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Original Article

Impaired Aerobic Capacity in Thai Dyslipidemias

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ABSTRACT *Introduction:* **Cardiovascular disease (CVD) is the leading cause of death in Thailand. Dyslipidemias have been known to be high risk for CVD. This may be determined by an impaired aerobic capacity which is associated with CVD. However no study investigated this event in Thai dyslipidemias. Therefore the present study aimed to 1) determine the aerobic capacity in Thai dyslipidemias and 2) investigate effects of gender and age on aerobic capacity in Thai dyslipidemias.**

Methods: **Seventy-five dyslipidemias and 87 healthy sedentary subjects in urban, Khon Kaen province, Thailand were recruited. All of them were divided by age into 2 groups 1) 20-40 years and 2) 40-60 years. The former comprised of 41 men and 34 women and the latter were 31 men and 56 women. Blood sample was obtained after fasting over night and analyzed for total cholesterol (TC), triglycerides (TG), high density lipoprotein-cholesterol (HDL-C), and low density lipoprotein-cholesterol (LDL-C). At least 1 week after blood sampling, each subject underwent a maximum oxygen consumption ($\dot{V}_{O2,max}$) test to determine aerobic capacity.**

Results: **Combined data showed significant lower aerobic capacity in the dyslipidemia (28.2 ± 0.9 ml/kg/min) than the control group (32.6 ± 1.0 ml/kg/min) (p=0.01). The dyslipidemia group (28.6 ± 1.3 ml/kg/min) aged 40-60 years tended to have lower aerobic capacity than the control group (31.6 ± 1.3 ml/kg/min, p=0.09). However, there was no significant difference in aerobic capacity between groups in younger subjects.**

Conclusion: **This study demonstrates that aerobic capacity is impaired in Thai dyslipidemias, especially type III. The mechanism which is responsible for this may be the loss of EDNO-mediated hyperemia resulting from hypertriglycerides and hypercholesterol. Men had greater aerobic capacity than women at all ages. In addition, aerobic capacity declined with age especially the dyslipidemias type IIa.**

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Key words: **maximum oxygen consumption, dyslipidemias, lipid profile**

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in Thailand. Up-to-date it has been known that dyslipidemias who have one or more of these abnormal blood lipid concentrations; high levels of total cholesterol (TC), triglycerides (TG), low density lipoprotein-cholesterol (LDL-C) or low levels of high density lipoprotein-cholesterol (HDL-C) are at high risk of CVD as a result of atherosclerosis[1-3]. Both abnormal lipid profile[4] and CVD[5, 6] were shown to be associated with impaired aerobic capacity. The overall power of the heart as an oxygen pump and of the muscle cells' ability to utilize oxygen and fuel sent to them via the cardiovascular system is measured by maximum oxygen consump-

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tion ($\dot{V}_{O2,max}$) test, which determines aerobic capacity. The reduction in exercise capacity may be attributable to dilator dysfunction, attenuated elaboration of aortic endothelial derived nitric oxide (EDNO), associated with an endothelium-dependent vasoconstriction and a reduced exercise-induced NO production assessed by urinary nitrate excretion. These findings lead us to speculate that EDNO production contributes significantly to exercise-induced hyperemia and that a loss of EDNO-mediated hyperemia results in a decreased oxygen transport capacity of the vasculature and an attenuated aerobic capacity. Aerobic capacity has also been demonstrated to be lower in women and the elderly than men and the younger respectively. Recent published study showed that the increased prevalence of heart failure with preserved ejection fraction in elderly persons and particularly in elderly women may be attributable to combined ventricular-vascular stiffening[7]. The above previous studies were done in Caucasian. No study investigated this event in Thai dyslipidemias although there is an ethnic difference in heart health behaviors, risk factors for coronary heart disease,and cardiovascular fitness[8]. Therefore the present study aimed to 1) determine the aerobic capacity in Thai dyslipidemias and 2) investigate effects of gender and age on aerobic capacity in Thai dyslipidemias.

METHODS

Subjects. Seventy-five dyslipidemias and 87 healthy sedentary subjects in urban, Khon Kaen province, Thailand were recruited. All of them were divided by age into 2 groups 1) 20-40 years and 2) 40-60 years. The former comprised of 41 men and 34 women and the latter comprised of 31 men and 56 women. Three types of dyslipidemias including, type I, Type IIa, type IIb and type III participated in this study. Dyslipidemias type IV and V which are characterized by chylomicrons and very low density lipoprotein (VLDL) were not recruited because chylomicrons and VLDL were not measured. Subjects were excluded if they had CVD, orthopedic problem, neuromuscular disorder, liver and kidney disorders, infection, diabetes mellitus and current medication use. All subjects participated in a routine medical examination in which a medical history by completion of health-risk questionnaire, a 12-lead electrocardiograph to examine cardiac function before experiment. All subjects signed an informed consent form approved by the Ethical Committee of Khon Kaen University.

Experimental protocol. Each subject underwent a graded exercise test on an electrically braked cycle ergometer. Expired-air collection and analysis were performed using a gas analysis system which volume and percent gas were calibrated every experimental day. The subject's $\dot{V}_{O2,max}$ was measured during about the 12th to 15th min of an incremental test in which workload was increased every 3 min from the beginning until exhaustion. First workload and increment were determined from an estimation of physical fitness based on daily physical activity. The first work rate was 20-30 watt and 40-50 watt for women and men, respectively. The incremental work rate for women was 20-30 watt and for men was 30-40 watt. Expired air samples and the heart rate were obtained throughout the test. The highest oxygen uptake value ($\dot{V}_{O2,max}$) of the subject was determined when any of the following criteria was achieved: 1) the subject's $\dot{V}_{O2}$ reached a plateau with an increase in workload, or 2) the heart rate reached 90% of age-predicted maximum (220-age), or 3) the subject's respiratory exchange ratio ≥ 1.15.

Statistical analysis. Data are expressed as mean ± SE. Descriptive statistis was used to express the baseline subject characteristics. Group differences were evaluated by Students't test whereas analysis of correlation between lipid levels and aerobic capacity in dyslipidemia group was determined by Pearson correlation test. Significance was defined as $p \leq 0.05$.

RESULTS

Anthropometric and body composition characteristics

Effect of dyslipidemias. Seventy-two men aged 49 ± 1.2 years and ninety women aged 43 ± 0.8 years participated in this study. Combined data showed that control group had lower body mass, body mass index, fat mass, fat free mass and waist to hip ratio than dyslipidemia group (Table 1). There was no significant difference in height and percentage of body fat between groups (Table 1).

Effect of gender. In dyslipidemia group, at all ages, men had higher height, body mass, fat free mass, waist circumference and waist to hip ratio and less percentage of body fat than women. There was no significant dif-

Table 1 Anthropometric of all subjects in control and dyslipidemia groups

	Control	Dyslipidemias
Age (yrs)		
Men	47.0 ± 1.6	45.0 ± 1.4
Women	42.0 ± 0.9	50.0 ± 1.8
Sex		
Women	n = 56	n = 41
Men	n = 31	n = 34
Height (cm)	159.8 ± 0.8	161.4 ± 0.9
Body mass (kg)	57.9 ± 1.1	63.4 ± 1.2##
BMI (kg/m^2)	22.7 ± 0.4	24.4 ± 0.4 #
% BF	30.6 ± 0.5	31.6 ± 0.4
FM (kg)	17.9 ± 0.5	20.2 ± 0.6 #
FFM (kg)	39.9 ± 0.7	43.2 ± 0.8 #
Waist circumference (cm)		
Men	84.4 ± 1.2	85.4 ± 1.0
Women	72.1 ± 1.1	77.0 ± 1.5 #
Hip circumference (cm)	92.9 ± 0.7	95.5 ± 0.7 #
Waist/hip ratio	0.76 ± 0.01	0.82 ± 0.01##

Values are expressed as means ± SE; n=162.

BMI, body mass index; %BF, percentage of body fat; FM, fat mass; FFM, fat free mass.

Significantly different from control group (P<0.01);

 # Significantly different from control group (P<0.05).

ference in body mass index, fat mass and hip circumference between men and women at all ages in the same group (Table 2). When compared between gender within dyslipidemia group, at particular age, results were similar to all-age data. There was additional non significant gender difference in, percentage of body fat and body mass at aged 20 to 40 and 40 to 60 years respectively (Table 2).

Effect of age. In dyslipidemia group, all subjects aged 20 to 40 years had lower waist circumference and hip circumference than subjects aged 40 to 60 years (Table 3). There was no significant age difference in any anthropometric characteristics in men in the dyslipidemia group (Table 3). In dyslipidemia group, all women aged 20 to 40 years had lower height, body mass, fat mass, fat free mass, waist circumference, hip circumference and waist to hip ratio than women aged 40 to 60 years (Table 4). There was no significant difference in body mass index and percentage of body fat between women aged 20 to 40 years and 40 to 60 years (Table 4).

Aerobic capacity

Effect of dyslipidemias. Combined data showed that control group had higher $\dot{V}_{O2,max}$ (32.7 ± 1 and 28.8 ± 0.9 ml/kg/min respectively, P<0.01) than dyslipidemia

Table 2 Anthropometric of men and women at all ages in control and dyslipidemia groups

	Control		Dyslipidemias	
	Men	Women	Men	Women
Age (yrs)	47.0 ± 1.6	42.0 ± 0.9	50.0 ± 1.8	45.0 ± 1.4
Sex	n = 31	n = 56	n = 41	n = 34
Height (cm)	166.8 ± 1.0	159.3 ± 0.6	166.7 ± 1.0	155.0 ± 0.8**
Body mass (kg)	67.8 ± 1.3	52.8 ± 1.0	67.0 ± 1.3	59.0 ± 2.0 **
BMI (kg/m^2)	24.4 ± 0.5	21.9 ± 0.5	24.4 ± 0.3	24.4 ± 0.7
% BF	29.3 ± 0.9	31.3 ± 0.6	30.3 ± 0.5	33.2 ± 0.7**
FM (kg)	20.0 ± 0.8	16.8 ± 0.7	20.4 ± 0.6	20.0 ± 1.1
FFM (kg)	47.6 ± 0.8	36.1 ± 0.5	46.5 ± 0.8	39.1 ± 1.1 **
Waist circumference (cm)	84.4 ± 1.2	72.1 ± 1.1	85.4 ± 1.0	77.0 ± 1.5 **
Hip circumference (cm)	95.4 ± 0.7	91.7 ± 0.9	95.3 ± 0.6	95.7 ± 1.5
Waist/hip ratio	0.9 ± 0.01	0.8 ± 0.01	0.9 ± 0.01	0.8 ± 0.01 **

Values are expressed as means ± SE; n=162.

BMI, body mass index; %BF, percentage of body fat; FM, fat mass; FFM, fat free mass.

**** Significantly different from men in the same group (P<0.01).**

Table 3 Anthropometric of all subjects aged 20-40 and 40-60 years in dyslipidemia group

	Dyslipidemias	
	Aged 20-40 years (n = 23)	**Aged 40-60 years (n = 52)**
Age (yrs)	36.4 ± 0.7	50.2 ± 0.9
Height (cm)	160.7 ± 1.9	161.6 ± 1.0
Body mass (kg)	59.5 ± 2.4	64.7 ± 1.4
BMI (kg/m^2)	23.3 ± 0.5	24.8 ± 0.4
% BF	30.4 ± 0.8	32.0 ± 0.5
FM (kg)	18.3 ± 1.0	20.9 ± 0.7
FFM (kg)	41.2 ± 1.5	43.8 ± 0.9
Waist circumference (cm)	76.9 ± 1.9	83.2 ± 1.1^{+}
Hip circumference (cm)	92.0 ± 1.2	96.7 ± 0.9^{+}
Waist/hip ratio	0.83 ± 0.01	0.86 ± 0.01

Values are expressed as means ± SE; n=75.

BMI, body mass index; %BF, percentage of body fat; FM, fat mass; FFM, fat free mass.

$^{+}$Significantly different from all subjects aged 20-40 years (P<0.05).

Table 4 Anthropometric of men and women aged 20-40 and 40-60 years in dyslipidemia group

	Aged 20-40 years		Aged 40-60 years	
	Men	**Women**	**Men**	**Women**
Age (yrs)	35.5 ± 1.4	37.1 ± 0.7	51.9 ± 0.8	49.3 ± 1.1
Sex	n =11	n = 12	n = 30	n = 22
Height (cm)	166.8 ± 2.0	151.0 ± 0.9 $^{++}$	166.5 ± 1.5	156.2 ± 0.9$^{*, \#\#}$
Body mass (kg)	67.2 ± 2.4	50.8 ± 2.5 $^{++}$	66.9 ± 1.5	61.9 ± 2.5*
BMI (kg/m^2)	24.1 ± 0.5	21.1 ± 0.9	24.5 ± 0.4	25.1 ± 0.9
% BF	30.0 ± 0.6	31.0 ± 1.5	30.4 ± 0.6	34.0 ± 0.8 $^{\#\#}$
FM (kg)	20.2 ± 1.1	16.1 ± 1.5	20.5 ± 0.7	21.3 ± 1.3*
FFM (kg)	47.0 ± 1.3	34.7 ± 1.2 $^{++}$	46.4 ± 0.9	40.6 ± 1.3 $^{*, \#\#}$
Waist circumference (cm)	82.4 ± 1.9	70.6 ± 2.4 $^{+}$	86.4 ± 1.1	79.2 ± 1.8 $^{*, \#\#}$
Hip circumference (cm)	94.8 ± 1.0	88.8 ± 2.0	95.5 ± 0.7	98.1 ± 1.7 *
Waist/hip ratio	0.9 ± 0.02	0.79 ± 0.01 $^{+}$	0.9 ± 0.01	0.81 ± 0.01$^{*, \#\#}$

Values are expressed as means ± SE; n=75.

BMI, body mass index; %BF, percentage of body fat; FM, fat mass; FFM, fat free mass.

$^{+}$Significantly different from men aged 20-40 years (P<0.05);

$^{++}$Significantly different from men aged 20-40 years (P<0.01);

$^{\#\#}$Significantly different from men aged 40-60 years (P<0.01);

*** Significantly different from aged 20-40 years in the same gender (P<0.05).**

group (Fig. 1). Both men and women in control group had higher $\dot{V}_{O2,max}$ (34.8 ± 1.3 and 30.3 ± 0.9, 26.9 ± 1 and 31.4 ± 1 ml/kg/min respectively, P<0.05) than men and women respectively in dyslipidemia group (Table 5). Control group had higher $\dot{V}_{O2,max}$ (32.7 ± 1 and 22.1 ± 1.3 ml/kg/min respectively, P<0.01) than dyslipidemias type III only (Fig. 1). All men in control group had higher $\dot{V}_{O2,max}$ than men in dyslipidemias type I, IIb and III. All women in control group had higher $\dot{V}_{O2,max}$ than women in dyslipidemias type I, IIb and III (Table 5).

Effect of gender. In control group, there was no significant difference in $\dot{V}_{O2,max}$ between men and women at all ages. In dyslipidemia group, men had higher $\dot{V}_{O2,max}$ than women at all ages (Table 5). In dyslipidemias type IIb, men had higher $\dot{V}_{O2,max}$ than women at all ages.

Effect of age. Combined data showed that there was no significant age difference in $\dot{V}_{O2,max}$ between all subjects in both groups. In dyslipidemias type IIa, all subjects aged 20 to 40 years had higher $\dot{V}_{O2,max}$ than subjects aged 40 to 60 years (Table 6). There was no significant age difference in $\dot{V}_{O2,max}$ between subjects in the other types of dyslipidemia group (Table 6).

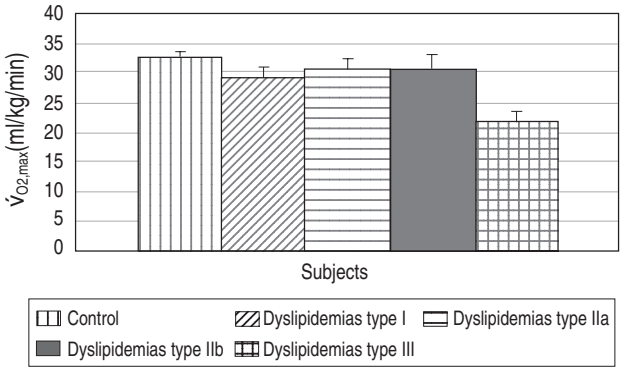

Fig. 1 Aerobic capacity of all subjects in control and dyslipidemia groups (control, n=87; dyslipidemias type I, n=18; dyslipidemias type IIa, n=26; dyslipidemias type IIb, n=14; dyslipidemias type III, n=10). Values are expressed as means ± SE; $\dot{V}_{O2,max}$, maximum oxygen consumption; * Significantly different from control group (P<0.05).

DISCUSSION

This is the first study in Thai dyslipidemias that demonstrated their impaired aerobic capacity, especially type III. Moreover, among these patients, men had greater aerobic capacity than women especially at all ages. In addition, aerobic capacity declined with age especially the dyslipidemias type IIa.

Aerobic capacity. The graded maximum oxygen test used to determine maximum oxygen consumption or aerobic capacity in the present study is the most accurate, reproducible and commonly used as a measure of cardiorespiratory function[9]. It determines the capacity of the heart and lung as an oxygen supply and pump and of the muscle cells' ability to utilize oxygen and fuel sent to them via the cardiovascular system. The increase in consumed oxygen and produced carbon dioxide by active skeletal muscle during exercising is many folds greater than during resting. Individuals who have high aerobic capacity will have high cardiac output and muscular oxy-

Table 5 Aerobic capacity of men and women at all ages in control and dyslipidemia groups

	$\dot{V}_{O2,max}$ (ml/kgBM/min)		$\dot{V}_{O2,max}$ (ml/kgFFM/min)	
	Men	Women	Men	Women
Control	34.8 ± 1.3	31.4 ± 1.0	45.8 ± 1.4	40.6 ± 0.9
Dyslipidemias	30.3 ± 0.9#	26.9 ± 1.0 *,#	39.9 ± 0.9#	37.7 ± 0.8*,#
Classifications				
Type I	30.7 ± 1.9#	24.8 ± 2.4#	38.9 ± 2.1#	35.3 ± 2.8#
Type IIa	35.8 ± 1.6	28.2 ± 1.5*	46.7 ± 2.4	38.7 ± 1.8**
Type IIb	30.4 ± 3.0#	25.4 ± 2.4#	39.3 ± 3.7#	35.3 ± 2.8#
Type III	25.0 ± 2.1##	21.4 ± 2.0##	35.7 ± 0.8##	32.4 ± 1.9##

Values are expressed as means ± SE; (control, men, n=31 women, n=56; dyslipidemias type I, men, n=14 women, n=4; dyslipidemias type IIa, men, n=10 women, n=16; dyslipidemias type IIb, men, n=7 women, n=7; dyslipidemias type III, men, n=4 women, n=6);

$\dot{V}_{O2,max}$, maximum oxygen consumption;

*** Significantly different from men at all ages (P<0.05);**

**** Significantly different from men at all ages (P<0.01);**

 # Significantly different from control group in the same gender (P<0.05);

Significantly different from control group in the same gender (P<0.01).

Table 6 Aerobic capacity of all subjects aged 20-40 years and 40-60 years in control and dyslipidemia groups

	$\dot{V}_{O2,max}$ (ml/kgBM/min)		$\dot{V}_{O2,max}$ (ml/kgFFM/min)	
	Aged 20-40 years	Aged 40-60 years	Aged 20-40 years	Aged 40-60 years
Control	35.0 ± 1.5	31.6 ± 1.0	46.6 ± 1.6	35.9 ± 1.9 ++
Dyslipidemias	28.5 ± 1.0	26.3 ± 0.9	41.2 ± 1.3	34.4 ± 2.7 +
Classifications				
Type I	28.0 ± 0.9	30.0 ± 2.2	40.8 ± 1.2	41.6 ± 2.2
Type IIa	35.2 ± 1.9	28.6 ± 1.6 +	46.8 ± 2.4	40.3 ± 1.9 ++
Type IIb	25.0 ± 0.7	33.1 ± 1.8	33.3 ± 1.0	44.2 ± 2.3
Type III	25.0 ± 1.2	21.4 ± 1.6	33.0 ± 1.9	30.1 ± 2.1

Values are expressed as means ± SE; (control, n=87; dyslipidemias type I, n=18; dyslipidemias type IIa, n=26; dyslipidemias type IIb, n=14; dyslipidemias type III, n=10).
$\dot{V}_{O2,max}$, maximum oxygen consumption;
+ Significantly different from all subjects aged 20-40 years (P<0.05);
++ Significantly different from all subjects aged 20-40 years (P<0.01).

gen uptake mainly from EDNO-mediated hyperemia.

Aerobic capacity and dyslipidemia. Dyslipidemias type III is characterized by an elevation of concentration of TC and TG due to a defect in VLDL remnant clearance. These individuals had difficulty in removing TG rich VLDL remnant particles. In the present study, only dyslipidemias type III had significantly lower aerobic capacity than the healthy control subjects. This result is consistent with the study of Thomas and colleges which reported that VLDL and TG were inversely associated with $\dot{V}_{O2,max}$[10, 11]. This may be due to hypertriglycerides and hypercholesterol which strongly correlated with a loss of EDNO-mediated hyperemia[12]. This may result in a decreased oxygen transport capacity of the muscular vasculature and an attenuated aerobic capacity in the present study.

Aerobic capacity and gender. In the present study, men had higher aerobic capacity than women at all ages. This may be due to the greater body mass, fat mass and mitochondrial enzyme activity and lower fat free mass in women than men. This gender difference in aerobic capacity is well-described in published data and is attributed to higher body fat composition, lower hemoglobin content and small heart size of women[13]. In addition the lower $\dot{V}_{O2,max}$ in the women was reported to be due to decreased maximal stroke volume associated with female gender[14]. It was previously demonstrated that aerobic capacity is negatively correlated with body mass and fat mass[15, 16] and positively correlated with fat free mass[17, 18]. This may explain the greater aerobic capacity in men than women in the present study. Moreover, women in dyslipidemia group in this study had greater TC, TG and LDL-C concentrations than men. Thus, hypertriglycerides and hypercholesterol in these women may contribute to a greater loss of endothelium-dependent vasorelaxation, leading to lower aerobic capacity than men. Although estrogen was not measured in the present study it was known to be decreased in postmenopausal period[19]. Estrogen was reported to have a TG lowering effect[20, 21]. Therefore, the reduction of estrogen during postmenopausal period may contribute to hypertriglycerides. All of above may be responsible for the lower aerobic capacity in women than men at middle age in the present study. It is noted that $\dot{V}_{O2,max}$ in men still is higher than women even when normalize by FFM. This may show that there are other factors as mentions above influencing $\dot{V}_{O2,max}$ for example muscle mitochondrial enzyme activity and hemoglobin content.

Aerobic capacity and age. The present study demonstrated the lower aerobic capacity in both men and women in dyslipidemia group at middle age than the younger. The age-related decrement in aerobic capacity is likely multifactorial[13, 22]. This may be due to the reasons mentioned above that aerobic capacity is inversely correlated with body mass and fat mass[15, 16] and positively correlated with fat free mass[17, 18]. First, it may

be due to a decline with age in central factor (cardiac function) of maximum oxygen consumption which results in decreased maximum heart rate. This may contribute to a decline in blood delivery to active muscles. Second, it may be attributable to the decrease with age in skeletal muscle blood flow from a decrease in both capillary density and capillary-to-fiber ratio[23], nutrition and hormone level[24]. Third, it may be due to a decline with age in mitochondrial enzyme activity[25]. Last, it may result from the higher body mass and fat mass and lower percentage of muscle mass.

CONCLUSION

The remarkable result of this study is that aerobic capacity is impaired in Thai dyslipidemias, especially type III. The mechanism which is responsible for this may be the loss of EDNO-mediated hyperemia resulting from the hypertriglycerides and hypercholesterol. In dyslipidemias, men had greater aerobic capacity than women at all ages. This may be explained by many reasons. In addition, aerobic capacity declined with age especially the dyslipidemias type IIa.

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