

## Maximum oxygen consumption in patients with suspected coronary artery disease

### สมรรถภาพการใช้ออกซิเจนในผู้ที่สงสัยว่าเป็นโรคหลอดเลือดหัวใจ

Thapanee Reangrit (ฐาปณี เรียงฤทธิ)\*, Dr.Panakaporn Wannanon (พญ.ปานคพร วรรณานนท์)\*\*, Dr.Tawan Suwanich (นพ.ท้าวัญ สุวานิช)\*\*\*, Dr.Pongsak Intharapetch (นพ.พงษ์ศักดิ์ อินทรเพชร)\*\*\*, Montana Donsom (มณฑนา ดอนโสม)\*\*\*\*, Jatuporn Wichitsranoi (จตุพร วิชิตสระน้อย)\*\*\*\*\*, Dr.Naruemon Leelayuwat (ดร.นฤมล ลีลานุวัฒน์)\*\*

#### ABSTRACT

Coronary artery disease (CAD) is a major killer and is the most common cause of mortality and morbidity in the entire world. Previous study has shown that the aerobic capacity determined by maximum oxygen consumption ( $\dot{V}O_{2,max}$ ) during the exercise stress test (EST) is a well-documented risk predictor of cardiovascular and total mortality. Therefore, we examined aerobic capacity in Thai patients with suspected CAD (N = 29, mean age 54 years, 24 male, 5 female). The 12-lead ECG heart rate and blood pressure were measured throughout this study. Results indicate that subjects with positive EST had lower  $\dot{V}O_{2,max}$  than those with negative EST ( $17.94 \pm 9.76$  and  $32.81 \pm 16.24$  ml/kg/min). This could be attributed to an inability to adapt their coronary flow adequately to higher metabolic demands during the maximal exercise.

#### บทคัดย่อ

โรคหลอดเลือดหัวใจเป็นสาเหตุสำคัญที่ทำให้ประชากรเสียชีวิต รายงานวิจัยในอดีตแสดงให้เห็นว่าสมรรถภาพการใช้ออกซิเจน ซึ่งวัดจากการใช้ออกซิเจนสูงสุดขณะการออกกำลังกาย เป็นตัวบ่งชี้ที่สำคัญบอกถึงอัตราเสี่ยงที่มีโอกาสเกิดโรคหัวใจและหลอดเลือด ทั้งนี้การตรวจสมรรถภาพหัวใจโดยการออกกำลังกาย เป็นวิธีการตรวจเบื้องต้นสำหรับการวินิจฉัย ทำนายความรุนแรง และ พยากรณ์โรคหลอดเลือดหัวใจ ดังนั้นงานวิจัยนี้ต้องการศึกษาสมรรถภาพการใช้ออกซิเจนสูงสุด โดยใช้การตรวจสมรรถภาพหัวใจโดยการเดินสายพาน ในกลุ่มผู้ป่วยคนไทยที่สงสัยว่าเป็นโรคหลอดเลือดหัวใจ จากการศึกษาพบว่า ในกลุ่มผู้ป่วยที่มีผลการตรวจสมรรถภาพหัวใจโดยการเดินสายพานเป็นบวก จะมีค่าสมรรถภาพการใช้ออกซิเจนสูงสุดน้อยกว่ากลุ่มที่แสดงผลเป็นลบ ซึ่งอาจเกิดจากการไหลเวียนของเลือดในหลอดเลือดหัวใจไม่เพียงพอกับความต้องการใช้ออกซิเจนที่เพิ่มขึ้นขณะออกกำลังกาย

**Key Words :** coronary artery disease, exercise stress test, maximum oxygen consumption

**คำสำคัญ :** โรคหลอดเลือดหัวใจ การตรวจสมรรถภาพหัวใจโดยการออกกำลังกาย การใช้ออกซิเจนสูงสุด

\*Student, Ms.D. of Medical Physiology, Faculty of Medicine, Khon Kaen University

\*\*Assistant Professor, Faculty of Medicine, Khon Kaen University

\*\*\*Doctor, Sirikit cardiac center, Khon Kaen University

\*\*\*\*Physical therapist, Sirikit cardiac center, Khon Kaen University

\*\*\*\*\*Student, Ph.D. of Biomedical Sciences, in Biomedical Sciences, Graduate School, Khon Kaen University

## Introduction

Coronary artery disease (CAD) is a major killer and is the most common cause of mortality and morbidity in the entire world (Reddy, 1993). CAD is a disease characterized by narrowing or blockage of the arteries and vessels providing oxygen and nutrients to the heart caused by atherosclerosis. Diagnostic tests are many tests include electrocardiogram and exercise stress test. If the tests are positively diagnosed specific vessels and severity will be confirmed by cardiac catheterization or coronary angiogram. Exercise stress test is a screening test for diagnosis of CAD (Davis *et al.*, 1990; Detrano and Froelicher, 1988). During the test, cardiac muscle consumed large amount of energy. More blockage of the cardiac vessel is more severity of the disease. Interestingly, previous study have shown that the aerobic capacity determined by maximum oxygen consumption ( $\dot{V}O_{2max}$ ) during the exercise stress test is a well-documented risk predictor of cardiovascular and total mortality (Dorn *et al.*, 1999; Vanhees *et al.*, 1995). However, no study investigated aerobic capacity in Thai patients with suspected CAD. Therefore, this study aimed to determine aerobic capacity in Thai patients with suspected CAD.

## Materials and methods

### Subjects

This experimental study. The physician was evaluated patients with suspected CAD such as angina pectoris, shortness of breath or lightheadedness, irregular heart beats, or cardiovascular risk factors. That include the following: DM, dyslipidemia, hypertension or obesity. The physician may recommend an exercise stress test to diagnose CAD.

The 29 subjects were recruited. The 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. All subjects signed an informed consent form approved by the Ethical Committee of Khon Kaen University.

### Experimental protocol

All subjects were measured anthropometry and body composition. Then they underwent an exercise stress test on a treadmill (TM55 Ultradrive digital treadmill). All subjects were measured  $\dot{V}O_{2max}$  during exercise period. Expired air samples were obtained throughout the exercise period. The  $\dot{V}O_{2max}$  of the subject was determined when any of the following criteria is achieved: 1) the subject's  $\dot{V}O_2$  reached a plateau with an increase in workload, or 2) the heart rate reached 85% of age-predicted maximum (220-age), 3) the subject's Respiratory Exchange Ratio (RER)  $\geq 1.15$  or 4) they cannot perform the exercise (Lipton *et al.*, 2008).

### Grading of symptoms

Clinical symptoms during the test are determined "positive" when they meet the following criteria: chest pressure or pain during exercise that was not present before starting of the exercise, that resolved post exercise. Patients with no symptom, leg fatigue, musculoskeletal pain or shortness of breath were determined "negative" (Lipton *et al.*, 2008).

### Statistical analysis

Data were expressed as the mean and the standard deviation (mean  $\pm$  SD). Descriptive statistics

was used to express the baseline subject characteristics. Univariate comparisons between groups of continuous variables were performed using the Student's t-test for unrelated samples, and the Mann-Whitney U-test if data were not distributed in normal fashion. Qualitative variables were expressed as percentages. Significance level was set at 0.05. All calculations were performed using the SPSS statistical software package.

## Results

### Study population

Among 29 patients; 19 were categorized as “negative” and 10 as “positive”. Baseline characteristics are displayed in Table 1. Age was higher in patients with positive EST vs. negative EST . There were no significant differences in anthropometry (height, weight, waist circumference and hip circumference) and body composition (fat mass and fat free mass) between the negative and the positive groups. History of smoking and alcohol consumption was higher in patients with positive EST vs. negative EST .

Table 1. Baseline characteristics of subjects

Variables	negative (n=19)	positive (n=10)	P value
Age (yrs)	51.58±8.22	59.30±4.23	0.000*
Sex (M/F)	16/3	8/2	0.678
Height (cm)	161.47±7.73	162.00±5.87	0.520
Body mass (kg)	63.71±10.81	65.51±15.62	0.432
BMI	25.03±3.75	23.30±3.39	0.641
%body fat	24.04±4.08	23.82±4.29	0.768
FM (kg)	15.42±4.09	15.56±3.89	0.151
FFM (kg)	48.28±7.97	49.95±12.79	0.553
W/H ratio	0.88±0.06	0.88±0.08	0.655
History			
DM % (n)	10.53%(2)	10.00%(1)	0.343
HT % (n)	26.32%(5)	30.00%(3)	0.168
Heart disease % (n)	15.79%(3)	10.00%(1)	0.168

Smoking, amount / day (n)	1.8± 0.84(5)	3±1.41(2)	0.037*
Alcohol consumption , frequency/wk (n)	1.5±0.52(6)	2.5±.71(2)	0.037*
Exercise activity, (>3 times/wk), % (n)	47.37%(9)	50.00%(5)	0.037*

Values are expressed as means ± SD; n=29.

\*Significantly different from control group (P<0.05)

M, male; F, female; BMI, body mass index; %BF, percentage of body fat; FM, fat mass; FFM, fat free mass; W, waist; H, hip; DM, diabetes mellitus; HT, hypertension

### Exercise test

Results of the exercise test were shown in Table2. Peak heart rate and target heart rate were lower in positive than negative group (P=0.028; P=0.001 respectively). In contrast, the resting heart rate, mean arterial pressure, systolic blood pressure and metabolic equivalents were similar in negative and positive.

Table 2 Results of the exercise test of all subjects

Variables	negative (n=19)	positive (n=10)	P value
Resting HR (/min)	77.07±12.11	77.30±10.08	0.698
Peak HR (/min)	140.96±19.28	129±19.79	0.028*
Resting MAP (mm Hg)	90.17±9.86	91.53±15.89	0.544
Peak MAP (mm Hg)	103.83±15.23	110.30±12.42	0.777
Target HR (/min)	137.68±13.36	136.80±4.01	0.001*
Resting SBP (mm Hg)	125.00±21.72	129.80±19.46	0.346
Peak SBP (mm Hg)	162.96±38.86	164.70±17.80	0.927
MET (METs)	8.14±2.85	8.03±2.71	0.322

Values are expressed as means ± SD; n=29.

\*Significantly different from control group (P<0.05)

HR, heart rate; SBP, Systolic blood pressure; MAP, mean arterial blood pressure; METs, metabolic equivalents

### Aerobic capacity

The aerobic capacity of all subject were shown in Table 3. Subjects with positive EST had lower  $\dot{V}O_2\text{max}$  than those with negative EST (17.94 ± 9.76 and 32.81 ± 16.24 ml/kg/min). There was no significant gender difference in  $\dot{V}O_2\text{max}$  between the negative and positive groups. However, in the negative

group women tended to have lower  $\dot{V}O_{2max}$  than men ( $13.51 \pm 8.47$  and  $36.43 \pm 14.78$  ml/kg/min;  $P=0.078$ ).

Table 3 Aerobic capacity of all subjects

$\dot{V}O_{2max}$ (ml/kg/min)	negative (n=19)	positive (n=10)	P value
All subjects (29)	32.81 ± 16.24	17.94 ± 9.76	0.920
men (24)	36.43 ± 14.78	18.88 ± 10.82	0.390
women (5)	13.51 ± 8.47	14.16 ± 1.75	0.964

Values are expressed as means ± SD; n=29.

## Discussion

The results of this study showed that suspected CAD patients with both positive and negative results had lower aerobic capacity than healthy subjects. Sports authority of Thailand reported that  $\dot{V}O_{2max}$  value in healthy subjects. ( $>33.9$  ml/kg/min (men) ;  $> 30.9$  ml/kg/min (women)).

This may imply that individuals with negative result of the exercise stress test still have a high risk of cardiovascular disease when compare with healthy individuals. Moreover, high resting heart rate in these subjects ( $\geq 70$ /min) may confirm the CVD risk because heart rate is a modifiable risk factor for cardiovascular disease. Previous studies suggested that lowering resting heart rate has a beneficial impact on cardiovascular events, even in high-risk patients, and in addition to those procured by a high level of evidence-based therapy (Cucherat, 2007; Fox et al., 2008).

This study demonstrated that in the negative group, women tended to have lower  $\dot{V}O_{2max}$  than men. This may imply that women may be more prone to have CVD than men. A possible reason is that female's coronary arteries are smaller and more easily

occluded (Kitzman and Edwards, 1990). This could result in an inability to adapt their coronary flow adequately to higher metabolic demands during maximal exercise.

Of interest, these methodologic problems may explain the wide range of sensitivity (35 to 88 percent) and specificity (41 to 100 percent) found for exercise testing, because the variations could not be attributed to the usual explanations: definition of anatomic abnormality, stress test technique or definition of an abnormal test. Determining the true value of exercise testing requires methodologic improvements in patient selection, data collection and data analysis (Philbrick et al., 1980).

## Conclusions

Thai patients with suspected CAD patients had lower  $\dot{V}O_{2max}$  value than healthy individuals. This could be attributed to an inability to respond their coronary flow adequately to higher metabolic demands during maximal exercise.

## Acknowledgements

This study was supported by The Khon Kaen University's Graduate Research Fund Academic Year 2009. We appreciate all doctors, nurses and physical therapists in Queen Sirikit Heart Center of the Northeast Thailand for their medical assistance. We would like to thank Mr.Piyapong Prasetsri and Miss Yupaporn Kanpette for their kind laboratory assistance. We also would like to thank all subjects for their enthusiastic participation.

## References

1. Cucherat M. 2007. "Quantitative relationship between resting heart rate reduction and magnitude of clinical benefits in post-myocardial infarction: a meta-regression of randomized clinical trials." *Eur Heart J*: 28: 3012-9.
2. Davis RB, Boyd DG, McKinney ME, Jones CC. 1990. "Effects of exercise and exercise conditioning on blood platelet function." *Med Sci Sports Exerc*: 22: 49-53.
3. Detrano R, Froelicher VF. 1988. "Exercise testing: uses and limitations considering recent studies." *Prog Cardiovasc Dis*: 31: 173-204.
4. Dorn J, Naughton J, Imamura D, Trevisan M. 1999. "Results of a multicenter randomized clinical trial of exercise and long-term survival in myocardial infarction patients: the National Exercise and Heart Disease Project (NEHDP)." *Circulation*: 100: 1764-9.
5. Fox K, Ford I, Steg PG, Tendera M, Ferrari R. 2008. "Ivabradine for patients with stable coronary artery disease and left-ventricular systolic dysfunction (BEAUTIFUL): a randomised, double-blind, placebo-controlled trial." *Lancet*: 372: 807-16.
6. Kitzman DW, Edwards WD. 1990. "Age-related changes in the anatomy of the normal human heart." *J Gerontol*: 45: M33-9.
7. S, Beker A, Sommo L, et al. 2008. "High-frequency QRS electrocardiogram analysis during exercise stress testing for detecting ischemia." *Int J Cardiol*: 124: 198-203.
8. Philbrick JT, Horwitz RI, Feinstein AR. 1980. "Methodologic problems of exercise testing for coronary artery disease: groups, analysis and bias." *Am J Cardiol*: 46: 807-12.
9. Reddy KS. 1993. "Cardiovascular diseases in India." *World Health Stat Q*: 46: 101-7.
10. Vanhees L, Fagard R, Thijs L, Amery A. 1995. "Prognostic value of training-induced change in peak exercise capacity in patients with myocardial infarcts and patients with coronary bypass surgery." *Am J Cardiol*: 76: 1014-9.