

Novel Mathematic Indexes to Identify Subclinical Atherosclerosis in Different Obesity Phenotypes of Perimenopausal/Menopausal Women

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Background: Evidence shows that novel adiposity and atherosclerotic index perform better than individual lipids or traditional cardiometabolic risks in predicting cardiovascular disease (CVD). Identifying mathematic indexes both adiposity and atherogenic indexes can serve as a quick and simple tool for identifying subclinical atherosclerosis and monitoring population at risk of CVD.

Objective: To examine the relationship between atherogenic index and adiposity index to identify subclinical atherosclerosis using carotid intima media thickness (CIMT) in specific population groups of central obesity and general obesity phenotype in perimenopausal/menopausal women.

Material and Method: The cross-sectional study was conducted with 130 participants, aged 40 to 80 years, between August 2015 and January 2016 in Suranaree University of Technology Hospital, Thailand. CIMT was assessed using a high-resolution B mode ultrasound system. Traditional anthropometric parameters such as body mass index (BMI), waist circumference (WC), blood pressure, fasting plasma glucose, lipid profile, and CIMT were assessed in all participants. All atherogenic indexes and adiposity indexes were calculated.

Results: Data from 130 perimenopausal/menopausal participants with 41% being central obesity phenotype was reviewed. Most adiposity indexes such as visceral adiposity index (VAI), lipid accumulation product (LAP), and atherosclerotic index of plasma (AIP) were different between abdominal obesity and non-abdominal obesity $p = 0.01$, $p < 0.01$ and $p = 0.03$, respectively. The body adiposity index (BAI) and a surface-based body shape index (ASBI) were not different. CIMT was higher in abdominal obesity and different obesity phenotype ($p < 0.01$). In abdominal obesity BAI, LAP, and AIP were correlated with CIMT but only AIP was correlated with CIMT in non-abdominal obesity.

Conclusion: The presence of early atherosclerosis in perimenopausal/menopausal women with abdominal obesity can be predicted using BAI, LAP, and AIP. In perimenopausal/menopausal women with non-abdominal obesity, only AIP was correlated with CIMT.

Keywords: Mathematic index, Atherogenic index, Adiposity index, Subclinical atherosclerosis, Perimenopausal women, Menopausal women

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Cardiovascular disease (CVD) is the leading cause of mortality for women. As women are getting older age, increasingly exposed to high levels of major CVD risk. Decreasing estrogen levels during the transition has been linked to endothelial dysfunction and larger vessel diameters, markers of early adverse vascular changes factors, including a poor lipid profile

and weight gain⁽¹⁻⁵⁾. Lipids are known to change in association with both age and the menopausal transition⁽⁶⁾. There is growing recognition of the heterogeneity in CVD risk in obese individuals. Multiple studies have identified a metabolically benign obese phenotype that fulfills the criteria of clinical obesity by body mass index (BMI) or waist circumference (WC), but does not have the burden of adiposity-associated cardiometabolic risk factors found among those with the “at-risk” obese phenotype. In addition, using BMI as a measure of obesity has limitations, because it cannot distinguish between fat and lean tissue. However, additional analyses using WC, waist to hip

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ratio (WHR) and waist to height ratio (WHtR) were suggested to be used as a surrogate measure of abdominal adiposity. Abnormal carotid intima media thickness (CIMT) has correlated with marker of atherosclerosis.

The mathematic index of both adiposity and atherogenic indexes to identify subclinical atherosclerosis in difference of obesity perimenopausal/menopausal women is achieved.

Material and Method

Study population

Between August 2015 and January 2016, we recruited 130 individuals were recruited from the Suranaree University of Technology Hospital, Thailand. Women aged 40 to 80 years were eligible and were enrolled when they participated in their annual health examination. All participants underwent a complete cardiovascular evaluation after 8 hours of fasting blood sampling, including: 1) Medical history for acute myocardial infarction, congestive heart failure previous stroke, end stage renal disease, hypertension, diabetes mellitus, dyslipidemia or smoking; 2) Anthropometric analysis including weight, height, WC and hip circumference (HC); 3) Blood pressure measurement; 4) Serum glucose levels; 5) Plasma lipids profile including total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) level and evaluated ratios of LDL-C to HDL-C profile.

Study protocol

At the baseline visit, perimenopausal/menopausal women without hormonal replacement therapy were completed self-administered questionnaires that included information on demographic and medication use, medical history, and family history of CVD and diabetes. Additionally, each woman underwent a physical examination that included anthropometric and blood pressure measurements, and collection of fasting blood specimens (after 8 hours or longer of fasting). The study protocol was approved by the ethics committee of Suranaree University of Technology and informed consent was signed by each participant.

Laboratory measurement

Baseline serum specimens (stored at the central repository) were measured for levels of glucose and lipids. Serum glucose, TC, TG, HDL-C, and 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.

Definition of terms

Perimenopausal/menopausal women

Perimenopausal status is defined to age ≥ 40 years around menopause and had menstrual periods irregularity in the past 12 months. Menopausal status is defined to no menstrual periods within the last 12 months. Participants were also asked about their menstrual bleeding patterns in the 12 months prior to recruitment.

Carotid intima media thickness measurement

The measurement was carried out according to a validated procedure, using a high-resolution B-mode ultrasonography with phased array transducer (PLT-704SBT 7.5 MHz). A single cardiologist who was blinded to the clinical characteristics measured CIMT. The view of the far wall of the common carotid artery, carotid bulb, internal carotid artery using the automated edge detection lumen intima and the media adventitia interface at the far wall for CIMT. The mean CIMT of each of the six carotid segments was determined, and the average of these six mean measures was computed for the outcome variable in this analysis. The study define abnormal CIMT ≥ 0.9 mm marker of atherosclerosis based on the American Society of Echocardiography recommendations⁽⁷⁾.

Anthropometrics measurement

According to the World Health Organization's protocol. WC was measured with the participant in nonrestrictive undergarments, at the level of the natural waist, defined as the narrowest part of the torso as seen from the anterior aspect. For cases in which waist narrowing was difficult to determine, the measure was taken at the smallest horizontal circumference in the area between the ribs and the iliac crest. HC was measured around the widest portion of the buttocks, with parallel to the floor. WHR was calculated as WC divided by HC. BMI was calculated as weight in kilograms divided by height in square meters. BMI was categorized as obese (BMI >30 kg/m²), overweight (BMI 25.0-29.9 kg/m²), or normal weight (BMI <25 kg/m²).

Obesity phenotype

The WHO states that abdominal obesity is defined as a waist-hip ratio above 0.90 for males and

above 0.85 for females. Non-abdominal obesity or generalized obesity is define as BMI >30 kg/m².

Mathematic index

All mathematic indexes were calculated mathematical model that uses simple anthropometric and lipid (TG and high-density lipoprotein (HDL) cholesterol) parameters.

A surface-based body shape index (ASBI)⁽⁸⁾

$$ASBI = WC/[BMI^{2/3}/Height^{1/2}]$$

Visceral adiposity index (VAI)⁽⁹⁾

$$VAI_{Female} = WC/[36.58 + (1.89 \times BMI)] \times (TG/0.81) \times (1.52/HDL-C)$$

Body adiposity index (BAI)⁽¹⁰⁾

$$BAI = [HC (cm)/Height (m)^{1.5}] - 18$$

Lipid accumulation product (LAP)⁽¹¹⁾

$$LAP_{Female} = [WC (cm) - 58] \times TG (mmol/l)$$

Atherogenic index of plasma (AIP)⁽¹²⁾

$$AIP = \log (TG/HDL-C)$$

Statistical analysis

Statistical analyses were performed and continuous variables of the subjects at baseline were expressed as mean and standard deviation (SD) or median. Demographics, health history, median laboratory values, and compared among normal CIMT

and atherosclerosis CIMT ≥ 0.9 mm using the independent t-test. Pearson correlation was used to define the correlation between mathematic indexes and atherosclerotic parameters. All reported *p*-values were 2-tailed, and *p*<0.05 was considered statistically significant.

Results

Total 130 women that abdominal obesity has higher incidence than generalized obesity participants. Age, systolic blood pressure, diastolic blood pressure and fasting blood sugar (FBS) were higher in abdominal obesity than non-abdominal obesity but no difference in lipid parameters. CIMT was higher in abdominal obesity than non-abdominal obesity with statistically significant (*p*<0.01) (Table 1).

All adiposity indexes; VAI, LAP and AIP except BAI and ASBI were different between abdominal obesity and non-abdominal obesity *p* = 0.01, *p*<0.01 and *p* = 0.03, respectively. CIMT was higher in abdominal obesity phenotype (*p*<0.01) (Table 2).

In addition, the present study also observed that abdominal obesity BAI, LAP and AIP were correlated with CIMT but only AIP was correlated in non-abdominal obesity (Table 3).

Discussion

In our study, perimenopausal/menopausal women, only 22% were identified to atherosclerosis. In current study, participants who had coronary atherosclerosis is defined to CIMT 0.91±0.20 mm.

Table 1. Demographic and metabolic characteristics of the study population by obesity phenotype

Parameters	Abdominal obesity n = 53	Non-abdominal obesity n = 77	<i>p</i> -value
Age (years)	55.14±10.87	49.90±7.57	<0.01*
Diabetes mellitus (%)	6/130	2/130	0.16
Hypertension (%)	19/130	8/130	0.07
Dyslipidemia (%)	34/130	18/130	0.04*
Systolic Blood Pressure (mmHg)	128.33±16.26	121.31±14.93	0.02*
Diastolic Blood Pressure (mmHg)	71.30±9.02	66.59±10.03	0.01*
Glucose (mg/dL)	104.96±23.79	94.75±9.23	<0.01*
Creatinine (mg/dL)	0.79±0.14	0.84±0.12	0.13
Total Cholesterol (mg/dL)	223.94±46.52	217.78±45.63	0.48
Triglyceride (mg/dL)	132.49±74.61	110.47±46.32	0.07
Low-density lipoprotein cholesterol (mg/dL)	136.29±42.42	133.98±37.72	0.76
High-density lipoprotein cholesterol (mg/dL)	55.69±13.28	60.43±13.85	0.07
Carotid intima media thickness (mm)	0.75±0.16	0.67±0.12	<0.01*

* Significant difference at *p*<0.05

The authors define abnormal CIMT ≥ 0.9 mm due to correlation with marker of atherosclerosis. Correlation between both adiposity, atherogenic indexes and CIMT marker of early atherosclerosis were not found. This was reflected by higher levels of CIMT in perimenopausal/menopausal compare female gender in general population from previous study in Thailand 0.74 mm and 0.67 mm, respectively⁽¹²⁻¹⁴⁾. Regarding Korean population, Bae et al, Cho et al and the Atherosclerosis Risk of Rural Areas in Korea General Population (ARIRANG) Study already reported normative CIMT values showing that mean CIMT was 0.63 ± 0.11 mm⁽¹⁵⁾.

The study, age of participants in atherosclerosis higher than normal CIMT 10 years with statistically significant may affect to mean CIMT, which is similar to previous studies. Atherosclerosis Risk in Communities (ARIC) have shown different intima media thickness of carotid artery in age, gender, and geographical origin⁽¹⁶⁾. Therefore, the results presented in this study further extend the findings of previous investigations by including not only mean CIMT, but also carotid plaque that demonstrates associations with obesity phenotype and lipid parameters. In this study,

we confirmed that obesity is an important risk factor to identify early atherosclerosis same as previous studies in other Asian populations. Adiposity index was better in identifying the risk of diabetes and abnormal glucose metabolism than BMI, WC and WHtR⁽¹⁷⁻¹⁹⁾. In combination risk, high VAI scores and the hypertriglyceridemic waist phenotype are strongly associated with diabetes risk, in previous study⁽²⁰⁾. The different effect of mathematic index might be attributed to different study populations. It has reported that compared with Caucasians, Asians may have significantly higher risk of type 2 diabetes and CVD despite substantially lower BMI⁽²¹⁾. In meta-analysis and Asia-Pacific region that serum TG is an important and independent predictor of CVD risk^(22,23) and it uses in mathematic indexes such as VAI, BAI, LAP, and AIP formula. Variations in lifestyle may also have effects on the relationship between mathematic index and cardiovascular risk among different populations besides hereditary factors⁽²⁴⁾. Thus, the efficiency of index in predicting the risk of CVD still needs further verification from studies in different areas and different ethnicities.

Despite these limitations, our study confirmed that central obesity is an important risk factor of subclinical atherosclerosis among Thai population and found mathematic indexes of both adiposity and atherogenic indexes are more important in subclinical atherosclerosis. Mathematic index is a good and convenient surrogate marker for visceral adipose measurement and AIP and could be used in identifying the risk of subclinical atherosclerosis s in large scale epidemiologic studies.

The limitation of this study. Our results need to be interpreted within light of certain limitations. Our cross-sectional analysis cannot be used to determine causation. As our cohort consisted of women in perimenopausal/menopausal women, the results may

Table 2. Adiposity index parameters and atherosclerosis in different obesity phenotype (ANOVA)

Obesity phenotype Between Groups	F	p-value
BAI	1.690	0.20
VAI	6.210	0.01*
LAP	22.720	<0.01*
ASBI	0.077	0.78
AIP	4.780	0.03*
CIMT	8.700	<0.01*

* Correlation is significant at the 0.05 level.

Table 3. Adiposity and CIMT parameters in obesity phenotype

Adiposity Index	Abdominal obesity Phenotype			Non abdominal obesity Phenotype		
	Chi-square	df	p-value	Chi-square	df	p-value
BAI	2,919.00	2,756	0.02*	1,865.75	1,794	0.12
VAI	3,339.00	3,233	0.10	2,346.00	2,300	0.25
LAP	3,228.75	3,074	0.03*	2,295.00	2,208	0.10
ASBI	3,339.00	3,233	0.10	2,346.00	2,300	0.25
AIP	3,228.75	3,021	<0.01*	2,193.00	2,024	<0.01*

* Correlation is significant at the 0.05 level.

not be generalizable to younger women or men.

Conclusion

Until this is rectified, mathematic index which can easily be calculated from standard lipid profile and anthropometric parameter can act as an adjunct that significantly adds predictive value beyond that of the individual cardiometabolic risk factors but BAI cannot predict for subclinical atherosclerosis of both abdominal and non-abdominal obesity in perimenopausal/menopausal women.

What is already known on this topic?

The present study is not the first report of mathematic indexes and CIMT values but previous studies cannot be directly applied to abdominal and non-abdominal obesity of perimenopausal/menopausal specific subgroup in Thai population because of differences in ethnic groups and environmental factors provided for index cut off point in our study.

What this study adds?

It is important to observe a correlation between mathematic index and CIMT risk of developing subclinical atherosclerosis in non-overt CVD, which is of great significance in reducing the incidence of CVD among perimenopausal/menopausal women.

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Potential conflicts of interest

None.

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ดัชนีทางเมตทีเมติกใหม่ใช้ในการทำนายภาวะหลอดเลือดตีบแบบไม่แสดงอาการในสตรีวัยใกล้หมดประจำเดือน/วัยหมดประจำเดือนที่มีลักษณะความอ้วนที่แตกต่างกัน

ปัทมา ทองดี, พรทิพย์ นิมขุนทด

ภูมิหลัง: หลักฐานที่แสดงให้เห็นว่าค่าดัชนีไขมันและดัชนีความแข็งของหลอดเลือดเป็นปัจจัยเสี่ยงในการทำนายความเสี่ยงทางหัวใจและหลอดเลือดได้ดีกว่าปัจจัยเสี่ยงทางหัวใจและเมตาโบลิคเดิม การหาดัชนีทางการคำนวณ เมตทีเมติกใหม่ ทั้งค่าดัชนีไขมันและดัชนีความแข็งของหลอดเลือด เพื่อเป็นเครื่องมือที่ง่ายและสะดวกช่วยในการทำนายการเกิดหลอดเลือดตีบแบบไม่มีอาการ เพื่อใช้ในการติดตามประชากรที่มีความเสี่ยงต่อโรคหัวใจและหลอดเลือด

วัตถุประสงค์: เพื่อหาความสัมพันธ์ระหว่างค่าดัชนีไขมันและดัชนีความแข็งของหลอดเลือดในการบ่งชี้ภาวะหลอดเลือดตีบแบบไม่มีอาการ โดยใช้ค่าความหนาของไขมันที่หลอดเลือดแดงคาร์โรติดในกลุ่มจำเพาะที่มีอ้วนลงพุงและอ้วนแบบทั่วไปของสตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือน

วัสดุและวิธีการ: การศึกษาแบบตัดขวางผู้เข้าร่วมการศึกษา 130 คน อายุระหว่าง 40-80 ปี ตั้งแต่เดือนสิงหาคม พ.ศ. 2558 ถึง เดือนมกราคม พ.ศ. 2559 ในโรงพยาบาลมหาวิทยาลัยเทคโนโลยีสุรนารี ประเทศไทย ทำการวัดความหนาของไขมันชั้นในของหลอดเลือดแดงที่คอโดยใช้คลื่นเสียงความถี่สูง ทุกคนได้รับการวัดขนาดสัดส่วนร่างกายแบบดั้งเดิม ดัชนีมวลกาย รอบเอว ความดันโลหิต น้ำตาลในเลือด ระดับไขมัน และความหนาของไขมันที่หลอดเลือดคอ ค่าความค่าดัชนีความแข็งของหลอดเลือดและดัชนีไขมันสะสม

ผลการศึกษา: ข้อมูลจากสตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือน 130 คน พบว่า 41% มีภาวะอ้วนลงพุง ค่าดัชนีไขมันสะสม ดัชนีไขมันภายในสะสม ผลิตภัณฑ์ไขมันสะสม ดัชนีหลอดเลือดแข็งของพลาสมา ยกเว้นดัชนีไขมันของร่างกายและพื้นผิวร่างกายตามดัชนีรูปร่างที่มีความแตกต่างกันระหว่างอ้วนลงพุงและไม่อ้วนลงพุง $p = 0.01$, $p < 0.01$ และ $p = 0.03$ ตามลำดับ ค่าความหนาของไขมันเกาะหลอดเลือดคอสูงในลักษณะรูปแบบความอ้วนแตกต่างกัน ($p < 0.01$) ในภาวะอ้วนลงพุง ค่าดัชนีไขมันของร่างกาย ผลิตภัณฑ์ไขมันสะสม และดัชนีหลอดเลือดแข็งของพลาสมา มีความสัมพันธ์กับความหนาของไขมันที่หลอดเลือดที่คอ แต่มีเพียงค่าดัชนีหลอดเลือดแข็ง ของพลาสมาเป็นดัชนีเดียวที่มีความสัมพันธ์กับลักษณะที่ไม่ใช่อ้วนลงพุง

สรุป: การมีหลอดเลือดแดงของหัวใจตีบแบบไม่แสดงอาการระยะแรกในสตรีวัยใกล้หมดประจำเดือนและวัยหมดประจำเดือนที่มีภาวะอ้วนลงพุงสามารถคาดการณ์โดยใช้ดัชนีไขมันของร่างกาย ผลิตภัณฑ์ไขมันสะสมและดัชนีหลอดเลือดแข็งของพลาสมาและในกลุ่มที่ไม่อ้วนลงพุง มีเพียงค่าดัชนีหลอดเลือดแข็งของพลาสมาค่าเดียวที่มีความสัมพันธ์กับความหนาของไขมันที่หลอดเลือดที่คอ
