Application of Visceral Adiposity Index and Anthropometry to Identify Preclinical Atherosclerosis in Menopausal Status Women

Pattama Tongdee MD*, Ryan A. Loyd MD**,
Kaset Winwan MPolSc***, Porntip Nimkuntod MD****

** School of Obstetrics and Gynecology, Institute of Medicine, Suranaree University of Technology, Nakhon Ratchasima, Thailand*
*** School of Family and Community Medicine, Institute of Medicine, Suranaree University of Technology, Nakhon Ratchasima, Thailand*
**** Research Assistance, Nakhon Ratchasima, Thailand*
***** School of Internal Medicine, Institute of Medicine, Suranaree University of Technology, Nakhon Ratchasima, Thailand*

Background: *Obesity is associated with a major prevalence of cardiovascular risk factors and high risk of cardiovascular events and contributes to the increase in cardiovascular morbidity and mortality worldwide. Abdominal obesity is a main predictive factor of the metabolic syndrome, so it is certain that it represents a preferable marker of cardiovascular risk than generalized obesity. Visceral adiposity index (VAI) has recently been suggested to be used as a surrogate of visceral adiposity.*
Objective: *We compared the predictive abilities of the VAI with those of simple anthropometric measures in preclinical atherosclerosis, as assessed by ultrasonographic measurement of carotid intima media thickness (CIMT).*
Material and Method: *This is observational cross-sectional study involving 130 menopausal status women voluntarily recruited from Suranaree University of Technology Hospital, Thailand. Body mass index (BMI), waist circumference (WC), waist-hip ratio (WHR), waist-height ratio (WHtR) and lipid profile were determined. VAI was calculated. CIMT was assessed using a high-resolution B mode ultrasound system.*
Results: *Total 114/130 menopausal status participants, 16 participants were excluded from morbid obesity and high triglyceride >400 mg/dL. About 22.3% had preclinical atherosclerosis on carotid ultrasound. Positive correlation was found between CIMT and WC (r = 0.20, p = 0.04), and WHR (r = 0.25, p<0.01) and WHtR (r = 0.24, p = 0.01). However, there was no correlation between VAI and CIMT.*
Conclusion: *Using VAI instead of simple anthropometric measures may lead to loss of much information needed for predicting preclinical atherosclerosis. WC, WHR, and WHtR were both superior to VAI in predicting CIMT.*

Keywords: *Visceral adiposity index, Anthropometry, Preclinical atherosclerosis, Menopausal status women*

J Med Assoc Thai 2016; 99 (Suppl. 7): S30-S35
Full text. e-Journal: *http://www.jmatonline.com*

Premenopausal women appear to be protected from cardiovascular disease (CVD) compared with men of similar age. Although women below the age of 50 years rarely develop CVD, by age 70 years the incidence of CVD is equal in men and women, suggesting that estrogen deficiency causes a rapid acceleration in CVD risk. Framingham investigators found a 4-fold increase in CVD in the 10 years following natural menopause. Premature, surgically induced menopause has been shown to increase the risk for CVD(1). The metabolic syndrome (MS) has received more focus as the updated Adult Treatment Panel III guidelines emphasize treatment of the MS in addition to lowering of low-density lipoprotein cholesterol (LDL-C) levels(2). The MS may not be a single disease entity, but, rather, a constellation of closely related risk factors that together convey substantially increased cardiovascular risk after accounting for traditional CVD risk factors(3-5). Fat distribution have been observed in two pattern, the accumulation of fat at abdominal and gluteo-femoral region. The accumulation of fat in a central distribution has emerged as a cardiovascular risk factor independent of difference obesity phenotypes(6). Hormonal defect in menopausal transition has affected

Correspondence to:
Nimkuntod P, 111 School of Internal Medicine, Institute of Medicine, Suranaree University of Technology, Nakhon Ratchasima 30000, Thailand.
Phone: +66-81-7906061
E-mail: porntipnimk@sut.ac.th

to promotes the accumulation of gluteo-femoral fat[7] and increase in central fat[8]. The gender may be affected to adipose tissue distribution, which partially explain the greater CVD risk in men compared with premenopausal women. Waist circumference (WC) is a major clinical parameter used for the indirect evaluation of increased visceral fat[9]. Nevertheless, WC alone does not help in distinguishing between subcutaneous and visceral fat mass[10].

Visceral adiposity index (VAI) has recently been suggested to be used as a surrogate of visceral adiposity and its increase was strongly associated with cardiometabolic risk marker. The incident CVD risk corresponding to the VAI 2.3 was null. However, the slope of the dose-response association was steeper for VAI values smaller than 2.3 than those greater than 2.3. VAI values below 2.3 appeared to provide some protection against CVD[11]. Meanwhile, a given decrease in VAI levels below 2.3 would be accompanied by the same proportional reduction in risk of incident CVD regardless of the initial risk and previous reports showing the best cut-off point for VAI to be around 2.2[12]. VAI was significantly correlated to all MS factors and cardio- and cerebrovascular events. Amato et al[13] defined VAI as assuming VAI 1 in healthy non-obese subjects with normal adipose distribution and normal triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C) levels.

Material and Method

Study population

All 130 perimenopausal/menopausal participants without history of hormonal replacement therapy were individuals recruited from a physical examination center at Suranaree University of Technology Hospital in Thailand from February 2015 until January 2016. The study was approved by the Institutional Review Board of Suranaree University of Technology, and written informed consent was provided by all participants before enrollment.

Study protocol

At the baseline visit, women 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, total cholesterol (TC), TG, HDL-C, and LDL-C were measured by the central laboratories. Diabetes defined as self-reported diabetes treatment or a fasting glucose level $\geq$126 mg/dL was measured.

Definition of terms

Menopausal status women

Menopausal status women include perimenopausal and menopausal women. Participants were also asked about their menstrual bleeding patterns in the 12 months prior to recruitment, 1) Perimenopausal status of women age $\geq$40 years around menopause and had menstrual periods irregularity in the past 12 months, and 2) Menopausal status of those with no menstrual periods within the last 12 months.

Visceral adiposity index (VAI)

VAI score was calculated as described using the following sex specific equations[11], when TG level is expressed in mmol/l and HDL-C level is expressed in mmol/l.

Female VAI = WC/[36.58 + (1.89 x BMI)] x (TG/0.81) x (1.52/HDL-C)

Carotid intima media thickness (CIMT) 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, Toshiba) view of the far wall of the common carotid artery, carotid bulb, and 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.

Anthropometrics measurement

Body mass index (BMI) was calculated as weight in kilograms divided by height in square meters. 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. Waist-hip ratio (WHR) and waist-height ratio (WHtR) were calculated.

Statistical analysis

Statistical analyses were performed and continuous variables of the subjects at baseline were expressed as mean and standard deviation (SD). Differences between groups in univariate analysis were detected by the unpaired student's t-test for continuous variables and by the χ^2 test and Fisher's exact test (when appropriate) for categorical variables. The analysis of variance (ANOVA) trend analysis and the χ^2-test for trend were used to assess means and proportions of the population characteristics across the participants groups. All reported *p*-values were 2-tailed, and $p<0.05$ was considered statistically significant.

Results

The average age of normal range VAI <2.3 and abnormal range VAI ≥2.3 was 52.68±9.79 and 59.00±15.56 years old, respectively. No significant difference was observed in systolic blood pressure (SBP), diastolic blood pressure (DBP), BMI, WC, WHR, WHtR, and mean CIMT between both groups. However, for fasting blood sugar (FBS), it is found that high VAI was more likely to have higher fasting blood sugar (FBS) and TG than low VAI (Table 1).

Significant positive correlation was observed for WHtR with VAI ($p = 0.04$) and CIMT ($p = 0.01$). On the contrary, WC, WHR were correlated with CIMT

Table 1. Participants' characteristics according to baseline VAI

Baseline characteristics	VAI <2.3	VAI ≥2.3	*p*-value
Age (years)	52.68±9.79	59.00±15.56	0.37
Systolic blood pressure (mmHg)	125.05±16.11	133.00±2.83	0.49
Diastolic blood pressure (mmHg)	69.08±9.73	75.50±10.60	0.36
Waist circumference (cm)	83.07±9.96	85.09±5.39	0.78
Waist-height ratio	0.53±0.06	0.55±0.02	0.73
Waist-hip ratio	0.86±0.06	0.91±0.06	0.27
Body mass index (kg/m^2)	24.89±4.27	25.00±1.84	0.97
Fasting plasma glucose (mg/dL)	99.61±18.00	144.50±48.79	<0.01*
Creatinine (mg/dL)	0.82±0.13	0.77±0.09	0.63
Cholesterol (mg/dL)	220.71±46.19	248.00±31.11	0.41
Triglyceride (mg/dL)	117.17±49.41	229.00±63.64	<0.01*
High-density lipoprotein cholesterol (mg/dL)	58.10±13.62	41.35±0.49	0.09
Low-density lipoprotein cholesterol (mg/dL)	135.58±40.50	117.00±5.66	0.52
Carotid intima media thickness (mm)	0.71±0.15	0.68±0.11	0.79

* Significant difference at $p<0.05$.

Table 2. Correlation between anthropometric parameters and VAI, CIMT

Parameters	VAI		CIMT	
	r	*p*-value	r	*p*-value
Body mass index	0.13	0.18	0.03	0.74
Waist circumference	0.14	0.13	0.20	0.04*
Waist to hip ratio	0.17	0.07	0.25	<0.01*
Waist to height ratio	0.19	0.04*	0.24	0.01*
Carotid intima media thickness(mm)	-0.08	0.43	-	-

* Correlation is significant at the 0.05 level.

Table 3. Correlation between anthropometric parameters with VAI and CIMT

VAI group	WC		WHtR		WHR		BMI	
	χ^2	*p*-value	χ^2	*p*-value	χ^2	*p*-value	χ^2	*p*-value
<2.3	4.83	0.03*	3.11	0.08	4.83	0.03*	<0.01	0.98
$\geq$2.3	-	-	-	-	-	-	2.00	0.16
Total	4.80	0.03*	3.10	0.08	4.80	0.03*	0.03	0.87

* Correlation is significant at the 0.05 level

but were not correlated with VAI (Table 2).

Discrimination between groups of normal and abnormal in VAI, CIMT range was correlated with WC, WHR anthropometric parameters ($p = 0.03$), ($p = 0.03$) respectively (Table 3).

Discussion

In this study, the VAI was independently associated with WC and WHR suggesting that the central obesity marker could be useful for predicting of VAI. In our study, VAI was correlated with both WC and WHR but was not correlated with the BMI. The finding suggest that these two measurements might reflect total fat accumulation but not visceral adiposity. WC is a major clinical parameter used for the indirect evaluation of increased visceral fat(10). Many longitudinal studies have shown that TG levels increase with the transition through the menopause(14) and the increase in TG also appears early in the postmenopausal period(15). TG increases in middle-age in women, but not in men(16). In this study, high FBS in VAI $\geq$2.3 than VAI <2.3 (p<0.01) same as previous study that high VAI scores and the hypertriglyceridemic waist phenotype are strongly associated with diabetes risk(17,18). In this study incidence of subclinical atherosclerosis were found lower than previous study (22.3 vs. 35.1%)(19).

Another important limitation to consider is the application of the VAI in non-Caucasian populations and numerical factors of the index arise from healthy Caucasian men and women. The application of VAI in the following populations: healthy or apparently healthy population with BMI <40 kg/m^2, one or two risk factors of the MS, polycystic ovarian syndrome (PCOS), and endocrine disorders(20).

The study has one or two metabolically unhealthy risk of MS in menopausal status women and excludes morbid obesity. Accumulation of excess abdominal fat with transition through the menopause plays a central role in connecting the MS with the metabolic alterations of menopause because main harm caused by obesity is visceral adipose accumulation(21). This subset of women may require targeted management to prevent future cardiovascular risk. Current evidence implies that multiple risk factors for CVD emerge in the postmenopausal period, but features of the MS may be present even before menopause.

Conclusion

Although VAI is not a diagnostic tool for subclinical atherosclerosis by using CIMT marker, the simplicity of WC and BMI measurement and TG and HDL-C assessment, make it an easily applicable index for the evaluation of visceral fat dysfunction. VAI might therefore be a useful tool in daily clinical practice and in high risk population studies for the assessment of cardiometabolic risk associated with visceral obesity.

What is already known on this topic?

The present study is not the first report adiposity index correlation with early atherosclerosis CIMT values in but previous studies cannot be directly applied to low cardiovascular risk factors of perimenopausal/menopausal group in Thailand and because of differences in ethnic groups and environmental factors provided for cardio-metabolic risks in our study.

What this study adds?

VAI, in our study, will not allow the application of early atherosclerosis comparable with simple anthropometric parameter in individual specific menopausal status participants.

Acknowledgements

We thank all who participated in the study, the staff at cardiovascular clinic and menopause clinic of Suranaree University of Technology Hospital who assisted the study. This study is supported by the grant from Suranaree University of Technology.

Potential conflicts of interest

None.

References

1. Gohlke-Barwolf C. Coronary artery disease—is menopause a risk factor? Basic Res Cardiol 2000; 95 (Suppl 1): I77-83.
2. Executive Summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 2001; 285: 2486-97.
3. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA 2002; 288: 2709-16.
4. Nimkuntod P, Tongdee P. Association between subclinical atherosclerosis among hyperlipidemia and healthy subjects. J Med Assoc Thai 2015; 98 (Suppl 4): S51-7.
5. Nimkuntod P, Tongdee P. Plasma low-density lipoprotein cholesterol/high-density lipoprotein cholesterol concentration ratio and early marker of carotid artery atherosclerosis. J Med Assoc Thai 2015; 98 (Suppl 4): S58-63.
6. Krotkiewski M, Bjorntorp P, Sjostrom L, Smith U. Impact of obesity on metabolism in men and women. Importance of regional adipose tissue distribution. J Clin Invest 1983; 72: 1150-62.
7. Poehlman ET, Toth MJ, Gardner AW. Changes in energy balance and body composition at menopause: a controlled longitudinal study. Ann Intern Med 1995; 123: 673-5.
8. Hadaegh F, Harati H, Ghanbarian A, Azizi F. Association of total cholesterol versus other serum lipid parameters with the short-term prediction of cardiovascular outcomes: Tehran Lipid and Glucose Study. Eur J Cardiovasc Prev Rehabil 2006; 13: 571-7.
9. Mathieu P, Pibarot P, Larose E, Poirier P, Marette A, Despres JP. Visceral obesity and the heart. Int J Biochem Cell Biol 2008; 40: 821-36.
10. Pouliot MC, Despres JP, Lemieux S, Moorjani S, Bouchard C, Tremblay A, et al. Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. Am J Cardiol 1994; 73: 460-8.
11. Mohammadreza B, Farzad H, Davoud K, Fereidoun Prof AF. Prognostic significance of the complex “Visceral Adiposity Index” vs. simple anthropometric measures: Tehran lipid and glucose study. Cardiovasc Diabetol 2012; 11: 20.
12. Amato MC, Giordano C, Pitrone M, Galluzzo A. Cut-off points of the visceral adiposity index (VAI) identifying a visceral adipose dysfunction associated with cardiometabolic risk in a Caucasian Sicilian population. Lipids Health Dis 2011; 10: 183.
13. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, et al. Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. Diabetes Care 2010; 33: 920-2.
14. Jensen J, Nilas L, Christiansen C. Influence of menopause on serum lipids and lipoproteins. Maturitas 1990; 12: 321-31.
15. Matthews KA, Kuller LH, Sutton-Tyrrell K, Chang YF. Changes in cardiovascular risk factors during the perimenopause and postmenopause and carotid artery atherosclerosis in healthy women. Stroke 2001; 32: 1104-11.
16. Razay G, Heaton KW, Bolton CH. Coronary heart disease risk factors in relation to the menopause. Q J Med 1992; 85: 889-96.
17. Du T, Sun X, Huo R, Yu X. Visceral adiposity index, hypertriglyceridemic waist and risk of diabetes: the China Health and Nutrition Survey 2009. Int J Obes (Lond) 2014; 38: 840-7.
18. Chen C, Xu Y, Guo ZR, Yang J, Wu M, Hu XS. The application of visceral adiposity index in identifying type 2 diabetes risks based on a prospective cohort in China. Lipids Health Dis 2014; 13: 108.
19. Maturana MA, Franz RF, Metzdorf M, da Silva TR, Spritzer PM. Subclinical cardiovascular disease in postmenopausal women with low/ medium cardiovascular risk by the Framingham risk score. Maturitas 2015; 81: 311-6.
20. Amato MC, Giordano C. Visceral adiposity index: an indicator of adipose tissue dysfunction. Int J Endocrinol 2014; 2014: 730827.
21. Fontana L, Eagon JC, Trujillo ME, Scherer PE, Klein S. Visceral fat adipokine secretion is associated with systemic inflammation in obese humans. Diabetes 2007; 56: 1010-3.

การใช้ค่าดัชนีไขมันภายในสะสมและการวัดรูปร่างแบบทั่วไปในการทำนายการเกิดหลอดเลือดแดงแข็งระยะก่อนเกิดอาการทางคลินิกของสตรีช่วงวัยหมดประจำเดือน

ปัทมา ทองดี, ไรอัน เอ ลอยด์, เกษตร วิณวันก์, พรทิพย์ นิ่มขุนทด

ภูมิหลัง: *ความอ้วนมีความสัมพันธ์กับการเกิดปัจจัยเสี่ยงทางหัวใจและหลอดเลือด และความเสี่ยงสูงในการเกิดอาการทางโรคหัวใจทำให้เพิ่มอัตราการเสียชีวิตในโลก ภาวะอ้วนลงพุงเป็นตัวบ่งชี้ในการเกิดกลุ่มอาการเมตาโบลิก ดังนั้นเป็นตัวแทนที่ดีของความเสี่ยงทางหัวใจและหลอดเลือดมากกว่าอ้วนแบบทั่วไป ดัชนีไขมันภายในสะสม ปัจจุบันได้ถูกแนะนำให้นำมาใช้เพื่อเป็นตัวแทนของภาวะไขมันสะสม*

วัตถุประสงค์: *เพื่อประเมินความสามารถของดัชนีไขมันภายในสะสมกับการวัดรูปร่างแบบทั่วไปในการทำนาย ความหนาของไขมันที่หลอดเลือดแดงคาร์โรติด*

วัสดุและวิธีการ: *การศึกษาสังเกตแบบตัดขวาง สตรีช่วงวัยหมดประจำเดือน 130 คน ที่สมัครใจเข้าการศึกษาของโรงพยาบาลมหาวิทยาลัยเทคโนโลยีสุรนารี ประเทศไทย ดัชนีมวลกาย รอบเอว อัตราส่วนรอบเอวต่อความสูง อัตราส่วนรอบเอวต่อรอบสะโพก และค่าไขมันในเลือด คำนวณค่าดัชนีไขมันภายในสะสม มีการวัด ความหนาของไขมันที่หลอดเลือดแดงคาร์โรติดด้วยคลื่นเสียงความถี่สูง*

ผลการศึกษา: *114 คน ของสตรีช่วงวัยหมดประจำเดือน 130 คน โดยคัดออก 16 คนจากอ้วนรุนแรงและมีค่าไขมันไตรกรีเซอไรด์มากกว่า 400 มิลลิกรัมต่อเดซิลิตร พบมีความผิดปกติของหลอดเลือดแดงตีบแบบไม่มีอาการ 22.3% ค่าความหนาของไขมันที่หลอดเลือดแดงคาร์โรติด มีความสัมพันธ์กับรอบเอว ($r = 0.20$, $p = 0.04$) อัตราส่วนรอบเอวต่อรอบสะโพก ($r = 0.25$, $p<0.01$) อัตราส่วนรอบเอวต่อความสูง ($r = 0.24$, $p = 0.01$) แต่พบว่าไม่มีความสัมพันธ์ของค่าดัชนีไขมันภายในสะสมกับค่าความหนาของไขมันที่หลอดเลือดแดงคาร์โรติด*

สรุป: *การใช้ค่าดัชนีไขมันภายในสะสมแทนการวัดรูปร่างแบบดั้งเดิมอาจทำให้สูญเสียข้อมูลบางส่วนที่ใช้ในการทำนายหลอดเลือดแข็งก่อนเกิดอาการไป ค่ารอบเอว อัตราส่วนรอบเอวต่อรอบสะโพก และอัตราส่วนรอบเอวต่อความสูง สามารถทำนายการเกิดความหนาของไขมันที่หลอดเลือดแดงคาร์โรติดได้ดีกว่าดัชนีไขมันภายในสะสม*