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Fuel Utilization and Circulating Substrate at Various Exercise Intensities in Dyslipidemic Women

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ABSTRACT

Tunkamnerdthai O, Wongpan D, Krasuaythong N, Kanpettha Y, Leelayuwat N. Fuel Utilization and Circulating Substrate at Various Exercise Intensities in Dyslipidemic Women. **JEPonline** 2019;22(7):30-41. The purpose of this study was to investigate the effects of exercise intensity on fuel utilization and circulating substrate in dyslipidemic women**.** Ten women randomly cycled at the workload of 25, 65, and 85% maximum oxygen consumption for 15, 10, and 10 min, respectively, and rested for 20 min, 7 days apart. Expired gas was collected 5 min before exercise, and the last 5 min of the exercise and recovery. Subjects used higher carbohydrate (CHO) and fat during exercise than at rest ($P<0.05$). CHO use was the greatest and fat was the lowest during exercise at high-intensity than at low- and moderate-intensity exercise. Subjects relied more on CHO than fat during exercise at all intensities. Blood glucose concentrations were the highest at the end of high-intensity exercise and recovery. The results suggest that dyslipidemic women relied more on CHO than fat at rest and during exercise at all intensities. Blood glucose concentration peaked after high-intensity exercise.

Key Words: Activity, Lipid Profiles, Substrate Oxidation, Females

INTRODUCTION

Dyslipidemia comprising a combination of high low-density lipoprotein cholesterol (LDL-C), high triglycerides (TGs), and low levels of high-density lipoprotein cholesterol (HDL-C) (8,9) is a strong risk factor for cardiovascular disease (3,15) and all-cause mortality (16). Thus, treating dyslipidemia is essential to reduce all-cause mortality. In addition, dyslipidemia may affect substrate oxidation (carbohydrate (CHO) and fat) of dyslipidemic individuals. The substrate oxidation is influenced by substrate availability in the circulation (1,14). Interestingly, we have shown that dyslipidemic Thai men relied more on fat at rest and equally during low-intensity exercise and more on CHO during higher-intensity exercise (21). Furthermore, blood glucose concentrations were the highest during high-intensity exercise and recovery. However, we did not find any changes in lipid profiles and insulin concentration during exercise at various intensities in the male subjects. Another previous study, which was done with untrained hypercholesterolemic men, found unchanged or increased HDL-C and decreased TGs, depending on the duration of the assessment, after a single bout of exercise at high-maximal O_2 consumption (80% VO_2 peak) or low- (50% VO_2 peak) intensity exercise (7). Interestingly, there has been no study explored the substrate utilization and circulating substrate in women with dyslipidemia.

Besides, the crossover point (COP) occurs when the contribution of CHO becomes greater than lipid (4,5), while the highest lipid oxidation point (PLipoxmax) occurs at the highest peak of fat oxidation. COP and PLipoxmax were shown to be at low-intensity exercise by our previous study (21). However, the subjects in our previous study were dyslipidemic men. Therefore, the substrate utilization and contributions at rest and exercise at the different intensities in dyslipidemic Thai women should be investigated.

A crossover research design of this study should provide reliable results that can assist in selecting the appropriate intensity of exercise for improving substrate utilization in middle-aged dyslipidemic Thai women. This study aimed to explore bouts of 10 to 15 min exercise due to its popularity (11) and practicality for dyslipidemic Thai women.

Thus, the aims of this study were primarily to evaluate the effect of exercise intensity on substrate utilization and secondly on circulating substrate (blood glucose and lipoprotein-TGs) in Thai dyslipidemic women. We hypothesized that the subjects would have different levels of substrate utilization and circulating substrate during exercise at low-, moderate-, and high-intensities.

METHODS

Study Design

This study is a randomized crossover trial composed of 3 visits, each at least 7 days apart to prevent any carryover effect. All visits involved a similar procedure outside of exercise intensity. Subjects underwent exercise intensities of 25, 65, and 85% VO_2 max depending on the visit for 15, 10, and 10 min, respectively, and rested for 20 min.

Subjects

Ten healthy dyslipidemic women from Khon Kaen Province, Thailand, gave written informed consent to participate in this study. Any lipid profile abnormality qualified the women for participation in this study, such as total cholesterol (TC) concentration >240 $mg \cdot dL^{-1}$, TG concentration >200 mg·dL^{-1}, LDL-C concentration >160 mg·dL^{-1}, or HDL-C concentration <35 mg·dL^{-1}. None of the subjects had been taking medication.

Before starting the experiment, all subjects received a routine medical examination that consisted of medical history, anthropometric measurements (height and body composition) from Dual x-ray absorptiometry (DXA), 12-lead electrocardiograph measurements, and blood pressure measurements. Blood samples were also collected for routine blood chemistry and hematology test. The Khon Kaen University Ethical Committee approved this study, and it conformed to the standards set by the 1964 Declaration of Helsinki (HE531276).

Procedures

VO_2 Peak Test

One week before the first experimental trial, the subjects' VO_2 peak was measured on an electromagnetically braked cycle ergometer (Corival, Lode BV, Groningen, Netherlands) during an incremental exhaustive exercise test (21). Throughout the exercise test, Heart rate was monitored with an oscilloscope monitor (Diascope type DS 521, Simonsen and Weel, Denmark) and rating of perceived exertion was recorded (2).

Energy Intake and Expenditure Prior to Testing

A week before each visit, the subjects were asked to keep a diet and physical activity diary for 3 days - 2 weekdays and 1 weekend day. Dietary records were analyzed using INMUCAL software (Mahidol University, Thailand) in order to estimate daily food intake and the amount of physical activity.

Experimental Protocols

In the evening before every visit, the subjects ingested their usual meal. At 0800 hrs after an overnight fast, they arrived at the laboratory. They had abstained from smoking, caffeine, alcohol, and heavy exercise for 48 hrs before the day of the study. Upon arrival, the subjects rested in a supine position for 30 min. Then, they cycled on an ergometer at a randomly chosen workloads at the intensity of 25%, 65%, or 85% VO_2 max for 15, 10, and 10 min, respectively with at least seven days between each intensity, and then rested for 20 min (21).

Blood Analysis

All blood tubes were placed on ice immediately after the collection. Each blood sample was divided into three tubes: (a) 1 mL into a sodium fluoride tube for measurement of whole blood glucose levels; (b) 1 mL into an EDTA tube for measurement of lipid profiles; and (c) 6 mL into clotting tubes for measurement of estrogen and insulin levels. All methods have been shown in our previous study (21).

Statistical Analyses

A Kolmogorov-Smirnov test was used to assess the normal distribution of data changes. A paired Student's *t* test was used to compare non-time-dependent variables within each subject. A two-way repeated-measures analysis of variance (ANOVA) was used to compare changes in the dependent variables over time and exercise intensity. Duncan and Scheffe's *post hoc* tests were applied in cases of a significant ($P<0.05$) F ratio in order to locate the differences. ANOVA and regression analysis were used to test significant interactions. A P value of less than 0.05 was considered significant, and the reliability of the dependent measures was shown with intra-class correlations. All data are expressed as mean ± SD unless stated otherwise.

Power Calculation

Regarding the previous study (21), the fat oxidation rate was 0.32 $g \cdot min^{-1}$. To meet the requirement of 80% power at a significance level of 0.05, the calculated sample size was eight, and the dropout rate was set at 20%. Therefore, the completion of the study required at least ten subjects.

RESULTS

Subjects' Characteristics

All subjects were healthy, excluding an abnormal lipid profile (Table 1). The subjects showed similar energy intake and expenditure a week before every exercise test (Table 2). Target relative exercise intensities of 25, 65, and 85% VO_2 peak were matched experimentally with actual average VO_2 values of 30 ± 1.7, 63 ± 1.8, and 85 ± 1.7% VO_2 peak, respectively.

Table 1. Anthropometry and Body Composition of Dyslipidemic Women (N=10).

	Mean ± SD
Age (yr)	48 ± 4.39
Body Mass (kg)	59.2 ± 3.08
Height (m)	1.59 ± 3.37
BMI ($kg \cdot m^{-2}$)	23.10 ± 0.39
Waist Circumference (cm)	77.5 ± 4.60
Hip Circumference (cm)	94.2 ± 2.06
W/H Ratio	0.81 ± 0.04
% Body Fat	31.7 ± 1.63
Fat Mass (kg)	18.5 ± 1.33
Lean Body Mass (kg)	40.4 ± 2.35

BMI = Body Mass Index; **W/H** = Waist to Hip Circumferences Ratio

Physiological and Metabolic Parameters

Heart rate, oxygen uptake and energy expenditure increased from resting values during exercise at low-, moderate-, and high-intensities, with the highest values being at a high intensity (all $P<0.05$) (Table 3). Similarly, RPE also increased from resting values during exercise at moderate-and high-intensities, but there was no difference between exercise at low-intensity and resting value (Table 3).

Table 2. Dietary Composition, Total EI, and EE of Dyslipidemic Women (N = 10).

	Mean ± SD
Carbohydrate ($g \cdot d^{-1}$)	278.9 ± 33.2
% Carbohydrate (%total EI)	64.3
Fat ($g \cdot d^{-1}$)	69.5 ± 7.0
%Fat (%total EI)	16.0
Protein ($g \cdot d^{-1}$)	85.1 ± 1.5
% Protein (%total EI)	19.6
Total EI ($kJ \cdot d^{-1}$)	7,628.6 ± 511.5
Total EE ($kJ \cdot kg^{-1} \cdot BM \cdot d^{-1}$)	7,909.9 ± 297.6

EI = Energy Intake; **EE** = Energy Expenditure

Table 3. Physiological and Metabolic Parameters at Rest and During Exercise at Different Intensities of Dyslipidemic Women (N = 10).

	Intensity	**Mean ± SE**
Heart Rate ($L \cdot min^{-1}$)	**Rest**	74 ± 6.5
	25%	115 ± 4.3*
	65%	155 ± 4.7*@
	85%	188 ± 4.4*@$
Rating of Perceived Exertion (scale)	**Rest**	6
	25%	7 ± 0.4
	65%	16 ± 0.5*@
	85%	19.9 ± 0.5*@$
Oxygen Uptake ($mL \cdot kg^{-1} \cdot min^{-1}$)	**Rest**	2.5 ± 0.3
	25%	8.0 ± 41.4*
	65%	20.6 ± 1.8*@
	85%	26.7 ± 2.5*@$
Energy Expenditure ($kJ \cdot kg^{-1} \cdot min^{-1}$)	**Rest**	0.0 ± 50.004
	25%	0.28 ± 0.02*
	65%	0.33 ± 0.033@*
	85%	0.37 ± 0.033@$

*Significantly different from at rest (P<0.05); @Significantly different from during exercise at low-intensity (P<0.05); $Significantly different from moderate-intensity exercise at the same condition (P<0.05)

Interaction

There was a significant interaction between exercise intensity and time in substrate oxidation rates, substrate contribution, and plasma glucose concentration (P<0.05).

Substrate Utilization

CHO oxidation rates during exercise were significantly greater than baseline values at all intensities (baseline (rest): 0.08 ± 0.02 $g \cdot min^{-1}$; low-intensity: 1.4 ± 0.26 $g \cdot min^{-1}$; moderate-intensity: 1.5 ± 0.25 $g \cdot min^{-1}$; high-intensity: 2.44 ± 0.03 $g \cdot min^{-1}$, P<0.05) and showed a significant return to baseline values at recovery (0.09 ± 0.01 $g \cdot min^{-1}$, P<0.05).

Fat oxidation rates during exercise were also greater than baseline values at all intensities (rest: 0.035 ± 0.002 $g \cdot min^{-1}$; low-intensity: 0.5 ± 0.01 $g \cdot min^{-1}$; moderate-intensity: 1.25 ± 0.03 $g \cdot min^{-1}$; high-intensity: 1.35 ± 0.02 $g \cdot min^{-1}$, P<0.05) and showed a significant return to baseline values at recovery (P<0.05).

The contribution of CHO to total energy expenditure was the highest, and fat was the lowest during exercise at high-intensity (P<0.05) (Figures 1 and 2). Furthermore, the subjects relied more on CHO than fat as energy sources at rest (60 vs. 40%), and during exercise at all intensities, P<0.05 (Figure 2).

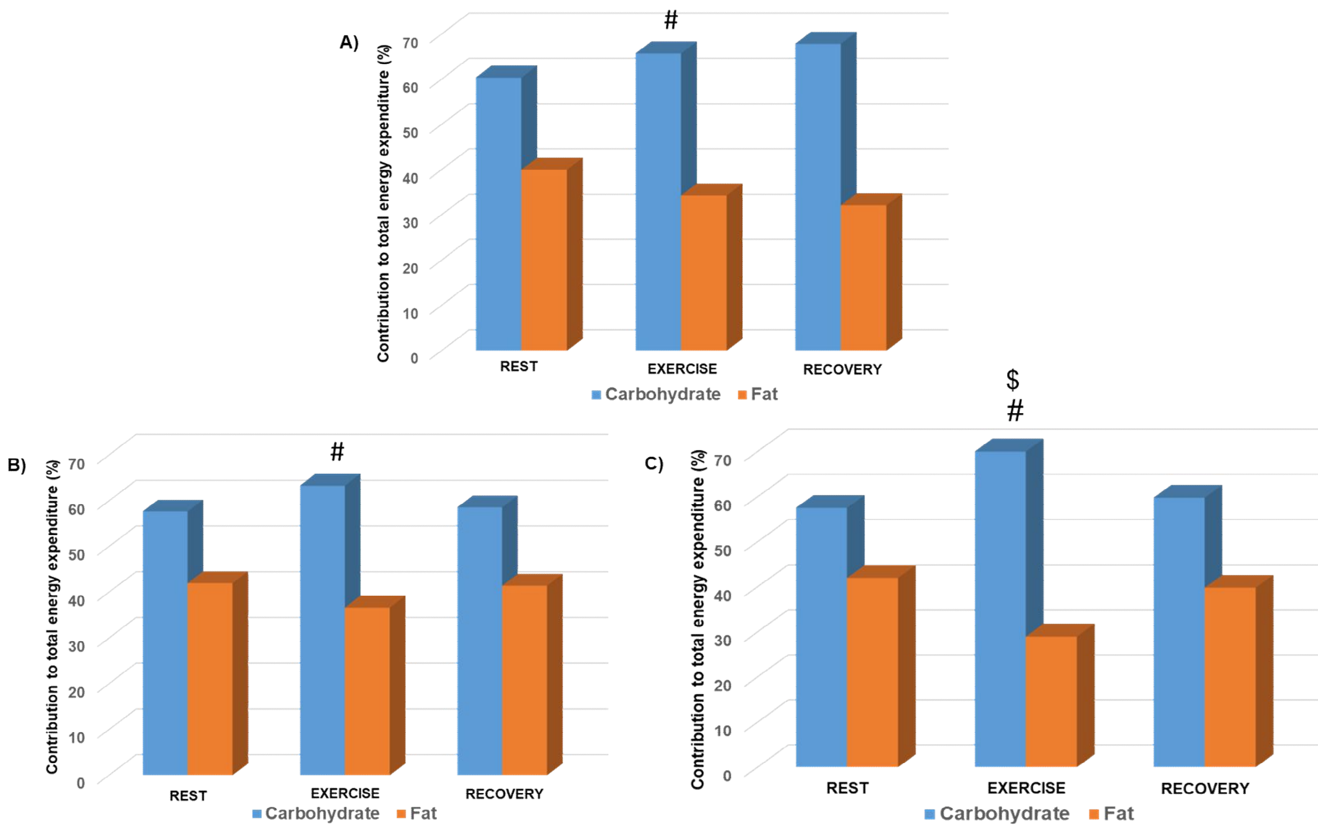

Figure 1. Percent of Substrate Contribution at Rest and During Exercise at Low (A), Moderate (B), and High Intensities (C) in Dyslipidemic Women. Data are expressed as mean (N = 10). $Significantly different from low- and moderate-intensities (P<0.05); #Significantly different from fat contribution at the same condition (P<0.05) Exercise intensity x time (P<0.05)

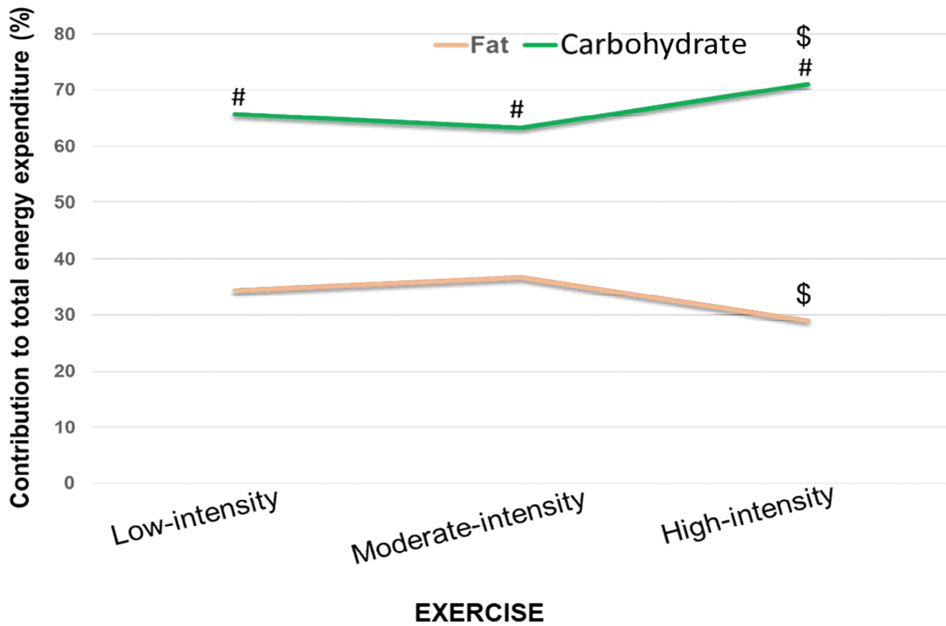

Figure 2. Percent of Substrate Contribution at Rest and During Exercise at Low, Moderate, and High Intensities in Dyslipidemic Women. Data are expressed as mean (N = 10). $Significantly different from low- and moderate-intensities (P<0.05); #Significantly different from fat contribution at the same intensity (P<0.05)

Plasma Glucose Concentration

Immediately after high-intensity exercise and at the end of recovery from the exercise, plasma glucose concentrations were higher than during the same points at low- and moderate-intensity exercise (Table 4). Plasma glucose concentrations did not change from resting values during exercise at any of low- and moderate-intensities.

Serum Insulin Concentration

There were no changes in serum insulin concentrations from resting values during exercise at any of the exercise intensities (Table 4).

Plasma Lipid Profile

Plasma lipid profiles showed no significant change at rest or during exercise at any intensity (Table 4).

DISCUSSION

This study is the novel study exploring fuel selection and circulating substrate at rest and during exercise at different intensities within dyslipidemic women. The significant findings from this study demonstrate that dyslipidemic women relied more on CHO than fat at rest and during exercise at all intensities. CHO and fat utilization increased when subjects exercised. The CHO utilization was the highest and fat utilization was the lowest at high-intensity exercise. Blood glucose concentrations peaked during and after the high-intensity exercise. However, exercise intensity did not influence insulin and lipid profiles concentrations.

The results of this study partially support our hypothesis, which hypothesized that the subjects would have different levels of substrate utilization and circulating substrate during exercise at low-, moderate-, and high-intensities. We found the significant increases in CHO and fat utilization during exercise in dyslipidemic women. The highest CHO and the lowest fat utilization were at the level of high-intensity exercise. This change is different from those in dyslipidemic men in our previous study (21). Although we did not observe statistically significant gender differences in substrate utilization at rest and during exercise, we found that the dyslipidemic men relied equally on carbohydrate and fat at low-intensity exercise and relied more on CHO than fat during higher-intensity exercise. The results of this study is similar to those in Thai normolipidemic subjects who relied more on CHO utilization at rest and during exercise at all intensities (12).

It is also noted that COP and PLipoxmax were at low-intensity exercise in the dyslipidemic men (21) and normolipidemic Thai subjects (12) whereas at moderate-intensity exercise in this study. In Western individuals with normolipidemia, fat utilization increased when the intensity of exercise increased from low- to moderate-intensity and decreased from moderate- to high-intensity, while CHO uses increased with the intensity of exercise (4,18,20). The greater utilization of CHO than fat at rest and during exercise in Thai subjects than seen previously in other populations may be due to the habitual higher dietary CHO intake of Thai subjects. However, the CHO contribution in Thai normolipidemic subjects is much higher and fat contribution is lower than dyslipidemic Thai subjects. The higher level of triglycerides of the dyslipidemic Thai subjects may be responsible for this phenomenon. The substrate utilization depends on its availability in blood circulation (6).

The highest effort at high-intensity exercise is comparable with the highest blood glucose concentration, which occurred immediately after high-intensity exercise and lasted at least 20 min. The role of increased gluconeogenesis resulting from the increased substrate, e.g., lactate induced by high-intensity exercise, implies an increased acidity of blood during high-intensity exercise, which would increase the functions of the cardiovascular and respiratory systems (as determined by HR, VO_2, and RPE). Although we did not analyze blood lactate concentration, these relationships have been well supported by previous research reviews (10, 17). Additional information is about a shorter exercise duration for the high-intensity exercise, as our subjects were middle-aged Thai women who would not be able to perform the exercise at such high-intensity for a long duration, i.e., longer than 5 min. Therefore, to be realistic, we set the duration at this high intensity only at 5 min for the subjects of this age who do not perform the exercise at this intensity.

Similarly, to the male counterpart, dyslipidemic women were not recommended to do exercise at high intensity because it may be harmful due to hyperglycemia after the exercise and the high effort required. Instead, the most appropriate intensity of exercise for dyslipidemic Thai women may be low- and moderate-intensity because of its capacity to increase CHO and fat utilization, as well as its practicality.

Table 4. Blood Chemistry Parameters Before (Baseline), Immediately (Exercise), and 20 Min After (Recovery) Exercise at Various Intensities in Dyslipidemic Women.

	Intensity of exercise								
	Low			Moderate			High		
	Baseline	Exercise	Recovery	Baseline	Exercise	Recovery	Baseline	Exercise	Recovery
Plasma Glucose ($mg \cdot dL^{-1}$)	82.1±9.2	81.1±9.0	78.2±9.3	80.2±8.1	78.6±7.8	76.5±6.3	79.8±8.8	85.5±14.2$^{@\$}$	84.0±13.8$^{@\$}$
Total Cholesterol ($mg \cdot dL^{-1}$)	276.8±39.3	272.2±34.4	272.6±39.7	264.1±56.7	270.8±57.6	267.7±59.7	252.0±70.5	274.5±81.6	266.8±78.8
Triglycerides ($mg \cdot dL^{-1}$)	200.3±91.2	196.6±76.7	205.9±86.6	181.1±77.5	187.5±65.2	177.3±81.4	178.2±68.7	180.3±64.2	177.7±69.4
HDL-C ($mg \cdot dL^{-1}$)	54.0±7.2	55.4±6.8	54.8±8.6	53.8±7.4	56.1±6.4	54.7±9.6	56.4±6.4	58.9±6.2	58.4±6.1
LDL-C ($mg \cdot dL^{-1}$)	161.5±59.3	149.3±48.7	158.2±58.6	147.8±50.2	150.0±55.9	146.6±48.5	134.8±72.9	156.3±74.8	155.7±68.7
Insulin ($\mu IU \cdot mL^{-1}$)	12.12±0.87	8.96±9.61	9.51±5.40	15.02±11.03	9.63±3.56	7.96±4.73	8.85±1.92	7.99±1.32	9.06±0.64

Data are expressed as mean ± SD (N = 10 women); **FBG** = Fasting Blood Glucose; **TC** = Total Cholesterol; **TG** = Triglycerides; **HDL-C** = High-Density Lipoprotein; **LDL-C** = Low-Density Lipoprotein; $^{@}$ Significantly different from low-intensity exercise in the same condition (P<0.05); $^{\$}$ Significantly different from moderate-intensity exercise in the same condition (P<0.05)

Furthermore, in this study, fat utilization during exercise was higher than resting values at all intensities. Thus, the PLipoxmax in this study was at moderate-intensity exercise. The higher level of lipoprotein-derived TGs in dyslipidemic women may be one factor that contributes to higher circulating fat availability in our subjects than in the previously studied young Thai subjects. This could lead to higher fat utilization at rest and during exercise all intensities, as seen in this study. Furthermore, higher dietary fat intake in this study's subjects (16.0%) relative to the subjects in our previous study (11.9 ± 1.0%) may explain the difference, as it is well known that chronic dietary interventions can affect substrate utilization during exercise (6,13,19).

Limitations in this Study

We used an indirect calorimetry method to measure whole-body substrate oxidation rate in this study. This method does not provide us the data of the specific sources of CHO and fat such as intramuscular glycogen and fat. We also did not analyze the molecular mechanism of CHO and fat metabolism. Therefore, further study using special techniques such as a biopsy of adipose tissue and muscle or radioisotope tracer is needed to determine molecular information about substrate utilization in dyslipidemic subjects.

CONCLUSION

The findings in the present study indicate that dyslipidemic Thai women relied more on CHO as an energy source at rest and during exercise at all intensities. Blood glucose concentrations peaked after high-intensity exercise. However, lipid profiles and insulin concentrations were not altered by the intensity of exercise.

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