Waist to Height Ratio for Predicting Hemodynamic Responses of Treadmill Exercise Stress Test in Perimenopausal/Menopausal Women

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Background: *Waist to height ratio (WHtR) is a simple screening measure for identifying overweight and obesity. It was recently proposed that the WHtR may represent a better parameter of cardiovascular risk, when compared to simple anthropometric parameters.*

Objective: *To investigate the hemodynamic responses of treadmill exercise stress test (EST) in perimenopausal and menopausal women with new central obesity parameter as WHtR.*

Material and Method: *This is a cross-sectional study of 76 perimenopausal/menopausal women. Main indicators included WHtR and hemodynamic parameters of treadmill EST. Statistical analysis was done by using Student's t-test and Pearson correlation. The p-value was taken as significant at 5% confidence level (p<0.05).*

Results: *Seventy-six perimenopausal/menopausal women, with average age of 50.26±8.36 years. Perimenopausal/menopausal women with lower WHtR values (<0.5) had different EST values in exercise duration time, functional capacity, rate pressure product (RPP), and heart rate recovery (HRR) after treadmill EST when compared to women with greater WHtR (≥0.5). No correlations of WHtR with 5-year survival or average annual mortality.*

Conclusion: *WHtR measurement is a simple and timesaving screening measure for central obesity that can be used to differential hemodynamic response in treadmill EST. WHtR ≥0.5 has abnormal hemodynamic response in HRR, which is associated with a strong adverse prognostic marker in premenopausal/menopausal population. Exercise capacity is lower in central obesity group.*

Keywords: *Waist to height ratio, Hemodynamic response, Treadmill exercise stress test, Perimenopausal women, Menopausal Women*

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Exercise stress testing (EST) is a fundamental non-invasive method to evaluate the severity of coronary artery disease (CAD) and to provide prognostic markers such as heart rate recovery (HRR), chronotropic index, and delayed systolic blood pressure response beyond ST-segment depression[1,2]. Incidence of CAD increases sharply after menopause in women. Perimenopausal and menopausal status are potential risk factors. Treadmill EST may be of clinical value when conducted in participants with estimated intermediate risk of developing CAD.

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Many hemodynamic response parameters were assessed to predict cardiovascular risk factor. Rate pressure product (RPP) is a major determinant of cardiac oxygen consumption. It is the product of heart rate (HR) with systolic blood pressure. It indicates that adequate stress was achieved and is an important indicator of ventricular function. It increases progressively with exercise. Peak rate pressure product is the rate pressure product at peak of exercise. Peak rate pressure product gives an accurate reflection of the myocardial oxygen demand and myocardial workload. The higher the peak rate pressure product, the more myocardial oxygen consumption. The ability to reach higher peak rate pressure product is associated with more adequate coronary perfusion. Thus, the low value of peak rate pressure product suggests significant compromise of coronary perfusion and decreased left ventricular function. HRR is mainly thought to be a function of parasympathetic or vagal reactivation, with a delayed decrease in HRR reflecting a reduction in vagal tone. Therefore, abnormal HRR after exercise is considered to be a measure of autonomic dysfunction. HR from peak exercise of less than 12 beats in 1 minute after cessation of the exercise test, while in the upright position, is most frequently used to define an abnormal HR recovery response.

This study aims to compare and associate hemodynamic response of EST in traditional anthropometric parameters of perimenopausal/ menopausal women, with different WHtR values.

Material and Method

Study population

This is a cross-sectional study involving 76 perimenopausal and menopausal participants who were recruited from cardiovascular clinic and menopause clinic, aged from 40 to 70 years without history of hormonal replacement therapy who underwent EST in Suranaree University of Technology Hospital between September 2015 and February 2016. For the assessment of guidelines for clinical exercise testing laboratories from American Heart Association, we selected sample by excluding participants with any of the following overt CVD and cardiovascular equivalence conditions: history of stroke including cerebral infarction or transient ischemic attack, myocardial infarction, heart failure, end stage renal disease, and inability to walk.

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, WHtR <0.5 and WHtR ≥0.5. The inclusion criteria were age 40 to 70 years, signed the consent form, and submitted to all laboratory and anthropometric tests. The exclusion criteria were having inability to walk and weakness of extremities. Informed consent was obtained from both groups and ethical clearance was obtained from the relevant authority.

Sample size was calculated from

$$n = \frac{Z_{1-\alpha/2}^{2}\, p\,(1-p)}{d^2}$$

In this formula, p is the prevalence of abnormal EST in perimenopausal and menopausal women of pilot study in Suranaree University of Technology Hospital (5%), d is the standard error (5%). The study has been reviewed and approved by the Ethics Committee for Research Involving Human Subjects, Suranaree University of Technology.

All patients fulfilling the inclusion criteria were recruited and underwent standard exercise test performed on a treadmill according to the modify Bruce protocol. The results of EST were interpreted by an experienced cardiologist as negative or positive result.

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.

The 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 were measured for levels of glucose and lipids. Serum 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.

Exercise stress test (EST)

All exercise tests were done on a motorized treadmill using the modify Bruce protocol. Exercise testing procedures outlined by the American Heart Association were followed for all assessments. All patients were continuously monitored with 12-lead electrocardiography (ECG), and hemodynamic measurements were made during each stage of the protocol. Blood pressure was measured with an automated sphygmomanometer with auditory confirmation and recorded during the third minute of each exercise staging when the heart rate was maximum and stabilized on the monitor of treadmill, immediately after cessation of exercise, at 1-minute, and at 5-minutes of recovery. Pulse rate was measured by examining brachial pulse at rest, immediately after cessation of exercise and after 5 minutes of recovery.

The following exercise test termination criteria were used, onset of severe typical angina, arrhythmias (frequent premature ventricular contractions, three 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

Perimenopausal women

Participants were also asked about their menstrual bleeding patterns in the 12 months prior to recruitment. Perimenopausal women are defined to women age $\geq$40 years around menopause and had menstrual periods irregularity in the past 12 months.

Menopausal women

Participants were also asked about their menstrual bleeding patterns in the 12 months prior to recruitment. Menopausal women are defined to those with no menstrual periods within the last 12 months.

Hemodynamic response abnormality measurements

Abnormal HRR (peak HR - HR at 1 min into recovery). Normal range $\leq$12 bpm.

Abnormal rate of chronotropic incompetence [(peak HR - rest HR)/(220-age- rest HR)]. Normal range <0.8.

Statistical analysis

The significance level for all variables studied was $p \leq 0.05$. Initially a descriptive analysis of the variables was carried out with central trend and dispersion measurements. Based on WHtR cut-point values, the sample was divided into <0.5 and $\geq$0.5 to compare relative anthropometric data, blood pressure and biochemical tests by student t-test. In addition, the correlation between WHtR and cardiovascular risk factors was evaluated, as well as the relative strength by means of Pearson correlation for lipid profile.

Results

The study population was represented by 76 perimenopausal/menopausal women. Average age of 50.26$\pm$8.36 years, and WHtR 0.52$\pm$0.06. Lipid profile slightly increases more than normal value in the study (Table 1).

The results show the characteristics of the participants according to WHtR with EST parameters levels. EST time, functional capacity, heart rate reserve, RPP at rest, RPP at peak, and HR recovery at 1 minute of EST parameters in perimenopausal/menopausal women with greater WHtR ($\geq$0.5) were statistically different when compared to women with lower WHtR (<0.5) groups ($p<0.01$, $p<0.01$, $p<0.01$, $p<0.01$, $p = 0.03$ and $p = 0.04$, respectively).

The WHtR has inverted correlations with exercise duration time, functional capacity, rate pressure product at rest, and heart rate recovery at 1 minute, all $p<0.01$. Nevertheless, no correlations among WHtR with 5-year survival and average annual mortality were found (Table 2).

No significant difference in heart rate recovery and chronotropic response were found between WHtR groups in perimenopausal/menopausal women (Table 3).

Discussion

The results of the present study pointed to the presence of correlation between WHtR and abnormal hemodynamic response, all exercise duration

Table 1. Anthropometric and cardio-metabolic characteristics

Anthropometric characteristics	Mean $\pm$ SD
Age (years)	50.26$\pm$8.36
Systolic blood pressure (mmHg)	122.08$\pm$13.34
Diastolic blood pressure (mmHg)	66.88$\pm$8.57
Height (cm)	155.93$\pm$5.29
Weight (kg)	60.42$\pm$11.75
Body mass index (kg/m^2)	19.35$\pm$3.58
Waist circumference (cm)	81.61$\pm$9.96
Waist to height ratio	0.52$\pm$0.06
Fasting blood sugar (mg/dL)	93.97$\pm$19.67
Total cholesterol (mg/dL)	202.93$\pm$40.48
Triglyceride (mg/dL)	126.88$\pm$81.82
High-density lipoprotein cholesterol (mg/dL)	50.86$\pm$15.16
Low-density lipoprotein cholesterol (mg/dL)	119.86$\pm$34.66
Peak rate pressure product	26,158.86$\pm$4,788.53
Heart rate recovery at 1 min (bpm)	23.18$\pm$8.81
Functional capacity METS	8.44$\pm$2.18
5 years survival (%)	91.56$\pm$4.50
Average annual mortality (%)	1.69$\pm$0.90

time, functional capacity RPP, and HRR after treadmill EST in perimenopausal/menopausal women. The results of abnormal hemodynamic responses may indicate an increased risk of non-predicting cardiovascular death and coronary events during follow up. The factors that may affect prognostic significance were blood pressure, heart rate responses to exercise, and duration of exercise testing. Confirming our initial hypothesis, women with greater WHtR had poorer exercise stress test parameters compared to women with lower WHtR values. The peak rate pressure product was significantly more in postmenopausal women without coronary artery disease as compared to postmenopausal women with coronary artery disease, indicating more compromised coronary perfusion in postmenopausal woman with coronary artery disease[3].

The effect of exercise on RPP in premenopausal and postmenopausal women with coronary artery disease was the percentage increase in RPP. RPP in postmenopausal women with CAD was significantly more than premenopausal women with CAD, indicating more compromised coronary perfusion in postmenopausal women[4]. This study, Perimenopausal and menopausal women with WHtR $\geq$0.5 had a significantly high RPP compared to <0.5, with statistical significance. This shows that the high WHtR, myocardial oxygen consumption is much higher at rest and they are more prone to ischemia due to stress and exercise. Previous study has shown a physiologic correlation between the RPP, the onset of angina pectoris, and the ECG abnormalities during exercise[5,6]. However, the large degree of natural variability of both HR and blood pressure makes it plausible that neither variable effectively reflects a given individual's level of exercise exertion[7]. Exercise capacity or the amount of work achieved before exhaustion is the most powerful predictor of survival[8,9].

Exercise functional capacity is lower in central obesity group. For the hemodynamic parameter, HRR at 1 minute in central obesity is higher than non-central obesity group. The differential HR recovery response is a strong adverse prognostic marker in both apparently healthy and patient populations, irrespective of differences in patient populations, medications, or baseline functional capacity[10-13]. High levels of sympathetic activity and low level of parasympathetic

Table 2. The correlation among anthropometric and EST hemodynamic parameters

Hemodynamic Correlation	WHtR	
	r	*p*-value
Exercise duration time	-0.33	<0.01*
Functional capacity (METS)	-0.33	<0.01*
Heart rate reserve	-0.26	0.02
Rate pressure product at rest	0.32	<0.01*
Rate pressure product at peak	0.20	0.09
Heart rate recovery at 1 min	-0.24	0.04*
Heart rat recovery at 5 min	-0.17	0.14
Chronotropic response	0.02	0.90
5 year Survival (%)	0.12	0.32
Average annual mortality (%)	-0.12	0.32

* Correlation is significant at the 0.05 level

Table 3. Exercise stress test (EST) characteristics of the groups with different WHtR values

EST characteristics	Waist to height ratio		*p*-value
	<0.5, n = 44	$\geq$0.5, n = 32	
EST time (min)	7.20±2.31	5.65 ± 1.87	<0.01*
Estimate functional capacity (METS)	9.26±2.32	7.84 ± 1.89	<0.01*
Heart rate reserve (bpm)	72.53±17.33	60.75 ± 13.64	<0.01*
Rate pressure product at rest	9.83±2.35	11.51 ± 1.69	<0.01*
Rate pressure product at peak	22.83±4.93	25.15 ± 4.39	0.03*
Heart rate recovery at 1 min (bpm)	25.63±8.79	21.41 ± 8.45	0.04*
Heart rat recovery at 5 min (bpm)	61.16±16.10	56.70 ± 10.27	0.15
Chronotropic response	0.80±0.22	0.77 ± 0.14	0.48
5 year survival (%)	91.51±3.85	91.58 ± 4.97	0.96
Average annual mortality (%)	1.69±0.77	1.68 ± 0.99	0.96

* Difference is significant at the 0.05 level

activity have been associated with obesity. Weight reduction has been associated to improve autonomic imbalance[14, 15]. Autonomic imbalance in overweight and obese may affect hemodynamic response during EST[16].

In central obesity, abnormal hemodynamic responses show that central obesity may affect to cardiovascular prognosis and physical fitness. Regular exercise and diet control for cardiovascular risks modification should be advised. Increased physical activity through regular combined exercise (resistance exercise combined with aerobic training) is more effective for mitigating obesity and improving health-related fitness at all ages than aerobic training alone in mitigating obesity. Additionally, physical activity may affect endotoxin concentrations and immune function[17-20].

There is a limitation of this study. Because the mean age of our study population was 50.26$\pm$8.36 years, the results might not be applicable to older or younger population.

Conclusion

Our findings showed that central obesity, high WHtR have abnormal hemodynamic response in HRR that shows a strong adverse prognostic marker in perimenopausal/menopausal population. Exercise capacity in central obesity is lesser than non-central obesity group. WHtR measurement is a simple and timesaving screening measure for central obesity that may affect hemodynamic response in treadmill EST.

What is already known on this topic?

The present study is not the first report of WHtR marker of central obesity but previous studies cannot be directly applied to perimenopausal/ menopausal specific subgroup in Thai population because of differences in ethnic groups and environmental factors provided for cardio-metabolic risks and hemodynamic response in our study.

What this study adds?

The diagnostic yield of EST as a screening tool for subclinical CAD in perimenopausal and menopausal women with abnormal WHtR is uncertain. However, it is important to observe that WHtR parameter has abnormal hemodynamic response in non-overt cardiovascular disease.

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Potential conflicts of interest

None.

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สัดส่วนรอบเอวต่อความสูงเพื่อใช้พยากรณ์การตอบสนองของระบบไหลเวียนโลหิตในการทดสอบสมรรถภาพหัวใจโดยการเดินสายพานในสตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือน

พรทิพย์ นิ่มขุนทด, ปัทมา ทองดี

ภูมิหลัง: *สัดส่วนรอบเอวต่อความสูงเป็นตัวชี้วัดการตรวจคัดกรองอย่างง่ายสำหรับการบ่งชี้ภาวะน้ำหนักเกินและโรคอ้วน การนำเสนอเร็วๆ นี้พบว่าสัดส่วนรอบเอวต่อความสูงอาจเป็นตัวแทนของความเสี่ยงโรคหัวใจและหลอดเลือด พารามิเตอร์ที่ดีขึ้นเมื่อเทียบกับสัดส่วนของร่างกายแบบดั้งเดิม*

วัตถุประสงค์: *เพื่อศึกษาการตอบสนองของการไหลเวียนโลหิตจากการทดสอบสมรรถภาพหัวใจโดยการเดินสายพานในสตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือนโดยการใช้สัดส่วนรอบเอวต่อความสูง*

วัสดุและวิธีการ: *การศึกษาแบบภาคตัดขวางในสตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือน 76 คน ตัวชี้วัดหลักสัดส่วนรอบเอวต่อความสูงและการตอบสนองของระบบไหลเวียนโลหิตจากการทดสอบสมรรถภาพหัวใจโดยการเดินสายพาน การวิเคราะห์ทางสถิติที่ได้กระทำโดยใช้แบบทดสอบทีเทสต์และค่าความสัมพันธ์เพียร์สัน ค่า p มีนัยสำคัญที่ระดับความเชื่อมั่นร้อยละ 5 ($p<0.05$)*

ผลการศึกษา: *สตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือน 76 คน อายุเฉลี่ย 50.26±8.36 ปี สตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือนที่มีสัดส่วนรอบเอวต่อความสูงต่ำกว่า 0.5 มีค่าค่าการทดสอบ สมรรถภาพหัวใจโดยการเดินสายพาน ทั้งระยะเวลาการออกกำลังกาย สมรรถภาพการออกกำลังกาย ผลิตภัณฑ์อัตราความดัน และการกู้คืนอัตราการเต้นหัวใจหลังจากการเดินสายพาน แตกต่างกับเมื่อเปรียบเทียบกับผู้หญิงที่มีค่าสัดส่วนรอบเอวต่อความสูงมากกว่าหรือเท่ากับ 0.5 พบว่าไม่มีความสัมพันธ์กันระหว่างสัดส่วน รอบเอวต่อความสูงกับการอยู่รอดใน 5 ปี และอัตราการเสียชีวิตโดยเฉลี่ยต่อปี*

สรุป: *สัดส่วนรอบเอวต่อความสูง เป็นการตรวจคัดกรองที่ง่ายและประหยัดเวลาสำหรับโรคอ้วนลงพุงที่สามารถนำมาใช้ในการพยากรณ์การบ่งชี้การตอบสนองของระบบไหลเวียนโลหิตในการทดสอบสมรรถภาพหัวใจโดยการเดินสายพาน ค่าสัดส่วนรอบเอวต่อความสูงมากกว่าหรือเท่ากับ 0.5 มีความผิดปกติในการตอบสนองของระบบไหลเวียนโลหิต ในการกู้คืนอัตราการเต้นของหัวใจหลังจากการเดินสายพาน ซึ่งเป็นการทำนายการพยากรณ์โรคที่ไม่ดีในสตรีวัยก่อนหมดประจำเดือนและสตรีวัยหมดประจำเดือน สมรรถภาพการออกกำลังกายน้อยกว่าในกลุ่มที่ไม่อ้วนลงพุง*