

## The Effect of Combined Training on Estradiol Levels and Metabolic Risk Factors in Overweight and Obese Postmenopausal Women

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### Abstract

**Objective:** Menopause is a normal biological process associated with hormonal and metabolic changes. The purpose of this study was to investigate the effect of combined training on estradiol levels and some metabolic risk factors in obese and overweight postmenopausal women.

**Materials and Methods:** In this quasi-experimental study, 24 postmenopausal women were randomly divided into experimental and control groups. Subjects of experimental group were performed 10 weeks of combined training including resistance and aerobic exercises. Control group did not participate in any exercise training. Fasting glucose, insulin, estradiol, HOMA-IR and body fat percentage measured at the beginning and after training.

**Results:** There were no significant differences in estradiol ( $P$ -value: 0.87), glucose ( $P$ -value: 0.09), insulin ( $P$ -value: 0.11), HOMA-IR ( $P$ -value: 0.08) and body fat percentage ( $P$ -value: 0.24) between experimental and control groups after combined exercise training.

**Conclusion:** This study showed that 10 weeks of moderate-intensity combined exercise training has no effect on serum estradiol level and insulin resistance in overweight/obese postmenopausal women.

**Keywords:** Estradiol, Metabolic risk factors, Combined training, Postmenopausal women

### Introduction

Menopause is a substantial stage in women's life that is associated with metabolic changes and possibly an increased risk of type 2 diabetes (1). After menopause, adipose tissue is the main source of estrogen biosynthesis through aromatase activity (2). On the other hand, it has been reported that among postmenopausal women

circulating levels of steroid sex hormones, especially estradiol, were positively associated with increased risk of type 2 diabetes (3). Therefore, concentrations of estradiol may play important roles in the pathogenesis of type2 diabetes in postmenopausal women (4). Given that obese postmenopausal women have higher circulating estrogen levels compared to

lean postmenopausal women (5), the relationship between menopause and the risk of type 2 diabetes in obese postmenopausal women may be partly due to increased levels of endogenous estrogens. It has also been suggested that insulin resistance plays a major role in the pathogenesis of type 2 diabetes (6) and is positively associated with circulating estradiol in postmenopausal women (7). Insulin resistance and hyperinsulinemia lead to impaired glucose uptake in the muscle and decreased glycogen synthesis in the liver (8). Hyperinsulinemia also increases the risk of developing type 2 diabetes by inhibiting the synthesis of sex hormone-binding globulin in the liver (9). A cross-sectional study, also suggested that serum fasting insulin and blood glucose concentrations are higher in postmenopausal women than premenopausal women (10).

The inverse relationship between the incidence of type 2 diabetes and physical activity is well known (11,12). It has been reported that those who perform 150 min/week of moderate physical activity have a 26% lower risk of developing type 2 diabetes mellitus than inactive individuals (13). However, the effects of exercise interventions on biomarkers of type 2 diabetes risk in postmenopausal women such as estradiol and insulin levels are not well known. In this regard, previous studies have reported desirable changes (14,15) or no changes (16) in the endogenous estrogens after long-term exercise training. There are also conflicting findings about the effect of exercise training on insulin in postmenopausal women. Some studies have reported that aerobic training causes decreased insulin levels and HOMA-IR in sedentary postmenopausal women (17,18). But another study has found no changes in levels of insulin and insulin sensitivity in healthy and sedentary postmenopausal women after combined aerobic and strength exercise training (19). On the other hand, considering the favorable effects of combined training on various aspects of health, the effects of these types of training have been less studied on type 2

diabetes biomarkers in postmenopausal women. Therefore, due to heterogeneous research findings and the need to investigate different types of exercise training, the purpose of present study was to investigate the effect of a period of combined training for 10 weeks on the estradiol levels and some metabolic risk factors in overweight and obese postmenopausal women.

## Materials and Methods

In this quasi-experimental study, twenty four overweight/obese postmenopausal women (body mass index  $>25 \text{ kg/m}^2$ ) were selected through purposive sampling method among the volunteers referring to health center in the Zarandieh city, Iran. The sample size was estimated using the Fleiss's formula as in other similar studies (20,21). The participants did not have any regular exercise training in the past 6 months and their last menstruation was at least one year ago. They did not have cardiovascular, metabolic, orthopedic diseases or other chronic diseases. Moreover, none of the participants were underwent hormone replacement therapy. Informed consent was obtained from all participants before their participation in study. They were then randomly assigned into experimental (n=14) and control (n=10) groups.

Physiological and biochemical variables were measured before and after training program. Height was assessed using a stadiometer (Kaveh, Iran). Body weight and body fat percentage were measured using the body composition analyzer (Omron, Finland). Maximal oxygen uptake ( $\text{Vo}_{2\text{max}}$ ) was estimated using the Rockport Fitness Walking Test (22). Overnight fasting blood samples were taken from the antecubital vein at baseline and 48 hours after the last training session. The blood samples were centrifuged at 2500-3000 rpm for 10 min. The serum was separated and stored at  $-70 \text{ }^\circ\text{C}$  for subsequent analysis. Serum estradiol was measured by electrochemiluminescence immunoassay kit (Roche, Germany). Insulin was evaluated by immunoradiometric assay kit (IM3210;

Immunotech, Czech Republic). Glucose level was assessed by glucose oxidase method kit (Pars Azmoon, Iran). Insulin resistance was calculated using the homeostatic model assessment of Insulin Resistance (HOMA-IR) (23).

The experimental group participated in a combined aerobic and resistance training program, four times per week for ten weeks. The aerobic training consisted of 25-45 minutes of walking/running at an intensity of 65-75% of maximal heart rate (MHR), two times per week. The aerobic exercise started with the intensity 65% of MHR for 25 minutes and gradually progressed to 75% of MHR for 45 minutes by the end of the 10<sup>th</sup> week. Resistance training including chest press, lat pull down, biceps and triceps curls, leg press, and leg extension and flexion were performed at 55-65% of one maximal repetition (1RM), 3 sets of 8-12 repetitions with a 2-3-min rest interval between sets. The resistance training was performed two times per week. A 10 minute warm up and 5 minute cool down was included before and after each training session.

### Statistical analysis

Normal distribution of data was evaluated by the Kolmogorov-Smirnov test. Independent T-test was used to test the difference in baseline characteristics between the groups. Pre- and post-training differences of all variable were assessed by paired T-test in each group. The analyses of covariance (ANCOVA) was used to compare changes between experimental and control groups. P values less than 0.05 were considered statistically significant. The statistical analyses were performed using SPSS 18 software.

### Ethical considerations

This study was approved by the ethics committee of Islamic Azad University of Karaj and registered in the Iranian Registry of Clinical Trial with registration number of IRCT20170918036257N1.

### Results

The baseline characteristics of the participants are presented in Table 1. There were no differences in age, height, weight, body mass index, body fat percentage and vo2max between the two groups ( $P$ -value > 0.05).

The ANCOVA test showed that there were no significant differences in estradiol ( $P$ -value: 0.87), glucose ( $P$ -value: 0.09), insulin ( $P$ -value: 0.11), HOMA-IR ( $P$ -value: 0.08), body mass index ( $P$ -value: 0.12) and body fat percentage ( $P$ -value: 0.24) between experimental and control groups after combined exercise training. Paired T-test also showed no significant differences between pre- and post-training of these variables in each group. In other words, ten weeks of combined training intervention had no significant effects on measured variables. The values of measured variables in the pre- and post-training are presented in Table 2.

### Discussion

In the present study, the effect of 10 weeks of combined training was investigated on circulating estradiol and some metabolic risk factors in overweight and obese postmenopausal women. The results showed that combined training had no effect on the levels of estradiol. Similar to this study, Yoon et al. (2018)

**Table 1. Physical characteristics in the two groups (means  $\pm$ SD)**

Variables	Experimental group	Control group	$P$ -value
Age (years)	54 ( $\pm$ 2.6)	55.5 ( $\pm$ 4.9)	0.37
Height (cm)	154.1 ( $\pm$ 2.8)	153.2 ( $\pm$ 4.9)	0.59
Weight (kg)	73.4 ( $\pm$ 11.7)	75.1 ( $\pm$ 9.3)	0.72
Body mass index(kg/m <sup>2</sup> )	30.9 ( $\pm$ 4.9)	32.1 ( $\pm$ 4.6)	0.58
Body fat (%)	43.4 ( $\pm$ 6.1)	43.4 ( $\pm$ 5.9)	0.98
Vo2max (ml/kg/min)	22.6 ( $\pm$ 5.6)	19.1 ( $\pm$ 6.4)	0.17

**Table2. Physiological and biochemical variables in pre and post training**

Variable	Experimental group		<i>P</i> -value (Within- group)	Control group		<i>P</i> -value (Within- group)	<i>P</i> -value (Between- group)
	Pre-training	Post-training		Pre-training	Post-training		
<b>BMI (kg/m<sup>2</sup>)</b>	30.9 (±4.9)	30.9 (±4.4)	0.97	32.07(±4.6)	31.03 (±3.3)	0.09	0.12
<b>Body fat (%)</b>	43.4 (±6.1)	43.3 (±6.1)	0.98	43.4 (±5.9)	46.1 (±5.7)	0.12	0.24
<b>Estradiol (pg/ml)</b>	13.9 (±3.2)	15.6 (±4.9)	0.37	15.3 (±3.6)	15.5 (±5.8)	0.94	0.87
<b>Glucose(mg/dl)</b>	85.3 (±16.7)	87 (±11.7)	0.77	82.9 (±11.5)	78.9 (±9.5)	0.44	0.09
<b>Insulin (µIU/ml)</b>	5.03 (±1.4)	5.4 (±1.1)	0.31	5.7 (±1.4)	5 (±0.6)	0.12	0.11
<b>HOMA-IR</b>	1.07 (±0.4)	1.16 (±0.4)	0.33	1.18 (±0.5)	0.97 (±0.12)	0.19	0.08

Also found no significant change in the estrogen level among obese postmenopausal women following 12 weeks of aerobic or resistance training (16). In contrast to our findings, Friedenreiche et al. (2010) showed that 1-year of moderate-to-vigorous intensity aerobic exercise (5d/wk) caused changes in estradiol levels among sedentary postmenopausal women (14). In the another study by Friedenreiche et al. (2015), serum levels of total and free estradiol decreased in inactive postmenopausal women after 12-month of moderate (150 min/week) or High (300 min/week) volumes of aerobic exercise training (15). These contradictions seem to be due to differences in type, intensity, duration, and volume of exercise training that may affect the changes in estradiol. Thus, in the present study, the intensity or duration of combined training may have not been adequate to make favorable changes in serum estradiol levels. On the other hand, it has been suggested that the effects of exercise training on estradiol levels are mediated by a decrease in body fat tissue (24). In this regard, Van Gemert et al. (2015) reported that exercise-induced weight loss led to desirable changes in levels of estradiol among postmenopausal women (25). Also, other studies have shown that weight loss reduces estrogens levels in postmenopausal women (26,27). In one of these, Campbell et al. (2012) found that greater weight loss created greater reductions on estrogens levels in overweight and obese postmenopausal women (27). Therefore, it is possible that physical activity without weight loss does not decrease estradiol levels. The combined training used in our study had no effects on body fat percentage and body mass index, probably due to the diet or short term of

training intervention. In the present study, the participants with no dietary intervention performed the exercise training for 10 weeks, while it has been reported that the combination of exercise and diet compared to exercise or diet alone, have a greater effect on weight and body fat percentage in postmenopausal women (28).

Moreover, in the present study, we found no significant effects of combined training on glucose, insulin and insulin resistance in overweight and obese postmenopausal women. Similarly, Van Gemert et al. (2015) reported that 1-year combined aerobic and strength training has no beneficial effect on the glucose, insulin and insulin sensitivity in healthy and sedentary postmenopausal women (19). In contrast, some studies have reported a decrease in insulin and insulin resistance after aerobic exercise training in postmenopausal women (17,18). It is possible that the intensity or duration of combined training used in the present study have not been adequate to affect insulin and insulin resistance since some studies have shown that intensity (29) and duration (30) of exercise training are important factors for improvement of insulin sensitivity. As Izadi et al. (2018) showed that high intensity interval exercise training compared with moderate continuous exercise training is more effective on insulin resistance in elderly patients with type2 diabetes (31). In another study, Houmard et al. (2004) reported that the duration of exercise should be considered as an important factor in improving insulin action in obese/overweight postmenopausal women (30). On the other hand, some other studies have suggested that the influence of exercise training on insulin levels is modulated through changes in body weight or body fat mass in

postmenopausal women (19,32). For instance, Van Gemert et al. (2015) concluded that exercise may affect insulin sensitivity by weight loss (19). Given these findings, the lack of change in insulin resistance in the present study may be due to inadequate weight or body fat mass changes.

### Conclusions

In conclusion, the findings of this study suggested that 10 weeks of moderate-intensity combined exercise training has no beneficial effects on serum estradiol level and metabolic risk factors in sedentary overweight/obese postmenopausal women. It appears that the levels of estradiol and insulin make no favorable changes in response to exercise

intervention that does not reduce body fat mass.

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### Conflict of Interest

Authors declare that they have no competing interests.

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