Neck Circumference as Simple Screening Measure for Predicting the Annual Mortality in Menopausal Status Women using Treadmill Exercise Stress Test

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Background: *Neck circumference (NC) is a simple screening measure for identifying overweight and obesity. It was recently proposed that the NC may be represent a better parameter of cardiovascular risk, when compared to fat stored in the visceral region.*
Objective: *To determine whether a single measure of NC might be used to identify hemodynamic response, annual mortality rate in treadmill exercise stress test (EST) and traditional anthropometric parameters in perimenopausal/menopausal women.*
Material and Method: *This is a cross-sectional study of 76 perimenopausal/menopausal women. Main indicators included NC, body mass index (BMI), waist circumferences (WC), waist to hip ratio (WHR), average annual mortality rate, and hemodynamic response during 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: *The research included 76 perimenopausal/menopausal women with an average age of 50.26 ± 8.36 years. Perimenopausal/menopausal women with lower NC values (<35 cm) presented no difference in EST values when compared to women with higher NC values ($\geq$35 cm). Average annual mortality had inverted correlation with NC ($p = 0.04$). The other traditional parameters, BMI and WHR did not correlate with the annual mortality rate. The hemodynamic response of the treadmill exercise parameters in rate pressure product, heart rate recovery, and functional capacity did not correlate with NC.*
Conclusion: *NC measurement is simple and timesaving screening measure that may be added to prognostic parameters for prediction of annual mortality. Average annual mortality in treadmill EST had inverted correlation with NC. The other traditional anthropometric parameters did not correlate with prognostic variables of treadmill EST.*

Keywords: *Neck circumference, Average annual mortality, Treadmill exercise stress test, Menopausal status women*

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Excessive body fat is a risk factor for developing non-communicable chronic degenerative diseases, and it is associated with the incidence of diabetes[1], cardiovascular diseases (CVD)[2,3] and early death[4,5]. It was recently proposed that the neck circumference (NC) may represent a better parameter of cardiovascular risk, when compared to fat stored in the visceral region[6,7], possibly because visceral fat is not the major source of free fatty acids circulating levels[8]. Furthermore, it was demonstrated that the upper part of the body (neck) is responsible for greater release of systemic free fatty acids from the visceral region, mainly in obese individuals[9]. Currently, there are limited data of NC for the prognostic parameters in the menopausal transition both perimenopausal and menopausal women.

This study aimed to compare and associate hemodynamic response, annual mortality prognosis of treadmill exercise stress test (EST) and traditional anthropometric parameters in perimenopausal/menopausal women, with different NC values.

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Material and Method

Study population

The study involved 76 perimenopausal and menopausal subjects recruited from cardiovascular clinic and menopause clinic, aged 40 to 70 years who underwent EST in Suranaree University of Technology

Hospital from September 2015 until February 2016. Exercise testing procedures outlined by American Heart Association (AHA) guidelines for clinical exercise testing laboratories were followed for all assessment. The sample was selected 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 from September 2015 until February 2016, in perimenopausal and menopausal women at the Suranaree University of Technology Hospital, Thailand. After signing the informed consent forms, 76 women voluntarily participated in the investigation. The sample was divided into two groups: NC <35 cm and NC ≥35 cm. Previous studies based on the Asian population of China, Taiwan and including this study, used 35 cm as the cut-off point for an abnormal value in females. The inclusion criteria were ages 40 to 70 years; signed the consent form and participated in all laboratory and anthropometric tests. The exclusion criteria were having neck deformity, goiter, and hypertrophy of parotid glands. Informed consent was obtained from both groups and ethical clearance was obtained from the relevant authorities.

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 an abnormal EST in perimenopausal and menopausal women of the pilot study in Suranaree University of Technology Hospital (5%), and 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 the treadmill EST according to the modified Bruce protocol. The results of EST were interpreted by an experienced cardiologist as negative or positive results.

Laboratory measurement

Baseline serum specimens (stored at the central repository) 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. Diabetes was 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 modified Bruce protocol. Exercise testing procedures outlined by the AHA 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.

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 heart rate (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 defined as perimenopausal and menopausal women. Participants were also asked about their menstrual bleeding patterns in the 12 months prior to recruitment. Perimenopausal women are defined as women age ≥40 years and around menopause and have menstrual period irregularity in the past 12 months. Menopausal women are defined as women those with no menstrual periods within the last 12 months.

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 NC values, the sample was divided into <35 cm and ≥35 cm to compare relative anthropometric data, blood pressure and

biochemical tests by independent t-test. In addition, the correlation between NC 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, with average age of 50.26±8.36 years and normal functional exercise capacity 8.44 METS (Table 1).

The results show the characteristics of the study participants according to NC with hemodynamic response parameters during treadmill EST. Lower NC groups (<35 cm) had not differences in hemodyamic parameters with higher NC groups (≥35 cm) in perimenopausal/menopausal women (Table 2).

NC had inverse correlation with average annual mortality rate (p = 0.04). Nevertheless, no correlations among NC and hemodynamic response of treadmill exercise parameters in the rate pressure product, heart rate recovery and functional capacity variables were found (Table 3).

Table 1. Anthropometric and cardio-metabolic characteristics

Anthropometric characteristics	Mean ± SD
Age (years)	50.26±8.36
Systolic blood pressure (mmHg)	122.08±13.34
Diastolic blood pressure (mmHg)	66.88±8.57
Height (cm)	155.93±5.29
Weight (kg)	60.42±11.75
Body mass index (kg/m^2)	19.35±3.58
Waist circumference (cm)	81.61±9.96
Waist to hip ratio	0.83±0.05
Neck circumference (cm)	33.51±3.14
Fasting blood sugar (mg/dL)	93.97±19.67
Total cholesterol (mg/dL)	202.93±40.48
Triglyceride (mg/dL)	126.88±81.82
High-density lipoprotein cholesterol (mg/dL)	50.86±15.16
Low-density lipoprotein cholesterol (mg/dL)	119.86±34.66
Peak rate pressure product	26,158.86±4,788.53
Heart rate recovery at 1 min (bpm)	23.18±8.81
Functional capacity METS	8.44±2.18
Average annual mortality (%)	1.69±0.90

Discussion

The results of the present study pointed to the presence of correlation between NC and average annual mortality rate using treadmill EST in perimenopausal/menopausal women. Initial hypothesis, women with higher NC presented more cardiovascular risk factors and poor prognosis than lower NC values. The NC cut-off points for evaluating overweight or obesity have been defined differently in different studies but previous studies of Asian population including this study used 35 cm as the cut-off point for an abnormal value[10]. For the results of this study, hemodynamic responses in treadmill EST had no differential between the two groups of NC. The discrepancy with the results of this study may be due to different diagnostic cut-off point standards or study populations.

In this study, high NC group (NC ≥35 cm) had high rate pressure product (RPP) compared with low NC group but no statistical significance. This shows that the high NC, myocardial oxygen consumption is much higher at rest and they are more prone to ischemia due to stress and exercise. Previous studies have shown a physiologic correlation between the RPP, the onset of angina pectoris, and the ECG abnormalities during exercise[11,12]. 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[13].

Exercise capacity, or the amount of work achieved before exhaustion, is the most powerful predictor of survival[14,15]. NC did not correlate with exercise time and exercise capacity in this study but central obesity parameters, WHR has inverted correlation. The cut-off points of <5 METs in women and <7 METs in men, it is more logical and accurate to assess each individual relative to age and sex based standard protocol. HR from peak exercise of more than 12 beats, 1 minute after cessation of the exercise test, while in the upright position, is most frequently used to define an abnormal HR recovery response and a strong adverse prognostic marker in both apparently healthy and patient populations, irrespective of differences in patient populations, medications, or baseline functional capacity[16-19]. An exaggerated systolic blood pressure response to exercise could indicate an increased risk for future hypertension, left ventricular hypertrophy, and cardiovascular events[20]. NC may add clinical value when conducted in participants with estimated intermediate risk of developing coronary artery disease (CAD) especially in perimenopausal/menopausal women.

The limitation in this study, predicting average annual mortality, calculated by using the treadmill EST

Table 2. Hemodynamic parameters in Treadmill exercise stress test between NC groups

Exercise Stress Test Parameters	Neck circumference		*p*-value
	<35 cm	≥35 cm	
Peak rate pressure product	25,632.71±5,323.06	27,060.82±3,610.38	0.21
Rate pressure product at rest	10.65±2.30	11.07±1.87	0.41
Rate pressure product at peak	23.92±5.00	24.61±4.30	0.54
Heart rate recovery at 1 min (bpm)	23.50±9.01	22.64±8.46	0.69
Heart rate recovery at 1 min (bpm)	59.94±14.12	56.25±11.11	0.24
Functional capacity METS	8.72±2.20	7.95±2.07	0.14

* Difference is significant at the 0.05 level

Table 3. The correlation among anthropometric and EST parameters

Correlation	NC		BMI		WHR	
	r	*p*-value	r	*p*-value	r	*p*-value
Exercise time	-0.08	0.47	-0.13	0.25	-0.33	<0.01*
Functional capacity(METS)	-0.11	0.36	-0.15	0.19	-0.32	<0.01*
Rate pressure product at rest	0.13	0.28	0.18	0.13	0.22	0.06
Rate pressure product at peak	0.06	0.63	0.09	0.44	0.22	0.06
Heart rate recovery at 1 min	-0.13	0.26	-0.21	0.06	-0.12	0.3
Heart rat recovery at 5 min	-0.18	0.12	-0.26	0.03*	0.03	0.81
Average annual mortality	-0.23	0.04*	-0.17	0.15	-0.02	0.90

NC = neck circumference, BMI = body mass index, WHR = waist to hip ratio
* Correlation is significant at the 0.05 level.

program in a cross-sectional study had no clinical mortality.

Conclusion

Our findings showed that the average annual mortality used to predict the prognostic parameter was found to correlate with NC using treadmill EST. In the cut-off point NC 35 cm, hemodynamic response had no differential between the two groups in perimenopausal/menopausal women. NC may add clinical value when conducted in participants with CAD risk factors.

What is already known on this topic?

The present study is not the first report of NC but previous studies cannot be directly applied to the perimenopausal/menopausal specific subgroup in the Thai population because of differences in ethnic groups and environmental factors provided for cardio-metabolic risks and EST 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 NC is uncertain. However, it is important to observe a correlation between NC with prognosis parameter in average annual mortality in non-overt CVD.

Acknowledgement

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Potential conflicts of interest

None.

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ความยาวเส้นรอบวงคอการคัดกรองแบบง่ายเพื่อการทำนายอัตราการเสียชีวิตโดยเฉลี่ยต่อปีของสตรีวัยหมดประจำเดือนโดยใช้การทดสอบสมรรถภาพหัวใจเดินสายพาน

พรทิพย์ นิ่มขุนทด ปัทมา ทองดี

ภูมิหลัง: *ความยาวเส้นรอบวงคอเป็นการตรวจคัดกรองอย่างง่ายสำหรับการระบุภาวะน้ำหนักเกินและโรคอ้วน เมื่อเร็วๆ นี้พบว่าความยาวของเส้นรอบวงคออาจเป็นตัวแทนของพารามิเตอร์ที่ดีขึ้นของความเสี่ยงโรคหัวใจและหลอดเลือด เมื่อเปรียบเทียบกับไขมันที่เก็บในอวัยวะภายใน*

วัตถุประสงค์: *เพื่อศึกษาว่าการวัดความยาวของเส้นรอบวงคออย่างเดียว สามารถใช้ในการทำนายการพยากรณ์โรคอัตราการเสียชีวิตโดยเฉลี่ยต่อปีในการทดสอบสมรรถภาพหัวใจเดินสายพาน เปรียบเทียบกับสัดส่วนของร่างกายแบบดั้งเดิมในสตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือน*

วัสดุและวิธีการ: *การศึกษาแบบภาคตัดขวางในสตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือน ตัวชี้วัดหลัก ได้แก่ เส้นรอบคอ ดัชนีมวลกาย รอบเอว และสัดส่วนรอบเอวต่อรอบสะโพก การวิเคราะห์ทางสถิติที่ได้กระทำโดยใช้การทดสอบทีเทสต์และความสัมพันธ์ของเพียร์สันค่า p มีนัยสำคัญทางสถิติที่ระดับความเชื่อมั่นร้อยละ 5 ($p<0.05$)*

ผลการศึกษา: *สตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือน 76 คน อายุเฉลี่ย 50.26±8.36 ปี สตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือนที่มีค่าความยาวของเส้นรอบวงคอน้อยกว่า 35 เซนติเมตร ค่าการทดสอบสมรรถภาพหัวใจเดินสายพานไม่แตกต่างกัน เมื่อเปรียบเทียบกับกลุ่มที่มีค่าความยาวของเส้นรอบวงคอ มากกว่าหรือเท่ากับ 35 เซนติเมตร ความยาวของเส้นรอบวงคอมีความสัมพันธ์ผกผันกับอัตราการเสียชีวิต โดยเฉลี่ยต่อปี ($p = 0.04$) การวัดสัดส่วนแบบดั้งเดิม ดัชนีมวลกาย สัดส่วนรอบเอวต่อรอบสะโพก ไม่มีความสัมพันธ์กับอัตราการเสียชีวิตโดยเฉลี่ยต่อปี การตอบสนองของการไหลเวียนเลือดในการเดินสายพานทดสอบสมรรถภาพหัวใจ ทั้งผลคูณของชีพจรและความดัน อัตราการกู้คืนของชีพจรและสมรรถภาพหัวใจ ไม่มีความสัมพันธ์กับความยาวของเส้นรอบวงคอ*

สรุป: *ความยาวเส้นรอบวงคอเป็นตัวชี้วัดที่ง่ายและประหยัดเวลาในการตรวจคัดกรองที่สามารถใช้ในการพยากรณ์โรค ในการทดสอบสมรรถภาพหัวใจเดินสายพาน พบว่าอัตราการเสียชีวิตเฉลี่ยต่อปีมีความสัมพันธ์กับความยาวของเส้นรอบวงคอ การประเมินความสัมพันธ์ของสัดส่วนร่างกายแบบดั้งเดิมมีความสัมพันธ์กับการพยากรณ์โรคในการทดสอบ สมรรถภาพหัวใจเดินสายพาน แต่ไม่สัมพันธ์เช่นเดียวกับความยาวของเส้นรอบวงคอ*