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Effects of endurance training on cardiorespiratory fitness and substrate partitioning in postmenopausal women

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Abstract

We examined the effect of endurance training on energy substrate partitioning during rest and exercise in postmenopausal women. Ten healthy sedentary (55 ± 1 years old) subjects completed 12 weeks of endurance exercise training on a cycle ergometer (5 d/wk, 1 h/d, 65% peak oxygen consumption [V_{O_2}peak]). Whole-body energy substrate oxidation was determined by indirect calorimetry during 90 minutes of rest and 60 minutes of cycle ergometer exercise. Subjects were studied at 65% V_{O_2}peak before training and after training at the same absolute exercise intensity (same absolute workload as 65% of pretraining V_{O_2}peak) and same relative exercise intensity (65% of posttraining V_{O_2}peak). After training, V_{O_2}peak increased by 16.3% ± 3.9% and resting heart rate decreased by 4 beats per minute ($P < .05$). During exercise at same absolute intensity, mean arterial pressure decreased by 8 mm Hg ($P < .05$), heart rate decreased by 19 beats per minute ($P < .05$), energy derived from carbohydrate decreased by 9.6%, and the energy derived from lipid increased by 9.2% ($P < .05$). Lactate concentration was lower at the same absolute and relative exercise intensities ($P < .05$). Changes in substrate partitioning during exercise were accomplished without changes in dietary composition, body weight, or body composition. We conclude that endurance training in healthy postmenopausal women who remain in energy balance results in many of the classic cardiopulmonary training effects, decreases the reliance on carbohydrate, and increases lipid oxidation during a given submaximal exercise task without a reduction in body weight.

1. Introduction

Previous studies examining the effects of endurance training have shown that, although both younger men and women can increase their cardiorespiratory capacity after training, younger women oxidize proportionately more lipid and less carbohydrate during exercise [1]. Although studies on young women [1] have demonstrated that endurance training increases cardiorespiratory capacity and decreases carbohydrate oxidation during exercise tasks of given absolute and relative exercise intensities, it is unclear whether the same training responses occur in postmenopausal women. Age-related changes in body composition and a decline in aerobic capacity [2] may dampen the cardiorespiratory training response in postmenopausal women relative to premenopausal levels. As well, the decline in estrogen levels at menopause alters the hormonal milieu and may have a significant effect on altering energy substrate partitioning (percentage carbohydrate/percentage lipid) during rest and exercise. In young women, estrogen has been shown to decrease carbohydrate oxidation during exercise [1,3,4] and can alter glucose metabolism by decreasing gluconeogenesis, glycogenolysis, and insulin-binding capacity, thereby shifting the substrate partitioning toward lipid metabolism [5]. Therefore, the decline in estrogen at menopause may lead to an increased reliance on carbohydrate and decreased reliance on lipid during rest and exercise. Endurance training may help override the effects of estrogen withdrawal on substrate partitioning by increasing lipid oxidation.

To date, most studies examining the effects of endurance training on substrate partitioning in older individuals have been of a mixed gender study design [6,7], so it is unclear

There is no conflict of interest with regard to this research.

The study protocol was approved by the University of California Committee for the Protection of Human Subjects (CPHS 2005-10-29), and subjects provided written informed consent.

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whether the effect of endurance training on metabolism is the same in older men and women. Sial et al [6] found that, compared with young subjects (age, 26 ± 2 years), fat oxidation during exercise was significantly lower in older (age, 73 ± 2 years) subjects during 60 minutes of cycle ergometer exercise performed at either the same absolute or relative exercise intensity. However, Sial et al [7] found that 16 weeks of endurance training (age, 74 ± 2 years; 3 men and 3 women) caused an increase in fat oxidation and a decrease in carbohydrate oxidation in elderly persons at the same absolute exercise intensity. A pre- vs posttraining comparison at similar relative exercise intensities was not reported. Those findings can be interpreted to mean that endurance training may be capable of overriding the negative effects of estrogen withdrawal on substrate partitioning. However, because of the mixed gender study design of these previous studies [6,7], the effects of endurance training on postmenopausal women remain unclear.

To evaluate the idea that exercise training would override the effects of menopause and estrogen withdrawal on energy substrate partitioning and cardiovascular fitness during rest and exercise, we determined the effects of 12 weeks of moderate-intensity endurance training in sedentary, but otherwise healthy, postmenopausal women. We predicted that exercise training would enhance lipid oxidation during physical activity and increase cardiovascular fitness in the absence of weight loss.

2. Methods

2.1. Subjects

Ten healthy, nonsmoking, weight-stable postmenopausal women (55 ± 0.61 years old) were recruited from the University of California campus and the surrounding community by posted notices and Internet advertisements. The women were considered to be postmenopausal if they had not menstruated for at least a year and their plasma follicle-stimulating hormone (FSH) levels were greater than 30 mIU/mL. Subjects were considered sedentary if they participated in less than 2 hours of regular strenuous activity per week for the previous year and if they had a peak oxygen consumption (V_{O_2}peak) between 15 and 35 mL kg^{-1} min^{-1} as determined by a continual progressive leg cycle ergometer stress test. The women were admitted into the study if they met the following criteria: (1) were diet and weight stable for at least 6 months, (2) did not have osteoporosis, (3) had not taken estrogen for at least 6 months or blood thinners such as aspirin for at least 3 months before the study, (4) had not had a hysterectomy, (5) had normal lung function (forced expiratory volume in 1 second of 70% or more), and (6) were disease and injury free as determined by a health history questionnaire and physical examination. Subjects were excluded if they had the metabolic syndrome, which is defined by the National Cholesterol Education Program–Adult Treatment Panel III [8]. The study protocol was approved by the University of California Committee for the Protection of Human Subjects (CPHS 2005-10-29), and subjects provided written informed consent.

2.2. Experimental design

Subjects underwent a total of 3 tests over the course of the study: one pretraining test and two posttraining tests. The testing consisted of a 90-minute rest period followed by 60 minutes of continuous pedaling on a cycle ergometer. The first test was performed at 65% of pretraining V_{O_2}peak (PRE). This task was selected because it is consistent in duration with the Institute of Medicine physical activity recommendations [9] and because, from practical experience, it was the most strenuous prolonged exercise task that sedentary participants were capable of performing. One of the posttraining tests was performed at the same absolute workload (65% of pretraining V_{O_2}peak), whereas the other posttraining test was performed at the same relative workload (65% of new V_{O_2}peak). The 2 posttraining tests were performed 2 weeks apart at weeks 10 and 12, respectively, of the training period. The order of the 2 posttraining tests was randomized, and training continued between the 2 tests.

2.3. Screening tests

Body composition was measured by using a dual-energy x-ray absorptiometry whole-body scanner (LUNAR, GE Medical Systems, Madison, WI). Waist circumference was determined at the smallest circumference between the xiphoid process and the anterior iliac crest, whereas the hip circumference was measured as the largest circumference around the buttocks.

A 12-hour fasting blood sample was taken from each of the prospective subjects to obtain measurements for a basic metabolic panel, FSH, triglycerides (TG), high-density lipoprotein (HDL), and total cholesterol. The FSH levels were used to confirm postmenopausal status, whereas levels of TG and HDL were used in conjunction with other parameters to assess whether the subjects had metabolic syndrome.

Three-day diet records (2 weekdays and 1 weekend day) were recorded and analyzed before and after the 12-week endurance-training program to monitor each subject's caloric intake and macronutrient composition and to ensure that the subjects had maintained the same dietary habits throughout the course of the study. Analysis of dietary records was performed using the Nutritionist III program (N-squared Computing, Salem, OR). Subjects were instructed not to alter their dietary habits or discretionary physical activity level (PAL) over the course of the study. Subjects were weighed before every training session and test and were told to increase their energy intake to compensate for the increase in energy expenditure to maintain weight stability.

The V_{O_2}peak tests were conducted under medical supervision as per the American College of Sports Medicine guidelines. The V_{O_2}peak was determined by a progressive test on an electronically braked cycle ergometer (Monark

Ergometric 839E, Vansbro, Sweden) with a power output that began at 50 W and was increased by 25 W every 3 minutes until volitional exhaustion. Respiratory gases were continuously monitored throughout the test using an open-circuit online automated gas analysis system (ParvoMedics TrueMax 2400, Salt Lake City, UT) that was calibrated before the test using room air and a certified calibration gas. Heart rate was monitored continuously using a Quinton 759 electrocardiogram (Seattle, WA), and blood pressure was measured by auscultation. Subjects were considered to have reached their V_{O_2}peak when the following criteria were met: (1) leveling off of oxygen consumption (V_{O_2}) with increasing workload, (2) a respiratory exchange ratio (RER) value greater than 1.1, and (3) a heart rate within 10% of their age-predicted maximum.

2.4. Experimental protocol

Subjects were instructed not to exercise on the day before testing and to only eat the standardized diet that was provided to them (2051 ± 58 kcal; 24% fat, 58% carbohydrate, and 18% protein). This standardized diet was based on the Institute of Medicine predictive equations for total energy expenditure (TEE) assuming a physical activity coefficient of 1.14 or PAL of 1.5, low active [9,10]. The physical activity coefficient is used in the prediction equations for TEE, whereas the PAL represents a measure of TEE in relation to basal energy expenditure (PAL = TEE/basal energy expenditure) [9]. Subjects were instructed not to drink caffeine-containing beverages 24 hours before testing. Subjects reported to the laboratory 9-hour fasted on the morning of the test, and catheters were then placed into the hand or wrist vein to obtain "arterialized" blood samples using the "heated hand vein" technique for measurements of fasting blood glucose [11].

After collection of the background blood and breath measurements, subjects were given a standardized breakfast (560 kcal; 60% carbohydrate, 26% fat, and 14% protein) to consume in the laboratory that consisted of a whole-wheat bagel, peanut butter, and orange juice. Because of a work conflict, 1 subject completed her testing in the afternoon, arriving at the laboratory at noon to begin each test. However, this subject consumed the same standardized pretest meal as the other subjects. A different standardized breakfast (565 kcal; 61% carbohydrate, 27% fat, and 12% protein) was provided to this subject to eat on the morning of the test. We choose to study subjects under postprandial conditions to mimic the normal free-living conditions and report data on postmenopausal women with stable exercise blood glucose levels and normal preexercise liver glycogen stores.

Respiratory gas exchange measurements and blood samples were collected during the test at 0, 60, 75, and 90 minutes of rest and during 15, 30, 45, and 60 minutes of exercise. Heart rates and blood pressures were recorded throughout rest and exercise at the same frequency as the blood and breath sampling.

2.5. Blood sampling and analyses

After background sampling, blood samples were taken at 60, 75, and 90 minutes of rest and at 15, 30, 45, and 60 minutes of exercise. Blood samples for analysis of glucose and lactate were immediately deproteinized with 8% perchloric acid, mixed thoroughly, and then stored on ice before centrifugation at 3000*g* for 10 minutes. Perchloric acid extracts for glucose and lactate analyses were stored at −0°C until further analysis. All samples from a given subject were analyzed at the same time in duplicate to reduce variability.

Hematocrit was measured at each of the time points using a circular microcapillary tube reader (no. 2201, International Equipment, Needham Heights, MA) and verified to be stable so as not to compromise the metabolite and hormone concentration measurements because of plasma shifts. Subjects drank tap water ad libitum during each test to maintain hydration status.

2.6. Calculations

Standard equations were used to estimate the energy derived from carbohydrate and lipid oxidation [12].

$$\text{Energy from carbohydrate oxidation (in kilocalories per minute)} = [((\text{NPRQ} - 0.707)/0.293) \times (\text{VO}_2) \times (5.05\text{kcal}/\text{O}_2)]$$

$$\text{Energy from lipid oxidation (in kilocalories per minute)} = [((1 - \text{NPRQ})/0.293)) \times (\text{VO}_2) \times (4.7\ \text{kcal}/\text{LO}_2)]$$

where RER is respiratory exchange ratio, V_{O_2} is oxygen consumption expressed in liters per minute, and NPRQ is the nonprotein respiratory quotient that was derived from the RER. The rates of carbohydrate oxidation, lipid oxidation, and energy expenditure were calculated using the NPRQ values for each time point. We made the assumption that the percentage contribution of protein to the resting metabolic rate was equivalent to the percentage of protein in the standardized diet and that the rate of protein oxidation would not be altered in the transition from rest to exercise.

2.7. Training protocol

The training intervention involved 60 minutes of supervised moderate-intensity exercise 5 d/wk for 12 weeks. The exercise consisted of pedaling on a cycle ergometer 4 d/wk and walking on a treadmill for 1 d/wk. The heart rate data from the V_{O_2}peak tests were used to estimate the target training heart rates needed to elicit 50% and 65% V_{O_2}peak. Duration and intensity of the exercise training were gradually increased. During the first 3 weeks of training, the exercise intensity was gradually increased from 50% to 65% V_{O_2}peak. The duration of the exercise training sessions was gradually increased from 30 to 60 minutes during the first 4 weeks. The number of supervised training sessions was increased gradually from 3 d/wk during the first 3 weeks to 5 d/wk during weeks 5 to 12. By week 5, subjects

were exercising for 60 minutes at 65% Vo_2peak 5 d/wk; this intensity and duration was continued throughout the course of the intervention. Interval training was added during the last 4 weeks such that, during training sessions, subjects performed four 1-minute bouts at a power output that elicited 100% Vo_2peak. Training took place at the study facility and was supervised by student personal trainers who were University of California–Berkeley students who had completed course work in exercise physiology and were Red Cross cardiopulmonary resuscitation certified. Trainers used Polar heart rate monitors (Polar, Oy, Finland) and data from the intermediate (5-week) Vo_2peak test to monitor and standardize the relative exercise intensity in training. Subjects were weighed before each training session and asked to increase their energy intake to maintain the same body weight. All subjects complied with the exercise training protocol and remained in the study for the entire duration.

2.8. Statistical analyses

Data are presented as group means ± SE. For evaluation of significance of responses to exercise and training, blood metabolite concentration values for the last 15 minutes of rest (75 and 90 minutes) and the last 30 minutes of exercise (30, 45, and 60 minutes) were averaged to give representative values. Significance of differences among the metabolite concentrations and substrate oxidation rates was determined using one-way analysis of variance with repeated measures, whereas glucose and lactate measurements over time were analyzed using a two-way analysis of variance with repeated measures. Significance of differences among the mean values in physical characteristics of the subjects were analyzed with paired Student *t* tests. Post hoc comparisons were made with Fischer protected least significant difference test. Statistical significance was defined as an α less than or equal to .05.

3. Results

3.1. Subjects

Physical characteristics and work capacities of the subjects before and after training are listed in Tables 1 and 2. Subjects were weight stable throughout the intervention. Measurement of body composition as determined by dual-energy x-ray absorptiometry indicated that training did not alter body composition.

The ergometric and physiologic parameters of subjects during rest and exercise before and after training are listed in Table 3. Maximal workload achieved during maximum oxygen consumption testing increased by 25.3% ± 3.4% and Vo_2peak increased by 16.3% ± 3.9% as a result of training ($P < .05$, Table 1). Because of the training effect, the posttraining test at the same absolute exercise intensity was equivalent to 55% of the posttraining Vo_2peak. Resting heart rate values were lower after training; and pulmonary minute ventilation, heart rate, diastolic blood pressure, and mean arterial pressure were all reduced during exercise at the same absolute ($P < .05$), but not relative, exercise intensity (Table 3).

Table 1
Subject characteristics before and after 12 weeks of endurance training

Variable	Pretraining	Posttraining	% Difference
Age, y	55 ± 0.61	–	–
Years postmenopausal	5 ± 0.95		
Height, cm	162.4 ± 1.44	–	–
Weight, kg	68.2 ± 4.50	67.7 ± 4.56	−0.78 ± 0.35
BMI, kg/m^2	25.9 ± 1.71	25.7 ± 1.71	−0.75 ± 0.36
Body fat, %	38.0 ± 2.90	38.0 ± 2.92	−3.28 ± 2.58
Fat mass, kg	25.5 ± 3.55	25.7 ± 3.78	−3.87 ± 3.12
Fat-free mass, kg	39.0 ± 1.30	39.1 ± 1.32	1.57 ± 1.03
Peak power output, W	117 ± 7.08	145 ± 6.21*	25.3 ± 3.38
Vo_2peak			
mL kg^{-1} min^{-1}	25.5 ± 1.80	29.4 ± 1.85*	16.3 ± 3.93
L/min	1.69 ± 0.08	1.95 ± 0.08*	16.3 ± 4.26

Values are means ± SE; n = 10. BMI indicates body mass index.
* Significantly different from pretraining, $P < .05$.

3.2. Diets

There were no changes in the total energy intake (1845 ± 124 and 1823 ± 98 kcal/d), percentage of energy intake as carbohydrate (48 %± 2.7% and 49% ± 2.7%), percentage of energy intake as fat (40% ± 2.2% and 42% ± 3.7%), and percentage of energy intake as protein (18% ± 1.1% and 18% ± 1.0% before and after training, respectively) as a result of the exercise intervention.

3.3. Blood glucose and lactate concentrations

There was no significant difference between the resting plasma glucose concentrations before and after training (Table 4). Before training, blood glucose concentrations decreased 22% from rest to exercise ($P < .05$). After training, the decrease in blood glucose concentration from rest to exercise was 16% during the same absolute exercise intensity and 30% during the same relative exercise intensity (Table 4). Blood glucose concentrations during the same relative exercise intensity were 16% lower than pretraining and 17% lower during the same absolute intensity ($P < .05$).

Training induced such a profound change in blood lactate concentration during exercise that lactate did not rise significantly over rest during the same absolute exercise intensity and was reduced by 45% during the same relative exercise intensity albeit a 35% increase in exercise power output ($P < .05$, Table 4). The lactate concentration during exercise before training was higher than both posttraining exercise tests at every exercise time point ($P < .05$, Fig. 1).

3.4. RER and substrate oxidation

Respiratory exchange ratio values increased in the transition from rest to exercise before training but not

Table 2
Metabolic risk factor characteristics of subjects before training

Variable	Pretraining
Cholesterol, mg/dL	193.2 ± 5.73
HDL, mg/dL	59.0 ± 3.84
LDL, mg/dL	115 ± 4.94
LDL/HDL ratio	2.05 ± 0.21
Cholesterol-HDL ratio	3.41 ± 0.26
TG, mg/dL	96.0 ± 7.48
12-h fasting plasma glucose, mmol/L	5.16 ± 0.13
Waist circumference, in	31.3 ± 1.57
Hip circumference, in	40.1 ± 1.14
Waist-hip ratio	0.78 ± 0.02
Systolic blood pressure, mm Hg	117 ± 3
Diastolic blood pressure, mm Hg	74 ± 2

Values are means ± SE; n = 10.

after training ($P < .05$, Table 4). Compared with pretraining, after training, RER was lower, indicating a decreased reliance on carbohydrate (Fig. 2A) and an increased reliance on lipid (Fig. 2B) during exercise at the same absolute, but not relative, intensity. Correspondingly, the energy from carbohydrate decreased and the energy from lipid increased during the same absolute exercise intensity compared with pretraining. Exercise energy expenditure during the same relative intensity after training was 16.7% greater than that during the same absolute intensity ($P < .05$), but there was no significant difference between pretraining and absolute intensity (Table 4).

4. Discussion

In previous studies on young women treated similarly as were the postmenopausal women enrolled in the current investigation, endurance training increased cardiorespiratory capacity and decreased total carbohydrate oxidation at the same absolute and relative exercise intensities [1]. Now we report that 12 weeks of supervised endurance training induced classic physiologic adaptations (ie, increased V_{O_2}peak, decreased resting heart rate, and decreased exercise heart rate during the same absolute, but not relative, exercise intensity) in postmenopausal women. In addition, endurance training resulted in decreased carbohydrate and increased lipid oxidation rates at the same absolute, but not relative, exercise intensity. The physiologic and metabolic adaptations seen in our study can be attributed to the effects of endurance training alone because our subjects remained diet and weight stable throughout the intervention.

4.1. Dietary controls and energy balance

Previous studies that have been conducted on postmenopausal women have been varied with regard to maintenance of dietary composition and weight stability. For example, Irwin et al [13] found that postmenopausal women who underwent an exercise training intervention had significant changes in body weight, total body fat, and intraabdominal fat compared with unexercised controls. To induce weight loss in some studies, investigators purposely altered subject diets via caloric restriction [14], whereas in other studies, investigators used a combination of exercise training and caloric restriction to decrease the subjects' body weight [13,14].

Because caloric restriction and weight loss can independently affect metabolism, we successfully isolated the effects of endurance training on parameters of metabolic and cardiovascular fitness. Nonetheless, with limitations, our data can be contrasted with those obtained in studies using a mixed gender study design including older women [7]. Given the variability in the extant literature on training effects on older men and postmenopausal women, we sought to control diet and body weight and study women within the first years following menopause.

Table 3
Ergometric and physiologic parameters of subjects during rest and exercise, before and after training

Variable	Rest		Exercise		
	Pretraining	Posttraining	PRE	ABT	RLT
Workload, W	–	–	55.5 ± 5.98	55.6 ± 6.02	74.9 ± 4.07†,‡
V_{O_2}, mL kg^{-1} min^{-1}	3.46 ± 0.14	3.55 ± 0.16	16.8 ± 1.18*	16.3 ± 1.29*	18.7 ± 1.38*,†,‡
V_{CO_2}, mL kg^{-1} min^{-1}	3.21 ± 0.14	3.32 ± 0.15	16.2 ± 1.19*	15.1 ± 1.25*	17.7 ± 1.30*,†,‡
Minute ventilation, L/min	6.96 ± 0.46	7.48 ± 0.36	29.2 ± 1.64*	26.0 ± 1.60*,†	30.9 ± 1.72*,‡
Heart rate, bpm	71.7 ± 2.66	68.2 ± 2.08*	133.8 ± 5.68*	114 ± 4.99*,†	133.7 ± 3.84*,‡
Blood pressure, mm Hg					
Systolic	117 ± 3	117 ± 3	148 ± 5*	138 ± 6*	150 ± 4*,‡
Diastolic	74 ± 2	70 ± 2	76 ± 2	69 ± 3†	73 ± 2‡
Mean arterial	88 ± 2	86 ± 2	100 ± 2*	92 ± 3*,†	99 ± 3*,‡
Hematocrit, %	39 ± 0.72	38 ± 0.48	40 ± 0.60*	39 ± 0.57*	40 ± 0.55*

Values are means ± SE; n = 10. ABT indicates same absolute workload (65% of pretraining V_{O_2}peak); RLT, same relative workload (65% of new V_{O_2}peak); V_{CO_2}, carbon dioxide production.

* Significantly different from resting conditions at $P < .05$.

† Significantly different from pretraining 65% (PRE) at $P < .05$.

‡ Significantly different from posttraining (ABT) at $P < .05$.

Table 4
Metabolite concentrations, substrate oxidation rates, and substrate partitioning of subjects during rest and exercise

Variable	Rest		Exercise		
	Pretraining	Posttraining	PRE	ABT	RLT
RER	0.93 ± 0.01	0.93 ± 0.01	0.96 ± 0.02*	0.93 ± 0.01†	0.95 ± 0.01‡
NPRQ	0.97 ± 0.01	0.98 ± 0.01	0.97 ± 0.01	0.93 ± 0.012*,†	0.96 ± 0.01*,‡
Plasma glucose, mmol/L	6.85 ± 0.39	6.48 ± 0.32	5.36 ± 0.27*	5.42 ± 0.26*	4.51 ± 0.16*,†,‡
Plasma lactate, mmol/L	1.31 ± 0.08	1.23 ± 0.04	4.03 ± 0.70*	1.55 ± 0.39†	2.20 ± 0.18*,†
EE, kcal/min	1.15 ± 0.06	1.17 ± 0.03	5.70 ± 0.27*	5.27 ± 0.24*	6.15 ± 0.34*,‡
Energy from CHO, kcal/min	0.77 ± 0.06	0.81 ± 0.05	4.80 ± 0.32*	3.96 ± 0.34*,†	5.06 ± 0.38*,‡
Energy from lipid, kcal/min	0.09 ± 0.02	0.07 ± 0.02	0.61 ± 0.15*	1.01 ± 0.16*,†	0.79 ± 0.15*,‡

Values are means ± SEM; n = 10. EE indicates energy expenditure; CHO, carbohydrate.
* Significantly different from resting conditions at $P < .05$.
† Significantly different from pretraining 65% (PRE) at $P < .05$.
‡ Significantly different from posttraining (ABT) at $P < .05$.

4.2. Cardiorespiratory training adaptations

The 16% increase in Vo_2peak seen in our study is consistent with previously observed aerobic training effects on postmenopausal women [15,16]. Although physiologically significant, the 16% increase in Vo_2peak is less than the 25% increase found in younger premenopausal women who underwent a similar training protocol [1], indicating that the cardiovascular training response is dampened in women after menopause. One of the contributing factors may be an inability of postmenopausal women to increase their peak cardiac output and stroke volume [17]. Spina et al [17,18] found that, whereas exercise training increased peak stroke volume and improved left ventricular systolic function in young women after 9 to 12 months of endurance training, these same improvements were not seen in the older women (60-70 years old) despite their significant improvements in cardiovascular fitness. Similarly, O'Donnell et al [16] reported that 12 weeks of endurance training in postmenopausal women increased Vo_2peak but did not result in changes in stroke volume, cardiac output, or total peripheral resistance. Estrogen deficiency may partly account for the blunted cardiovascular response in postmenopausal women [17] because previous studies on healthy postmenopausal women have found significant improvements in left ventricular ejection fraction, stroke volume, and cardiac output after hormone replacement therapy [19]. Together, these findings may help explain why the cardiovascular adaptations to endurance training in postmenopausal women were dampened relative to premenopausal women.

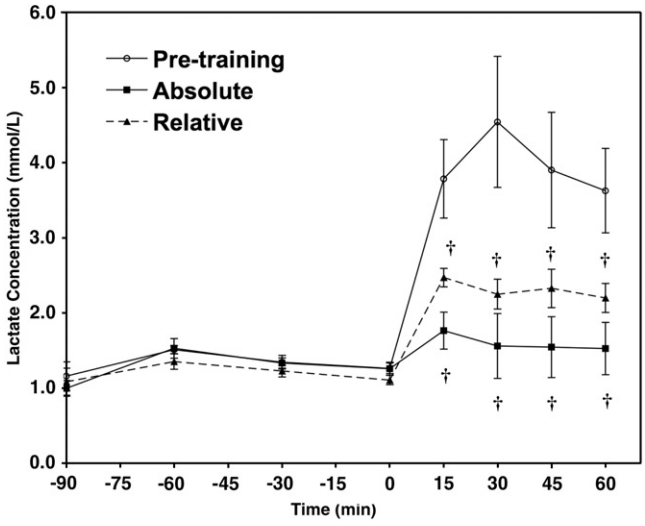

Fig. 1. Blood lactate concentrations (in millimoles per liter) over time in middle-aged (55 ± 0.6 years old) postmenopausal women at rest and during exercise before and after 12 weeks of endurance training. Exercise commenced at time 0. Values are means ± SE. †Significantly different from pretraining 65% (PRE) at $P < .05$.

The significant 4–beat per minute (bpm) decrease in resting heart rate after training may be attributed to a decrease in the intrinsic heart rate or an increase in vagal tone. The 19-bpm decrease in heart rate at the same absolute exercise intensity is less than the 27-bpm decrease seen in young premenopausal women [1], providing further evidence for the dampened cardiopulmonary training response in postmenopausal women. However, despite the dampened training response, the postmenopausal women in the present study still demonstrated significant improvements in cardiovascular adaptations such as a 7–mm Hg decrease in the diastolic pressure and an 8–mm Hg decrease in mean arterial pressure at the same absolute workload. Together, these findings indicate that healthy normotensive postmenopausal women have the ability to induce significant improvements in cardiovascular parameters after endurance training.

4.3. Energy substrate partitioning

The 12-week training intervention resulted in many of the classic metabolic adaptations seen in previous studies. Specifically, after training, the postmenopausal women had a decrease in lactate concentration at the same absolute and relative exercise intensities, and a decrease in RER and an increased reliance on lipid as an energy source during the same absolute exercise intensity.

The decrease in carbohydrate oxidation during submaximal exercise after endurance training may be partly

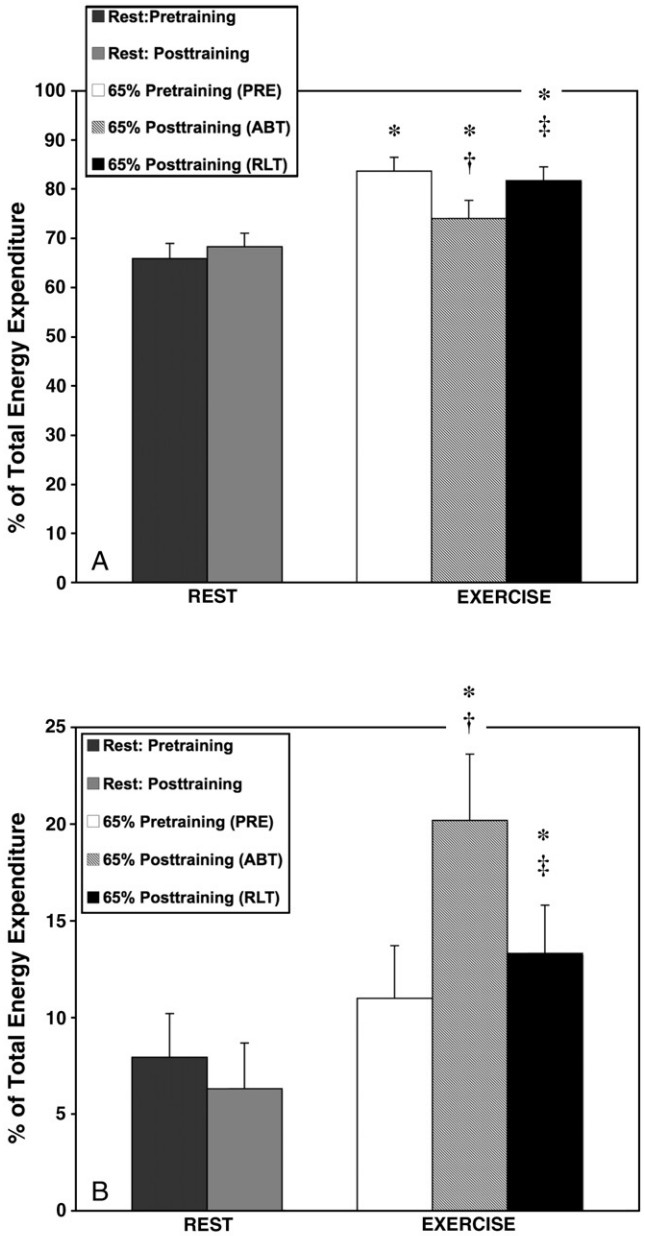

Fig. 2. Percentages of energy expenditure derived from carbohydrate oxidation (A) and lipid oxidation (B) in middle-aged (55 ± 0.6 years old) postmenopausal women at rest and during exercise before and after 12 weeks of endurance training. Values are means ± SE. *Significantly different from resting conditions at $P < .05$. †Significantly different from pretraining 65% (PRE) at $P < .05$. ‡Significantly different from posttraining (ABT) at $P < .05$.

attributed to a slower rate of glycogenolysis and an increased capacity of muscle to oxidize lipid in postmenopausal women. Endurance training increases the mitochondrial content and the sensitivity of respiratory control such that a given exercise can be accomplished at a higher adenosine triphosphate (ATP) to adenosine diphosphate ratio, leading to a decrease in the glycolytic flux and the rate of muscle glycogenolysis [20,21]. Molé et al [22] showed that, after rats underwent a treadmill training program, they had an increase in the enzymatic capacity of muscle to oxidize lipid as shown by increased amounts of carnitine palmitoyl transferase, palmitoyl coenzyme A dehydrogenase, and mitochondrial ATP-dependent palmitoyl coenzyme A synthetase. These peripheral adaptations seen with endurance training increase the capacity for ATP production and help promote the increase in lipid utilization during submaximal exercise after endurance training.

In addition to peripheral adaptations, a decrease in the sympathetic system activation after endurance training may have also contributed to alterations in substrate partitioning in our study population. Previous studies have demonstrated that the sympathetic system activation is proportional to the relative exercise intensity and that the magnitude of this hormonal response declines with training [23]. Therefore, in contrast to previous endurance studies on postmenopausal women that have only taken posttraining measurements at the same absolute exercise intensity [7,16], our measurements of relative exercise intensity allow us to compare the pre- and posttraining conditions in the context of a relatively similar hormonal environment [24]. Obtaining measurements at the same relative exercise intensity gives a standard by which investigators are able to compare results from studies involving different age groups and fitness levels. Our finding of a decrease in carbohydrate oxidation at the same absolute, but not relative, exercise intensity indicates that both hormonal and peripheral training adaptations may account for the training-induced alterations in postmenopausal women.

Our finding of a decrease in RER at the same absolute exercise intensity after endurance training is similar to studies in younger men [25] and older individuals [7]. However, our findings differ from the results of Friedlander et al [1] who found that an endurance-training program resulted in a significant reduction in RER at the same absolute and relative exercise intensities in young women. Furthermore, the training response at the same absolute exercise intensity was dampened in postmenopausal women because young women had a 22% average decline in total carbohydrate oxidation vs an 11.5% average decline seen in postmenopausal women [1]. These findings indicate that, although postmenopausal women respond to training, the magnitude of training-induced adaptations in energy-substrate partitioning is less than that in similarly treated young women.

Because estrogen has been shown to have significant effects on carbohydrate and lipid metabolism, the lower levels of estrogen at menopause may partly account for the dampened metabolic training response in postmenopausal women compared with younger women. Specifically, estrogen has been shown to have an effect of decreasing carbohydrate oxidation by decreasing muscle glycogenolysis in humans [3,5]. Studies in rats have demonstrated that estrogen can increase free fatty acid availability to the muscle during exercise [26] and shift the substrate

partitioning toward lipid [27,28]. Because of the known lipolytic effects of estrogen, the withdrawal of estrogen at menopause may make postmenopausal women more resistant to training-induced alterations in substrate partitioning in comparison to premenopausal women and may partly explain the smaller decline in total carbohydrate oxidation at the same absolute exercise intensity after training and lack of a training effect on substrate partitioning at the same relative exercise intensity.

Our finding that resting metabolic rate did not change after training is similar to other studies on postmenopausal women [29]. Because lean body mass has been shown to have an association with resting metabolic rate [30], we may not have seen a change in resting metabolic rate because there was not a significant change in fat-free mass (Table 1). Furthermore, unlike results from other studies [1,31], we did not see a significant increase in fat oxidation at rest after training. Friedlander et al [1] reported an increase in resting fat oxidation in young women after training. Our finding of an unchanged resting RER is similar to that seen in young men who underwent a similar endurance-training program as ours [1]. Thus, the decrease in estrogen at menopause may partly account for this finding, as our results tend to parallel those seen in younger men rather than younger women. The unaltered resting metabolic rate or change in resting RER after endurance training further underscores that postmenopausal women may be resistant to some of the beneficial effects of endurance training that are commonly seen in premenopausal women.

The resting RER and substrate oxidation data that we report are on 3-hour postprandial postmenopausal women, whereas other studies on postmenopausal women and elderly subjects have reported values on overnight-fasted individuals [6,7]. One notable difference was that the resting RER values of our subjects were significantly higher than those seen in other studies in which younger men and women underwent a similar training and testing protocol (0.93 vs 0.84 [younger women] or 0.86 [younger men]) [1,32]. The higher resting RER may be attributed to several age-related factors including subclinical gastroparesis and developing insulin resistance [33]. Menopause is associated with an increase in fasting insulin levels [34] and an increase in incidence of impaired glucose tolerance [33]. Concern is that this pattern of increased carbohydrate oxidation and diversion of lipid to storage could contribute to the increase in central adiposity [35] and the weight gain [36] that are commonly seen after menopause.

Although the sample size of our study was small and the exercise intervention was short, we report similar increases in cardiovascular fitness as seen in other studies with more subjects [15,16]. In addition, the exercise-training program in our study was physically demanding; and women recruited for the study were healthy and had to be in reasonable physical condition, thereby excluding a certain subset of postmenopausal women. We excluded women with the metabolic syndrome because the purpose of our study was to investigate the effects of endurance training on healthy postmenopausal women without metabolic abnormalities or on medications. Some of the strengths of our study include the following: (1) subjects remained diet and weight stable throughout the intervention, (2) all exercise training sessions were supervised, and (3) all subjects complied with the study protocol and completed the study.

5. Summary and conclusions

In summary, the main finding of this study was that 12 weeks of supervised endurance training in healthy postmenopausal women improved cardiorespiratory fitness, decreased blood lactate concentrations during exercise at the same absolute and relative exercise intensities, and increased reliance on lipid and decreased reliance on carbohydrate at the same absolute intensity after training. The results of this study indicate that, despite the changes in the hormonal milieu and the metabolic changes that occur at menopause, postmenopausal women have directionally similar, though blunted, training adaptations as those seen in younger women.

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