Association between Systolic Blood Pressure Recovery Ratio after Treadmill Exercise Stress Testing and Cardio-Metabolic Risk Factors among Menopausal Status

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Background: *Exercise Stress Testing (EST) is traditionally analyzed in prediction of the coronary artery disease (CAD). Systolic blood pressure (SBP) during recovery was related directly to risk of cardiovascular death after adjustment for age and other clinical and exercise test variables.*
Objective: *Determine the relationship between systolic blood pressure recovery ratio (SBPRR) and anthropometric and cardio-metabolic factors from laboratory among menopausal status.*
Material and Method: *The cross-sectional study was conducted between September 2015 and February 2016. Seventy-six perimenopausal and menopausal participants were recruited from Suranaree University of Technology Hospital in the study. Anthropometric indices, biochemical laboratory, and clinical parameters were measured. All participants underwent exercise as per Bruce protocol EST. The SBPRR was assessed by calculated SBP at 3 min/SBP at peak ratio.*
Results: *The 76 perimenopausal and menopausal participants had a mean age of 50.26±8.36 years. SBPRR were negatively correlated with HDL-C (r = -0.29, p = 0.02) and positively correlated with fasting blood sugar (FBS) (r = 0.28, p = 0.01). There was no difference among groups of SBPRR in perimenopausal/menopausal women except waist-hip ratio (p = 0.02) and HDL-C (p = 0.02). EST parameter peak rate pressure product, heart rate recovery at 1-minute, and functional capacity were not discriminating between SBPRR groups.*
Conclusion: *SBPRR measurement is non-invasive testing. The value of SBPRR correlate, negatively with HDL-C, positively with FBS and the traditional cardio-metabolic risk factors in perimenopausal/menopausal women.*

Keywords: *Systolic blood pressure recovery ratio, Exercise treadmill testing, Cardio-metabolic risk factor, Menopausal status*

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Exercise stress testing (EST) is a well-accepted examination for patients with suspected coronary artery disease (CAD), and exercise induced ST-segment deviation is commonly used for CAD detection. Disease prevention is predicated on the identification of risk factors in asymptomatic individuals. Screening tools that include additional biomarkers may yield better predictive value for hypertension, impaired glucose tolerance, and other cardiovascular disease (CVD) risk factors and help identify those individuals who may benefit from more in-depth assessment. In previous studies, the prognostic importance of ST-segment depression in exercise electrocardiogram (ECG), delayed slowing of heart rate (HR), and ventricular arrhythmias that appear during recovery are shown to be at least as valuable as the abnormal prognostic variables during exercise[1-3].

However, recent evidence shows that systolic blood pressure (SBP) changes during and after exercise were associated with CAD severity, risk of acute myocardial infarction, stroke, new onset hypertension, and cardiovascular mortality[4,5]. Although HR and blood pressure during recovery may reflect cardiovascular reactivity after exercise, SBP after exercise has not been documented previously in perimenopausal/menopausal women with change in

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hormonal that may affect hemodynamic response after exercise testing. Endothelial function plays a key role in determining the clinical manifestations of established atherosclerotic lesions and has shown to be associated with suppressed sympathetic tone, especially in prediabetic participants[6]. Abnormal heart rate recovery (HRR) and SBP response during recovery have been found to have diagnostic role for detecting cardiovascular risk.

The aim of this study was to investigate whether SBP changes after exercise predict cardio-metabolic risks in perimenopausal/menopausal women.

Material and Method

Study population

This is a cross-sectional study involving 76 perimenopausal and menopausal subjects recruited from non-invasive cardiovascular clinic and menopause clinic, aged from 40 to 70 years who underwent EST in Suranaree University of Technology Hospital between September 2015 and February 2016. Recommendations for clinical exercise testing laboratories from American Heart Association were followed. Exclusion criteria were myocardial infarction, unstable angina, uncontrolled hypertension, heart failure, moderate or severe aortic or mitral valve stenosis, percutaneous coronary intervention within three months, previous pacemaker implantation, or coronary artery bypass grafting.

The study has been reviewed and approved by the Ethics Committee for Research Involving Human Subjects, Suranaree University of Technology. Informed consent was obtained from both groups and ethical clearance was obtained from the relevant authority.

Study protocol

This is a cross-sectional study, carried out between September 2015 and February 2016, in perimenopausal and menopausal women in Suranaree University of Technology Hospital, Thailand. After signing the informed consent form, 76 women voluntarily participated in the investigation. The sample was divided into two groups according to SBPRR: <0.9 and ≥ 0.9. The inclusion criteria were age 40 to 70 years, signing the consent form, and submitted to all laboratory and anthropometric tests.

Anthropometry

The body mass measurement was taken with the individual wearing light clothes and bare feet, using digital scales with capacity of 150 kilograms (kg), and 100 gram divisions. Height was measured by a wall stadiometer with capacity of 2,200 millimeters (mm) and 1 mm divisions. Waist circumference (WC) was measured with the participant standing up, with minimal clothing as possible, midway between the last floating rib and the iliac crest.

Laboratory measurement

Baseline serum specimens (stored at the central repository) were measured for levels of glucose and lipids. Fasting blood sugar (FBS), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured by the central laboratories of Suranaree University of Technology Hospital. Diabetes, defined as self-reported diabetes treatment or a fasting glucose level 126 mg/dL, was measured.

Exercise stress test (EST)

All exercise tests were done on a motorized treadmill using the Bruce protocol[7]. Exercise testing procedures outlined by the American Heart Association were followed for all assessments[8]. All patients were continuously monitored with 12-lead ECG, and hemodynamic measurements were made during each stage of the protocol. Blood pressure was measured with an automated sphygmomanometer with auditory confirmation.

The following exercise test termination criteria were used: onset of severe typical angina, arrhythmias (frequent premature ventricular contractions; 3 or more beats of non-sustained ventricular tachycardia; new-onset atrial fibrillation, atrial flutter, or atrial tachycardia with rapid response; second-degree or third-degree heart block), hypotension, bradycardia or decrease in HR with same or greater workload, dyspnea, intermittent claudication, central nervous system symptoms, marked hypertension, more than 2 mm of horizontal or down-sloping ST segment depression or 1 mm or more of ST-segment elevation, and participant's request to stop or inability to keep up with the treadmill.

Definition of terms

Menopausal status

Menopausal status was referred to perimenopausal and menopausal women. Participants were also asked about their menstrual bleeding patterns in the 12 months prior to recruitment. Perimenopausal women are defined to women age ≥ 40 years around menopause and had menstrual periods irregularity in

the past 12 months. Menopausal women are defined to women those with no menstrual periods within the last 12 months.

Functional capacity

Participants who exercise testing that calculate via program of protocol. American Heart Association is defined the normal exercise capacity that ≥5 Metabolic equivalent task (METS) in women.

Systolic blood pressure recovery ratio (SBPRR)

The decline in SBP during recovery was assessed by calculating the ratio of SBP at 3 minutes of recovery to peak exercise.

Statistical analysis

All data are expressed as mean ± standard deviation (SD). Based on SBPRR values, the sample was divided into <0.9 and ≥0.9 to compare with anthropometric data, blood pressure and biochemical tests by student t-test. In addition, the correlation between SBPRR and cardiovascular risk factors was evaluated by Pearson correlation. The significance level for all variables studied was $p \leq 0.05$.

Results

Seventy-six perimenopausal/menopausal women who completed the EST protocol and reached the maximal exercise capacity were recruited for the study. The most common reasons for terminating exercise were fatigue. None of the participants had signs of myocardial infarction on the resting ECG or significant myocardial ischemia during stress exercise. None of the subjects reported experiencing chest pain during the EST. Participant's characteristics include mean age (50.26±8.36 years) and mean value of SBPRR (0.97±0.17). The patient population was divided into two groups according to the ratio of SBP at three minutes of recovery compared with SBP at peak exercise: <0.90 (n = 26) and ≥0.90 (n = 50). Participants with a recovery ratio ≥0.90 had higher waist-hip ratio (WHR) and lower HDL-C. Exercise characteristics of participants with SBPRR ≥0.90 revealed nominally a lower rate pressure product and functional exercise capacity (Table 1). There was no difference in lipid parameters among different results of SBPRR in perimenopausal/menopausal women.

Table 2 shown the results of study were positively correlated with FBS ($p = 0.01$) and negatively correlated with HDL-C ($p = 0.01$).

Discussion

The objective of the present study was to find the relationship between SBP after recovery and cardiovascular risk factors in perimenopausal/menopausal women. SBP changes during exercise and recovery period are analogous with blood pressure responsiveness to daily physical stress conditions. An exercise induced rise in SBP has been found to be a predictor of future hypertension, stroke, and CVD mortality in healthy populations[9]. This low risk population has no diabetes mellitus or poor control BP. Abnormal SBP recovery after exercise was not independently predictive of mortality after correcting for differences in baseline and exercise characteristics[10]. A delayed recovery of SBP has been noted by others to be associated with angiographic severity of CAD[11-13], the presence of perfusion abnormalities on thalium-201 scintigraphy[14], and the presence of CAD in patients with left ventricular hypertrophy and chronic heart failure[15,16]. Patients with paradoxical SBP increase after exercise and abnormally low SBP during EST are an important and significant predictor of CVD mortality[17-19]. The mechanism of delayed decrease in SBP after exercise may be a combination of various factors. Sympathetic drive could be responsible for SBP augmentation and delayed recovery in general. Increase in exercise SBP is achieved by cardiac output increase in healthy and delayed SBP recovery, mediated through vasoconstriction and increased level of circulating catecholamines in unhealthy participants[20]. In patients of CAD, during exercise, there is left ventricular asynergy, increase catecholamine release, and peripheral vasoconstriction compensatory to ischemia induced left ventricular systolic dysfunction. This may explain why patients with severe coronary disease have higher blood pressure during early recovery than those without disease.

The study of SBPRR has positively correlated with FBS and negatively correlated with HDL-C. The study has normal function capacity and may affect to SBP during and post exercise. The elevated SBP after exercise may reflect upon a person's physical fitness, aerobic capacity, over activity of sympathetic nervous system and attenuated vagal reactivation.

In asymptomatic perimenopausal/menopausal women, cardiac structure and function may remain normal at rest, but moderate to severe exercise may provoke cardiovascular abnormalities. Abnormal SBP response during recovery which correlated with FBS and HDL-C in the study may be used to diagnose role

Table 1. Anthropometric parameters, lipid profiles and EST difference between SBPRR groups

Cardio-metabolic risk factors	SBPRR		*p*-value
	<0.9, n = 26	≥0.9, n = 50	
Age (years)	52.23±8.51	49.24±8.18	0.14
Systolic blood pressure (mmHg)	122.09±14.01	122.02±13.08	0.96
Diastolic blood pressure (mmHg)	68.00±9.51	69.34±8.10	0.52
Anthropometry			
Weight (kg)	60.15±10.25	60.56±12.56	0.89
Body mass index (kg/m^2)	19.28±3.14	19.39±3.82	0.90
Waist circumference (cm)	79.88±8.61	82.50±10.59	0.28
Waist to hip ratio	0.81±0.06	0.84±0.05	0.02*
Laboratory			
Fasting blood sugar (mg/dL)	91.42±14.11	95.30±22.03	0.42
Total cholesterol (mg/dL)	208.81±46.62	199.88±37.03	0.37
Triglyceride (mg/dL)	123.15±83.53	128.82±81.71	0.78
High-density lipoprotein cholesterol (mg/dL)	56.27±17.28	48.04±12.25	0.02*
Low-density lipoprotein cholesterol (mg/dL)	125.19±35.17	117.08±34.42	0.34
Exercise stress test			
Peak rate pressure product	26,673.77±4,425.92	25,891.10±4,988.87	0.50
Heart rate recovery at 1 min (bpm)	23.04±7.29	23.26±9.58	0.92
Functional capacity METS	8.54±2.23	8.38±2.18	0.90

Table 2. Correlation between cardio-metabolic risk factors and SBPRR values

Cardio-metabolic risk factors	SBPRR	
	r	*p*-value
Age	-0.17	0.15
Systolic blood pressure	0.14	0.22
Diastolic blood pressure	0.11	0.33
Weight	0.21	0.07
Body mass index	0.19	0.10
Waist circumference	0.21	0.07
Waist to hip ratio	0.20	0.09
Fasting blood sugar	0.28	0.01*
Total cholesterol	-0.02	0.88
Triglyceride	0.14	0.23
High-density lipoprotein cholesterol	-0.29	0.01*
Low-density lipoprotein cholesterol	0.04	0.74
Peak rate pressure product	0.09	0.46
Heart rate recovery at 1 min	-0.10	0.38
Heart rate recovery at 5 min	-0.09	0.46
Functional capacity METS	0.02	0.86
5 year survival	-0.50	0.67

* Correlation is significant at the 0.05 level

for detecting CVD in the future.

The present study has some limitations. This cross-sectional design study limited extension of its interpretation to the causality of associations.

Conclusion

SBPRR after exercise treadmill testing correlations with FBS and HDL-C metabolic abnormalities in menopausal status.

What is already known on this topic?

Although the present study is not the first report of SBPRR and cardiometabolic risk factors, previous studies cannot be directly applied to evaluate the menopausal status. This is specific subgroup of menopausal status both perimenopausal/menopausal women to defined cardiovascular risk in stress testing.

What this study adds?

The study using two measures of blood pressure at different points of recovery, rather than comparing a recovery to an exercise measure, better prediction. It is important to observe a correlation between SBP after exercise testing and cardio-metabolic risk factors, which is of great significance to primary prevention in reducing the incidence of CVD among perimenopausal/menopausal women in the future.

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Potential conflicts of interest

None.

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ความสัมพันธ์ระหว่างอัตราการกู้คืนความดันโลหิตหลังจากการเดินสายพานทดสอบสมรรถภาพหัวใจและปัจจัยเสี่ยงทางหัวใจและเมตาบอลิกในช่วงวัยหมดประจำเดือน

พรทิพย์ นิ่มขุนทด, ปัทมา ทองดี

ภูมิหลัง: *การเดินสายพานทดสอบสมรรถภาพหัวใจเป็นการชาดการณ์ของโรคหลอดเลือดหัวใจ ความดันโลหิต ขณะหัวใจบีบตัวระหว่างการกู้คืนหลังจากการเดินสายพานเกี่ยวข้องโดยตรงกับความเสี่ยงของโรคหัวใจและหลอดเลือดที่ทำให้เสียชีวิตหลังการปรับอายุและตัวแปรทางคลินิกและการทดสอบออกกำลังกายอื่น ๆ*

วัตถุประสงค์: *เพื่อทดสอบว่าความสัมพันธ์ระหว่างอัตราการกู้คืนความดันโลหิต ขณะหัวใจบีบตัวกับสัดส่วนร่างกายและปัจจัยเสี่ยงทางหัวใจและเมตาบอลิกจากการตรวจทางห้องปฏิบัติการในช่วงวัยหมดประจำเดือน*

วัสดุและวิธีการ: *การศึกษาภาคตัดขวางระหว่างเดือนกันยายน พ.ศ. 2558 ถึง เดือนกุมภาพันธ์ พ.ศ. 2559 สตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือนจำนวน 76 คน ได้รับคัดเลือกจากโรงพยาบาลมหาวิทยาลัยเทคโนโลยีสุรนารีในการศึกษานี้ ดัชนีการวัดสัดส่วน การตรวจชีวเคมีทางห้องปฏิบัติการและค่าทางคลินิกถูกวัด ผู้เข้าร่วมวิจัยทั้งหมดได้ทำทดสอบสมรรถภาพหัวใจโดยการเดินสายพาน อัตราการกู้คืนความดันโลหิตขณะหัวใจบีบตัวถูกคำนวณโดยค่าความดันโลหิตขณะหัวใจบีบตัวที่ 3 นาที หารด้วยค่าความดันโลหิตขณะหัวใจบีบตัวที่จุดสูงสุด*

ผลการศึกษา: *สตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือนทั้งหมด 76 คน ค่าเฉลี่ยอายุและส่วนเบี่ยงเบนมาตรฐาน 50.26±8.36 ปี อัตราการกู้คืนความดันโลหิตขณะหัวใจบีบตัวมีความสัมพันธ์เชิงลบกับค่าไขมันเอชดีแอล ($r = -0.29$, $p = 0.002$) และมีความสัมพันธ์เชิงบวกกับระดับน้ำตาลในเลือด ($r = 0.28$, $p = 0.01$) ในสตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือน ไม่พบความแตกต่างระหว่างกลุ่มของอัตราการกู้คืนความดันโลหิตขณะหัวใจบีบตัว ยกเว้นกลุ่มที่มีปัจจัยเสี่ยงทางหัวใจและเมตาโบลิก มีความแตกต่างของอัตราส่วนรอบเอวต่อรอบสะโพก ($p = 0.02$) และไขมันเอชดีแอล ($p = 0.02$) ตัวแปรการเดินสายพานทดสอบหัวใจ อัตราผลิตภัณฑ์ ความดันสูงสุด การกลับคืนอัตราการเต้นหัวใจที่ 1 นาที และความจุหน้าที่ไม่มีความแตกต่างกันระหว่างการกู้คืนความดันโลหิตขณะหัวใจบีบตัว*

สรุป: *การวัดอัตราการกู้คืนความดันโลหิตขณะหัวใจบีบตัวเป็นการทดสอบที่ไม่รุกล้ำเข้าไปในร่างกาย สามารถนำไปใช้สัมพันธ์กับไขมันเอชดีแอลและระดับน้ำตาลในเลือด ซึ่งเป็นปัจจัยเสี่ยงทางหัวใจและเมตาบอลิกในสตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือน*