdan A, Bulut V. The effects of exercise on the immune system and stress hormones in sportswomen. Neuro Endocrinol Lett 2005;26:361-366.
- Karacan S. Effects of long-term aerobic exercise on physical fitness and postmenopausal symptoms with menopausal rating scale. Sci Sports 2010;25:39-46.
- Karvonen MJ, Kentala E, Mustala O. The effect of training of heart rate: a longitudinal study. Ann Med Exp Biol Fenn 1957;35:307-315.
- Kim JW, Kim DY. Effects of aerobic exercise training on serum sex hormone binding globulin, body fat index, and metabolic syndrome factors in obese postmenopausal women. Metab Syndr Relat Disord 2012; 10:452-457.
- Knopp RH. The effects of postmenopausal estrogen therapy on the incidence of arteriosclerotic vascular disease. Obstet Gynecol 1988;72(5



- Suppl):23S-30S.
- Lobo RA. Metabolic syndrome after menopause and the role of hormones. Maturitas 2008;60:10-18.
- Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-419.
- Nelson HD. Menopause. Lancet 2008;371:760-770.
- Oliveira PF, Gadelha AB, Gauche R, Paiva FM, Bottaro M, Vianna LC, Lima RM. Resistance training improves isokinetic strength and metabolic syndrome-related phenotypes in postmenopausal women. Clin Interv Aging 2015;10:1299-1304.
- Oliveria SA, Christos PJ. The epidemiology of physical activity and cancer. Ann N Y Acad Sci 1997;833:79-90.
- Orsatti FL, Nahas EA, Maesta N, Nahas-Neto J, Burini RC. Plasma hormones, muscle mass and strength in resistance-trained postmenopausal women. Maturitas 2008;59:394-404.
- Pedersen BK, Hoffman-Goetz L. Exercise and the immune system: regulation, integration, and adaptation. Physiol Rev 2000;80:1055-1081.
- Perkins GL, Slater ED, Sanders GK, Prichard JG. Serum tumor markers. Am Fam Physician 2003;68:1075-1082.
- Pernis AB. Estrogen and CD4+ T cells. Curr Opin Rheumatol 2007;19:414-420.
- Poehlman ET. Menopause, energy expenditure, and body composition. Acta Obstet Gynecol Scand 2005;84:1131.
- Robinson MM, Dasari S, Konopka AR, Johnson ML, Manjunatha S, Esponda RR, Carter RE, Lanza IR, Nair KS. Enhanced protein translation underlies improved metabolic and physical adaptations to different exercise training modes in young and old humans. Cell Metab

- 2017;25:581-592.
- Robles Gil MC, Timón R, Toribio AF, Muñoz D, Maynar JI, Caballero MJ, Maynar M. Effects of aerobic exercise on urinary estrogens and progestagens in pre and postmenopausal women. Eur J Appl Physiol 2012; 112:357-364.
- Rosano GM, Vitale C, Marazzi G, Volterrani M. Menopause and cardiovascular disease: the evidence. Climacteric 2007;10 Suppl 1:19-24.
- Ryan MR, Shepherd R, Leavey JK, Gao Y, Grassi F, Schnell FJ, Qian WP, Kersh GJ, Weitzmann MN, Pacifici R. An IL-7-dependent rebound in thymic T cell output contributes to the bone loss induced by estrogen deficiency. Proc Natl Acad Sci USA 2005;102:16735-16740.
- Smith AJ, Phipps WR, Thomas W, Schmitz KH, Kurzer MS. The effects of aerobic exercise on estrogen metabolism in healthy premenopausal women. Cancer Epidemiol Biomarkers Prev 2013;22:756-764.
- Song YM, Sung J, Ha M. Obesity and risk of cancer in postmenopausal Korean women. J Clin Oncol 2008;26:3395-3402.
- Sturgeon C. Practice guidelines for tumor marker use in the clinic. Clin Chem 2002:48:1151-1159.
- Valko M, Leibfritz D, Moncol J, Cronin MT, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. Int J Biochem Cell Biol 2007;39:44-84.
- Wessel TR, Arant CB, Olson MB, Johnson BD, Reis SE, Sharaf BL, Shaw LJ, Handberg E, Sopko G, Kelsey SF, Pepine CJ, Merz NB. Relationship of physical fitness vs body mass index with coronary artery disease and cardiovascular events in women. JAMA 2004;292:1179-1187.
- Wideman L, Weltman JY, Hartman ML, Veldhuis JD, Weltman A. Growth hormone release during acute and chronic aerobic and resistance exercise: recent findings. Sports Med 2002;32:987-1004.