

การประเมินสมรรถภาพหัวใจ และหลอดเลือดขณะออกกำลังกายที่เพิ่มความหนักมากขึ้นในคนไทยที่มีสุขภาพดี

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Evaluation of Cardiovascular Performance During Incremental Exercise Testing in Healthy Thais

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หลักการและวัตถุประสงค์: การประเมินสมรรถภาพหัวใจและปอด (Cardiopulmonary exercise testing; CPET) ได้มีการนำมาใช้ในการประเมินทางคลินิกในผู้ป่วยโรคที่มีความเสี่ยงสูงต่อโรคทางระบบหายใจ และระบบหัวใจและหลอดเลือด แต่พบว่ยังไม่มีการศึกษาค่ามาตรฐานของการตอบสนองของหัวใจและหลอดเลือดในคนไทย การศึกษานี้จึงมีวัตถุประสงค์เพื่อทำการประเมินการตอบสนองของหัวใจและหลอดเลือดขณะออกกำลังกายสูงสุดในกลุ่มประชากรอาสาสมัครคนไทยสุขภาพดี 30 ราย (เพศชาย 15 ราย และหญิง 15 ราย) ที่มีอายุระหว่าง 20-40 ปี

วิธีการศึกษา: อาสาสมัครสุขภาพดีได้รับการทดสอบ CPET โดยมีการปรับเพิ่มความหนักของการออกกำลังกายจนกระทั่งอาสาสมัครไม่สามารถทำการทดสอบต่อไปได้

ผลการศึกษา: ขณะออกกำลังกายสูงสุดในอาสาสมัครเพศชายมี oxygen pulse ($\dot{V}O_2/HR$), cardiac output (\dot{Q}_t) และ stroke volume (SV) สูงกว่าในเพศหญิงคิดเป็นร้อยละ 65.9, 71.7 และ 66.6 ($p < 0.001$) ตามลำดับในอีกด้านหนึ่ง heart rate reserve (HRR) และ heart rate (HR) ไม่มีความแตกต่างระหว่าง เพศหญิง และเพศชาย นอกจากนี้พบว่า HR, $\dot{V}O_2/HR$ และ \dot{Q}_t เพิ่มขึ้น เมื่อ work rate (WR) เพิ่มขึ้น ทั้งในเพศชายและหญิง (เพศหญิง $r = 0.84$, $r = 0.62$ และ $r = 0.79$, $p < 0.001$ และเพศชาย $r = 0.91$, $r = 0.83$ และ $r = 0.81$, $p < 0.001$) อย่างไรก็ตามที่ WR ต่ำกว่า 150 วัตต์ เพศหญิงมี SV และ $\dot{V}O_2/HR$ ต่ำกว่าชาย

Background and Objective: Cardiopulmonary exercise testing (CPET) has been a promising utility for performance, and physiological and valuable clinical assessment in patients at high risk for respiratory and cardiovascular diseases. Reference values for cardiovascular responses to the CPET in healthy Thais have never been studied. This study aimed to evaluate cardiovascular responses at maximal exercise in 30 healthy Thai subjects (15 males, 15 females); aged between 20-40 years.

Materials and Methods: Healthy Thai volunteers underwent the CPET by using a treadmill ramp protocol and symptom limited.

Results: Oxygen pulse ($\dot{V}O_2/HR$), cardiac output (\dot{Q}_t) and stroke volume (SV) at maximal exercise in males were significantly higher than in females by 65.9%, 71.7% and 66.6% ($p < 0.001$), respectively. On the other hand, heart rate reserve (HRR) and heart rate (HR) at maximal exercise were not significantly different between genders. Moreover, HR, ($\dot{V}O_2/HR$) and \dot{Q}_t increased proportionally with increasing work rate (WR) in both genders (female; $r = 0.84$, $r = 0.62$ and $r = 0.79$, $p < 0.001$ & male; $r = 0.91$, $r = 0.83$ and $r = 0.81$, $p < 0.001$). SV and HR responses to WR below 150 watts were relatively lower in females than in males. The HR response was higher in females than males.

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สรุป: การศึกษานี้แสดงให้เห็นว่าการตอบสนองของหัวใจและหลอดเลือดจะเพิ่มขึ้นเมื่อ WR เพิ่มขึ้น ซึ่งมีความแตกต่างระหว่างเพศ จึงมีความจำเป็นในการศึกษาในกลุ่มประชากรที่มากขึ้นเพื่อให้ได้ค่าอ้างอิงมาตรฐานสำหรับคนไทย

คำสำคัญ: การทดสอบสมรรถภาพหัวใจและปอด, การตอบสนองของหัวใจและหลอดเลือด

Conclusions: The present study suggests that although cardiovascular responses increase with increased WR, they are different between genders. It is necessary to conduct a study in a large population so that reference values can be established for Thais.

Keywords: Cardiopulmonary exercise testing, cardiovascular responses

ศรีนครินทร์เวชสาร 2558; 30 (1): 2-8. ♦ Srinagarind Med J 2015; 30 (1): 2-8.

Introduction

Cardiopulmonary exercise testing (CPET) has been established as an important tool to evaluate patients with suspected and confirmed cardiovascular diseases¹. It has been proposed to be the gold standard technique for exploring putative mechanisms underlying exercise intolerance in patients with heart failure², screening out patients with exercise training contraindications, prescribing safe and efficacious exercise training and determining exercise capacity³. The cardiovascular responses to exercise, common physiological stress, can elicit cardiovascular abnormalities that are not present at rest, and it can be used to determine the adequacy of cardiac function⁴. Increases in heart rate (HR) with progressive exercise are initially mediated by early parasympathetic withdrawal and subsequent sympathetic activation^{5,6}. In healthy subjects, the heart rate reserve (HRR), the difference between the predicted maximal HR and the maximum heart rate (HRmax) achieved during exercise, is little or no HRR or less than 15 /min⁷ or 15 %.

Interestingly, there is an effectively linear increase in HR as a function of oxygen uptake ($\dot{V}O_2$) during ramp incremental exercise though departs from linearity might occur at higher exercise intensities⁸. This slope and position of the HR- $\dot{V}O_2$ relationship is a function of stroke volume (SV): the higher the SV the lower the HR and, typically, its rate of change. HR at a given $\dot{V}O_2$ is higher than normal in patients with lung disease, deconditioning, ventilatory limitation to exercise and reduced oxygen delivery or abnormal utilization⁷.

According to the Fick principle, SV would lead to a steeper HR response, defined as (peak HR - resting HR)/(peak $\dot{V}O_2$ - resting $\dot{V}O_2$) ($\Delta HR/\Delta \dot{V}O_2$ slope). Consequently, cardiac dysfunction, decreased arterial O_2 content can potentially increase $\Delta HR/\Delta \dot{V}O_2$ ⁷. Oxygen pulse ($\dot{V}O_2/HR$) reflects the amount of oxygen extracted per heart beat which is often considered a surrogate for stroke volume⁹. A low O_2 pulse therefore may reflect deconditioning, cardiovascular disease, and early exercise limitation due to ventilatory constraint or symptoms. Moreover, O_2 pulse has been demonstrated to be a powerful predictor of mortality in patients with cardiovascular disease^{10,11} and associated with exercise induced ischemia⁹. As exercise intensity increases, reflex control of cardiac output causes some characteristic changes in blood pressure (BP)¹². An abnormal rise with exercise in the face of normal resting BP is also indicative of abnormal blood pressure control. If BP does not increase with exercise, or in fact declines, a cardiac limitation or abnormality of sympathetic control of BP is suspected¹³.

Thus, it is obviously necessary to examine cardiovascular responses in healthy subjects and create reference values for cardiovascular responses to the CPET in Thais which have never been studied.

Objectives of the study

This study aimed to evaluate the ability of the cardiovascular system to perform its function during exercise in Thai males and females.

Materials and Methods

Study designs and Population

The study was analytical and descriptive approved by the Human Research Ethics Committee, KhonKaen University (HE561451) and informed consent was obtained from each participant. Thirty healthy subjects of both genders (15 males and 15 females) aged between 20-40 years were recruited. Number of subjects was calculated according to a previous study done by Fairbairn et al.¹⁴ All subjects completed a confidential health-screening questionnaire. They were healthy with BMI of 18.5–24.9 kg/m² (according to the WHO guidelines) and had no history of regular alcohol drinking or smoking. Those having history of cardiovascular (i.e. coronary heart disease, arrhythmia and chronic heart failure), neuromuscular, arthritic, pulmonary, severe microvascular, diabetes mellitus, hypertension or other debilitating diseases were not included in this study.

Experimental Protocols

Participants were asked to have 4 visits to our Laboratory Unit. On the first 3 visits, physical examination and the measurement of anthropometry and familiarization with a treadmill were obtained. On visit four, the CPET was performed on a motorized treadmill with an incremental exercise test method¹⁵. This included 2 minutes of resting, 3 minutes of warm-up, incremental phase until exhaustion or symptom limited maximal exercise tolerable WR using Stationary CPET (Quark CPET, Cosmed, Italy). The exercise work rate was increased in speed rate and inclination every 1 minute until exhaustion and finally 3 minutes of recovery phase was done.

Statistical Analyses

Data were expressed as mean \pm SD. An unpaired t-test was used to compare differences in characteristics and all parameters between males and females. The two-sample Wilcoxon rank-sum (Mann-Whitney) test was used when data deviate from normality. The STATA 10 Statistical software was used to perform the statistical analysis. A value of $p < 0.05$ was taken to be the threshold of statistical significance.

Results

There were no significant differences in age (27 ± 5 vs. 27 ± 3 yrs), BMI (21.3 ± 2 vs. 20.9 ± 2 kg/m²), SBP (119.6 ± 13.8 vs. 113.3 ± 17.0 mm Hg), DBP (76.3 ± 10.2 vs. 74.0 ± 8 mm Hg), HR (74 ± 10 vs. 80 ± 8 /min) and BP (91 ± 10 vs. 84 ± 8) between males and females. Moreover, males were taller (174.0 ± 10.0 vs. 159.2 ± 6.6) and heavier (64.6 ± 8.0 vs. 53.0 ± 5.5) than females ($p < 0.001$). The cardiovascular response parameters from CPET are demonstrated in Table 1 and Fig. 1. We observed linear relationships between HR, \dot{Q}_t and $\dot{V}O_2$ /HR but not SV with work rates in both genders (females; $r = 0.84$, $r = 0.62$ and $r = 0.79$, $p < 0.001$) and males; $r = 0.91$, $r = 0.83$ and $r = 0.81$, $p < 0.001$) (Fig. 1B & 1C, 1F & 1G, 1D & 1E). At a given $\dot{V}O_2$ at WR below 2,000 ml/min or WR below 150 watts, we found that HR was relatively higher in females compared to those of males (Fig. 1A). In contrast, SV, \dot{Q}_t and $\dot{V}O_2$ /HR responses with increasing WR were greater in males than those of females (Fig. 1H & 1I).

In addition, SV, \dot{Q}_t and $\dot{V}O_2$ /HR, but not HR or HRR, at maximal exercise in males were significantly higher than in females by 71.7% (17.0 vs. 9.9 L/min) and 66.6% (93.3 vs. 56.0 ml/beat), 65.9% (15.1 vs. 9.1 ml/beat), ($p < 0.001$), respectively. Additionally, females had higher HR response, e.g. $\Delta HR / \Delta \dot{V}O_2$ slope ($p < 0.001$) (Table 1).

Discussion

The main findings of this study were such that the cardiovascular responses increase with increased work rate and $\dot{V}O_2$ which were different between genders. Moreover, $\dot{V}O_2$ /HR, \dot{Q}_t and SV at maximal exercise in males were significantly higher than in females. These results are in agreement with the data obtained by Ogawa et al.¹⁶ showing SV and \dot{Q}_t at maximum exercise in males higher than in females. Therefore, in maximal exercise, the sex difference in \dot{Q}_t and SV may be due to the fact that females have greater body fat than in males^{16, 17}. Moreover, sex and sex hormones may influence cardiac function^{18, 19}.

Table 1 Cardiovascular responses to incremental exercise testing

Measurement		Males (n=15)		Females (n=15)	
		Rest	Max ex	Rest	Max ex
HR, /min	Mean ± SD	82 ± 11	182 ± 10	86 ± 8	179 ± 16
	Min, Max	65, 98	153, 196	76, 115	140, 200
	Median	83.4	183.4	94.1	184.9
HRR, %	Mean ± SD	-	5.6 ± 4.9	-	6.0 ± 7.8
	Min, Max	-	-1, 21.1	-	-2, 35
	Median	-	5.8	-	6.0
$\dot{V}O_2$, ml/min	Mean ± SD	357 ± 59	2745 ± 392	295 ± 59*	1611 ± 259***
	Min, Max	272, 453	2007, 3271	197, 350	1262, 2106
	Median	365.8	2846.9	279.6	1581.2
$\dot{V}O_2$ /HR, ml/beat	Mean ± SD	4.5 ± 0.7	15.1 ± 1.8	3.2 ± 0.8*	9.1 ± 1.6***
	Min, Max	3, 6	12, 18	2, 5	7, 13
	Median	4.4	15.6	3.3	8.8
$\Delta HR/\Delta \dot{V}O_2$ slope' /ml	Mean ± SD	-	0.042 ± 0.006	-	0.071 ± 0.009***
	Min, Max	-	0.032, 0.050	-	0.034, 0.061
	Median	-	0.042	-	0.044
\dot{Q}_t , L/min	Mean ± SD	5.2 ± 0.8	17.0 ± 2.4	3.8 ± 0.9	9.9 ± 1.6***
	Min, Max	4, 6	12, 21	3, 6	8, 13
	Median	5.2	17.5	3.7	9.8
SV, ml/beat	Mean ± SD	61 ± 7.8	93.3 ± 10.8	41.8 ± 7.4*	56.0 ± 9.9***
	Min, Max	45, 78	71, 109	31, 56	45, 81
	Median	62.9	95.6	42.7	54.9
SBP, mm Hg	Mean ± SD	119.6 ± 13.8	187.3 ± 17.0	116.1 ± 15.8	nm
	Min, Max	95, 184	149, 216	92, 139	nm
	Median	131.7	191.0	112.0	nm
DBP, mm Hg	Mean ± SD	76.3 ± 10.2	81.6 ± 17.4	75.6 ± 8.6	nm
	Min, Max	62, 99	56, 121	62, 86	nm
	Median	74.8	80.0	78.0	nm

HR, heart rate; HRR, heart rate reserve; $\dot{V}O_2$, oxygen uptake; $\dot{V}O_2$ /HR, oxygen pulse; ΔHR , HRmax ex - HR rest; $\Delta \dot{V}O_2$, $\dot{V}O_2$ max ex - $\dot{V}O_2$ rest; \dot{Q}_t , cardiac output; SV, stroke volume; SBP, systolic blood pressure; DBP, diastolic blood pressure; max ex, maximal exercise; nm, not measured. Data are expressed as mean ± SD, minimum, maximum and median. *p<0.05, **p<0.001 males vs. females

Moreover, cardiac output is the best index of cardiac function during exercise. In healthy subjects, \dot{Q}_t is a linear function of $\dot{V}O_2$. That \dot{Q}_t increases with exercise is to support the increasing metabolic demands of the tissues. Increases in cardiac output are initially accomplished by increases in stroke volume and HR and then at high intensity exercise almost exclusively by increases in HR¹³.

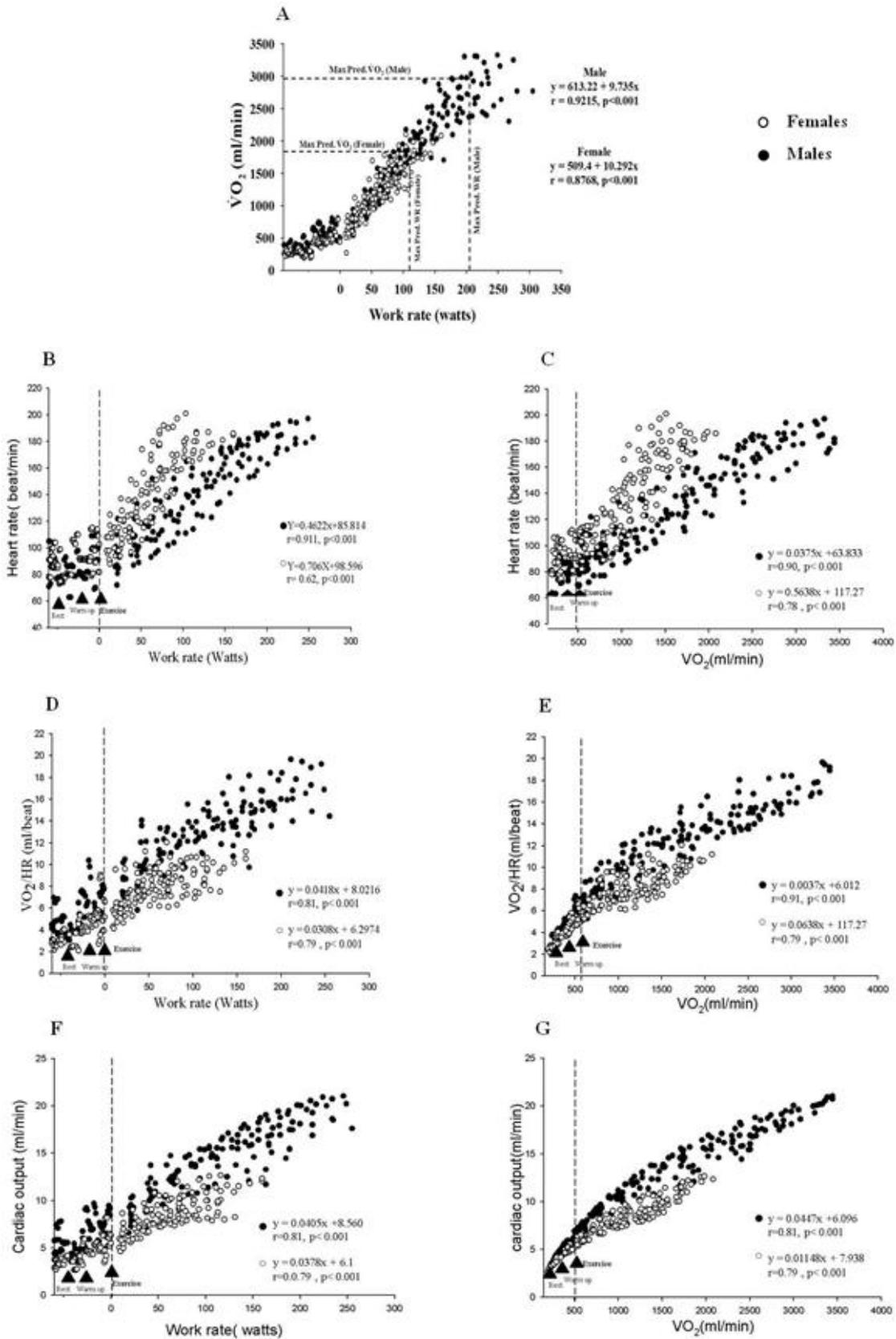
In addition, HRR and HR at maximal exercise were not significantly different between genders. Interestingly, the HR response to increasing oxygen uptake was greater in females compared to males.

Conclusions

In conclusion, we suggest that the cardiovascular response to increased WR is different between genders, i.e. it was greater in males than in females. A larger sample size is required in order to obtain normal values for different variables for the CPET.

Acknowledgements

This study was supported by grants from the Graduate School of KhonKaen University (Grant No. HE56211107), the Invitation Research Grant (I56301),



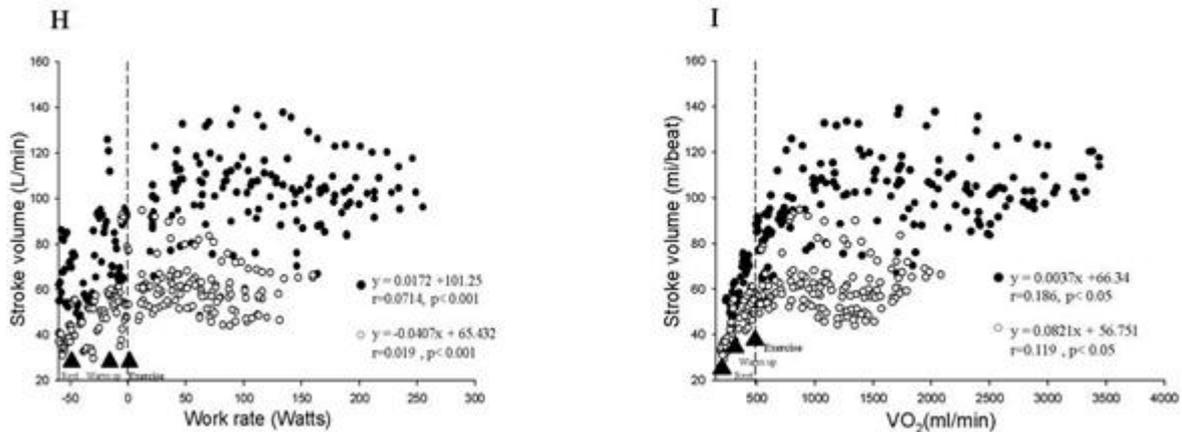


Figure 1 Cardiovascular responses to incremental exercise testing. A: Relationship between oxygen uptake ($\dot{V}O_2$) and work rate (WR); B, D, F, H: Relationships between heart rate (HR), oxygen pulse ($\dot{V}O_2/HR$), cardiac output (\dot{Q}_t), stroke volume (SV) and WR; C, E, G, I: Relationships between HR, $\dot{V}O_2/HR$, \dot{Q}_t , SV and $\dot{V}O_2$.

Faculty of Medicine, KhonKaen University. We thank Mr.Puttapol Chanchalad for his excellent technical support.

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