Evaluation of Metabolic Syndrome Risk in Korean Premenopausal Women

—— Not Waist Circumference but Visceral Fat ——

Yae Jung Hyun, PhD*,**; Oh Yoen Kim, PhD*,**; Yangsoo Jang, MD, PhD, FACC**,†,††; Jong-Won Ha, MD, PhD†; Jey Sook Chae, PhD*,**; Ji Young Kim, PhD*,**; Hyun Yang Yeo, MS‡; Jean Kyung Paik, MS*,‡‡; Jong Ho Lee, PhD, RD*,**,‡‡

Background In clinical practice, using the patient's waist circumference (WC) to evaluate visceral obesity may underestimate disorders with a metabolic origin. This study examined whether or not the WC derived from the cut-off point of the visceral fat area (VFA) can reflect the features of metabolic syndrome (MetS) in premenopausal women.

Methods and Results Computed tomography-scanned VFA, MetS components and the concentrations of high-sensitivity C-reactive protein (CRP) and adiponectin were measured in a total of 349 premenopausal women. The VFA at the L1 and the L4 sites was a significant index ($p<0.001$) of incremental MetS risk. Receiver-operating characteristic curve analysis showed that 75 cm^2 of VFA at L4 and 87.5 cm^2 at L1 were the optimal thresholds for discrimination of MetS risk. Significant differences in all MetS components, as well as CRP ($p<0.05$) and adiponectin levels ($p<0.005$), were observed when subjects were subdivided by the L4 VFA cut-off point (<75/≥75 cm^2), whereas there was a significant difference only in the triglycerides level in the groups divided by WC (WC <88/≥88 cm). Moreover, subjects with a lower WC – higher VFA showed a similar pattern in MetS components and lower adiponectin than those with a higher WC – higher VFA.

Conclusions This study clarified that VFA rather than WC is a major determinant of MetS risk in premenopausal women. (*Circ J* 2008; **72:** 1308 – 1315)

Key Words: Metabolic syndrome; Premenopausal women; Visceral fat; Waist circumference

A simple anthropometric measurement, such as waist circumference (WC) or waist to hip ratio (WHR), is widely used in clinical practice as a surrogate for central obesity in order to assess health status[1,2] However, for a given WC, body fat distribution differs significantly according to gender, menopausal status, age, and so forth[3,4] Particularly in premenopausal women, subcutaneous fat is relatively predominant over abdominal visceral fats[5] and so using WC to evaluate visceral obesity could underestimate metabolic disorders.

Metabolic syndrome (MetS) is a major public health challenge because of its implications in the increased risk of type 2 diabetes and cardiovascular disease (CVD)[6,7] During the past decade, various sets of diagnostic criteria for MetS have been proposed[8–11] and all share the major metabolic risk factors (RF) such as abdominal obesity, insulin resistance/glucose intolerance, dyslipidemia and hypertension. However, there are 2 major differences in the organization of the criteria and the emphasis on excessive adiposity[8–11] Thus, discrepant cases are often reported in studies of the prevalence of MetS, or in the subjects' characteristics classified to MetS, depending on the definition used[12–14] Currently, the International Diabetes Federation (IDF) criteria[11] which define WC as an obligatory factor for diagnosing MetS, are under discussion for thier inability to detect metabolically abnormal but non-obese individuals[12,15]

In addition, a WHO expert consultation addressed the fact that Asians generally have a higher percentage of body fat and show greater abdominal obesity at a lower body mass index (BMI) than Caucasians[16] The consultation also identified an additional trigger point for public health action or clinical intervention as being 23 kg/m^2 BMI because the relative risk for type 2 diabetes or CVD in Asian populations is substantial, even below 25 kg/m^2 BMI.

Therefore, in order to evaluate the risk of MetS in premenopausal Asian women, the present study aimed to (a) elucidate the best marker of central obesity among the obesity-related anthropometric indices including computed tomography (CT) results, (b) define the optimal cut-off point of visceral fat area (VFA) in premenopausal women and (c) examine whether or not the WC derived from the cut-off point of the VFA can also reflect the features of MetS, particularly in subjects with BMI ≥23 kg/m^2.

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**National Research Laboratory of Clinical Nutrigenetics/Nutrigenomics, Yonsei University, **Yonsei University Research Institute of Science for Aging, Yonsei University, †Cardiology Division, Yonsei Cardiovascular Center, Yonsei University College of Medicine, ††Cardiovascular Genome Center, Yonsei Medical Institute, ‡Interdisciplinary Program: Science for Aging and ‡‡Brain Korea 21 Project, Department of Food & Nutrition, College of Human Ecology, Yonsei University, Seoul, Korea*

Mailing address: Jong Ho Lee, PhD, RD, Department of Food & Nutrition, College of Human Ecology, Yonsei University, 134 Shinchon-Ding, Sudaemun-Gu, Seoul, 120-749, Korea. E-mail: yhe909@yonsei.ac.kr

Methods

Study Subjects

A total of 349 premenopausal Korean women with a mean age of 36±0.5 years (range 20–56) and BMI of 26.7±0.2 kg/m^2 (range 23.0–37.8) were recruited from participants in a clinical study conducted by the National Research Laboratory of Clinical Nutrigenetics and Nutrigenomics (Program #R0A-2005-000-10144-0) in Yonsei University. All subjects had BMI 23 kg/m^2 qualifying them as overweight or obese according to the Asia-Pacific Guideline![6] Premenopausal was defined as not experiencing menopause, which were checked by self-report of the regularity of the menstrual cycle. Subjects were excluded from the study for the following: (1) CVD, peripheral vascular disease, or stroke; (2) diabetes (fasting serum glucose ≥126 mg/dl or 2-h serum glucose ≥240 mg/dl after a 75-g oral glucose tolerance test); (3) orthopedic limitations; (4) thyroid or pituitary disease; (5) pregnant or breast feeding or intending to become pregnant during the study, (6) infection according to medical questionnaire examination; (7) acute or chronic inflammatory disease. Written informed consent was given by all subjects and the protocol was approved by the Institutional Review Board of Yonsei University.

Definitions of MetS

MetS was defined according to the 2005 guidelines of the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) criteria[10] or the IDF criteria![11] The revised National Cholesterol Education Panel (NCEP) criteria proposed by the AHA/NHLBI defines MetS as the presence of ≥3 of the following clinical criteria: (1) WC ≥80 cm; (2) systolic blood pressure (BP) ≥130 mmHg and/or diastolic BP ≥85 mmHg or self-report of taking medication for hypertension; (3) high-density lipoprotein (HDL)-cholesterol (C) <50 mg/dl (1.29 mmol/L); (4) triglycerides (TG) ≥150 mg/dl (1.69 mmol/L) or self-report of taking medication for hyperlipidemia; and (5) fasting plasma glucose ≥100 mg/dl (5.6 mmol/L). The IDF defined MetS as the presence of central obesity (WC ≥80 cm) plus 2 other RF: the other 4 components of the IDF-MetS were the same as the AHA/NHLBI criteria.

Anthropometric Parameters and BP

Body weight and height were measured unclothed and without shoes in the morning for the calculation of BMI. WC was measured at the umbilicus after normal expiration with the subject standing and the hip girth was measured at the widest part of the hip, from which the WHR was calculated. BP was measured in the left arm of the seated patient with an automatic BP monitor (TM-2654, A&D, Tokyo, Japan) after a 20-min rest; the average of 3 measurements was recorded for each subject.

CT measurement of Abdominal Fat at the Level of the 1st and 4th Lumbar (L1 and L4) Vertebrae

Abdominal fat area was measured by CT scanning using a General Electric (GE) High Speed Advantage 9800 scanner (Milwaukee, WI, USA). Two cross-sectional images were obtained for each subject at the level of the L1 and L4 vertebra. Each CT slice was analyzed for the cross-sectional area of fat using a density control program available in the standard GE computer software. Parameters for total abdominal fat density at the levels of L1 and L4 were selected between the range of –150 and –50 Hounsfield units. Total abdominal fat area was divided into visceral (VFA) and subcutaneous fat areas (SFA) to calculate the specific areas of fat. By subtracting the abdominal visceral adipose tissue area from the total adipose tissue area, the abdominal subcutaneous area was obtained.

Serum Lipids, Glucose, Insulin and Homeostasis Model Assessment (HOMA)-Insulin Resistance (IR)

Fasting serum concentrations of total cholesterol and TG were measured using commercially available kits on a Hitachi 7150 autoanalyzer (Hitachi Ltd, Tokyo, Japan). After precipitation of serum chylomicrons, low-density lipoprotein (LDL) and very-LDL with dextran sulfate-magnesium, the HDL-C level was measured enzymatically. LDL-C was estimated indirectly using Friedewald's formula for subjects with serum TG concentrations <4.52 mol/L (400 mg/ml) and directly measured for subjects with serum TG concentration 4.52 mol/L. Glucose was measured by a glucose oxidase method using a Beckman Glucose Analyzer (Beckman Instruments, Irvine, CA, USA) and insulin by radioimmunoassay with a commercial kit from Immuno Nucleo Corporation (Stillwater, MN, USA). IR was calculated with the HOMA using the following equation: IR = {fasting insulin (μU/ml) × fasting glucose (mmol/L)}/22.5![16]

Plasma LDL Particle Size

The distribution of the particle sizes of LDL (d=1.019–1.063 g/ml) was performed by sequential flotation ultracentrifugation and examined by a pore-gradient lipoprotein system (CBS Scientific, Solana Beach, CA, USA) using commercially available non-denaturing polyacrylamide 2–16% gradient slab gels (Alamo Gels Inc, San Antonio, TX, USA). The relative migration (Rf) rates of each band were estimated using the following standards: latex beads (34 nm), thyroglobulin (17 nm), apoferritin (12.2 nm) and catalase (10.4 nm). The gels were scanned with a GS-800 Calibrated Imaging Densitometer (Bio-Rad Laboratories, Graz, Austria). LDL particle size was calculated using the Rf values of the standards as a reference.

Serum High-Sensitivity C-Reactive Protein (hs-CRP) and Plasma Adiponectin Levels

Serum hs-CRP levels were measured with an Express$^+$ autoanalyzer (Chiron Diagnostics Co, Walpole, MA, USA) using a commercially-available, hs-CRP-Latex (II) X2 kit (Seiken Laboratories Ltd, Tokyo, Japan) that allowed detection of CRP levels as low as 0.001 mg/dl and as high as 32 mg/dl. Plasma adiponectin concentration was measured, in duplicate, using an enzyme immunoassay (Human Adiponectin ELISA kit, B-Bridge International Inc, Sunnyvale, CA, USA).

Statistical Analysis

We used SPSS version 12.0 for Windows (SPSS Inc, Chicago, IL, USA) for all statistical analyses. Each variable was examined for normality, and non-normally distributed variables were tested after log-transformation. Results are expressed as mean±SE. Continuous variables were compared by general linear model followed by Bonferroni test, with age, BMI and smoking status as covariates, and frequency distributions were tested by chi-square test. A stepwise regression analysis was performed to identify the most significant indices representing body fat distribution of MetS risk. Excepting WC, MetS components were used as dependent variables and obesity-related anthropometric in-

Table 1 Characteristics of the Study Population

	Premenopausal women (n=349)
Age (years)	*36.4±0.48*
BMI (kg/m²)	*26.7±0.16*
Current smokers (n (%))	*30 (8.6)*
Body fat (%)	*35.8±0.28*
Waist (cm)	*87.5±0.38*
L1 VFA (cm²)	*87.7±1.79*
L1 SFA (cm²)	*146.9±2.30*
L4 VFA (cm²)	*74.1±1.29*
L4 SFA (cm²)	*207.4±2.58*
Systolic BP (mmHg)	*115.5±0.79*
Diastolic BP (mmHg)	*75.2±0.58*
Triglyceride (mg/dl)	*127.2±3.64*
HDL-C (mg/dl)	*49.4±0.65*
Fasting glucose (mg/dl)	*84.8±0.49*
Fasting insulin (μIU/ml)	*10.6±0.29*
HOMA-IR	*2.23±0.07*
LDL particle size (nm)	*26.1±0.05*
hs-CRP (mg/dl)	*0.74±0.07*
Adiponectin (μIU/ml)	*6.19±0.19*

Mean ± SE.
BMI, body mass index; VFA, visceral fat area; SFA, subcutaneous fat area; BP, blood pressure; HDL-C, high-density lipoprotein-cholesterol; HOMA, homeostasis model assessment; IR, insulin resistance = {fasting insulin (μIU/ml) × fasting glucose (mmol/L)}/22.5; LDL, low-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein.

dices, including CT results (BMI, % body fat, WC, WHR, VFA, and SFA at L1 and L4 levels), as well as age, were used as independent variables. Receiver-operating characteristic (ROC) curve analysis was applied to determine the cut-off point of VFA associated with an elevated risk of MetS. The optimal cut-off points were estimated as the mean values of VFA, together with 2 cases according to the number of RF for MetS, excepting WC (MetS RF 0–1, ≥2 or MetS RF 0–2, ≥3). The cut-off value producing the best combination of sensitivity and specificity was selected as the optimal threshold for each parameter. Next, the WC value corresponding to each VFA was calculated by simple regression analysis. In order to observe the contribution of VFA to MetS risk-related factors, we compared groups subdivided by WC and VFA by a general linear model followed by Bonferroni test with adjustment of age, BMI and smoking status. A p-value of less than 0.05 was considered to be statistically significant.

Results

Characteristics of the Study Population

Table 1 lists the characteristics of the study subjects. All were premenopausal women and the distribution of BMI was 32.7% were 23≤BMI<25 kg/m², 54.2% were 25≤BMI <30 kg/m² and 13.2% were ≥BMI 30 kg/m². The prevalence of AHA/NHBLI-MetS was 26.6% (n=93) and that of IDF-MetS was 27.8% (n=97). Among the frequencies of individual MetS components, a larger WC was the most frequent at 89.1%, elevated TG level was 26.4%, lower HDL-C was 53.9%, higher BP was 22.3% and higher fasting glucose was 5.4%. None of participants was taking lipid-lowering medications, but 6 subjects (1.7%) used antihypertensive medications.

Best Marker of the Risk of MetS

A stepwise linear regression analysis was performed to identify the most representative indices of body fat distribution for the risk of MetS. It was analyzed in 2 categories (MetS RFs 0–1, ≥2 and MetS RFs 0–2, ≥3) as dependent variables, with MetS components excluding WC, which was included as an independent variable (age, BMI, % body fat, WC, WHR, VFA, and SFA at L1 and L4 levels). We found that VFA at the L1 level (upper abdomen) (MetS RFs 0–1 and ≥2, β=0.29, p<0.001) as well as at the L4 level (lower abdomen) (MetS RFs 0–2 and ≥3, β=0.24, p<0.001) were the most relevant indices of incremental risk of MetS.

Optimal Cut-off Point of VFA for MetS

Based on the results from the stepwise regression test, we determined the optimal cut-off threshold of VFA as the mean values of 2 cases (MetS RFs ≥2 and MetS RFs ≥3) (Fig 1). The largest mean values of sensitivity and specificity for VFA at the L4 level detected in subjects with MetS RFs ≥2 was 72.5 cm² (sensitivity=0.69, specificity=0.62)

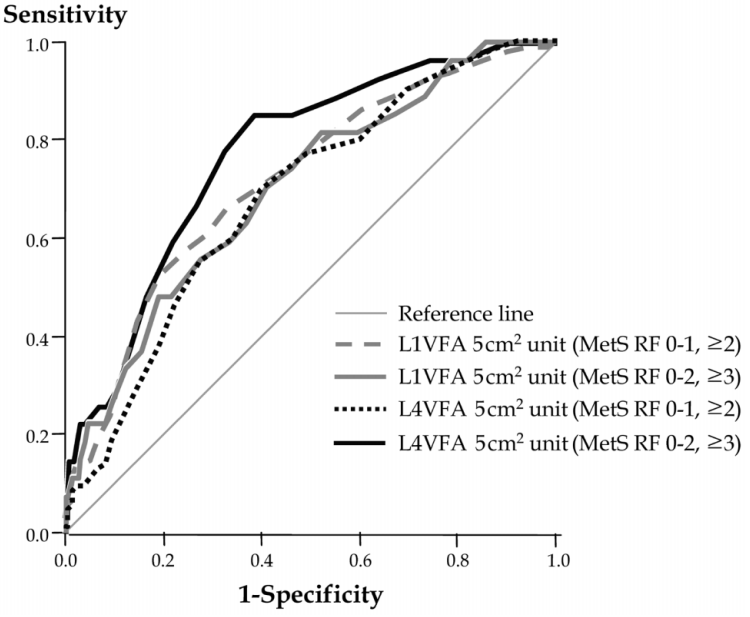

Fig 1. Receiver-operating characteristic curves for visceral fat area measured at 1st and 4th lumbar (L1VFA and L4VFA) for discrimination of metabolic syndrome (MetS) risk. MetS risk factors (RF) excluding waist circumference (triglycerides ≥150 mg/dl, high-density lipoprotein <50 mg/dl, blood pressure ≥130 or ≥85 mmHg, fasting glucose ≥100 mg/dl).

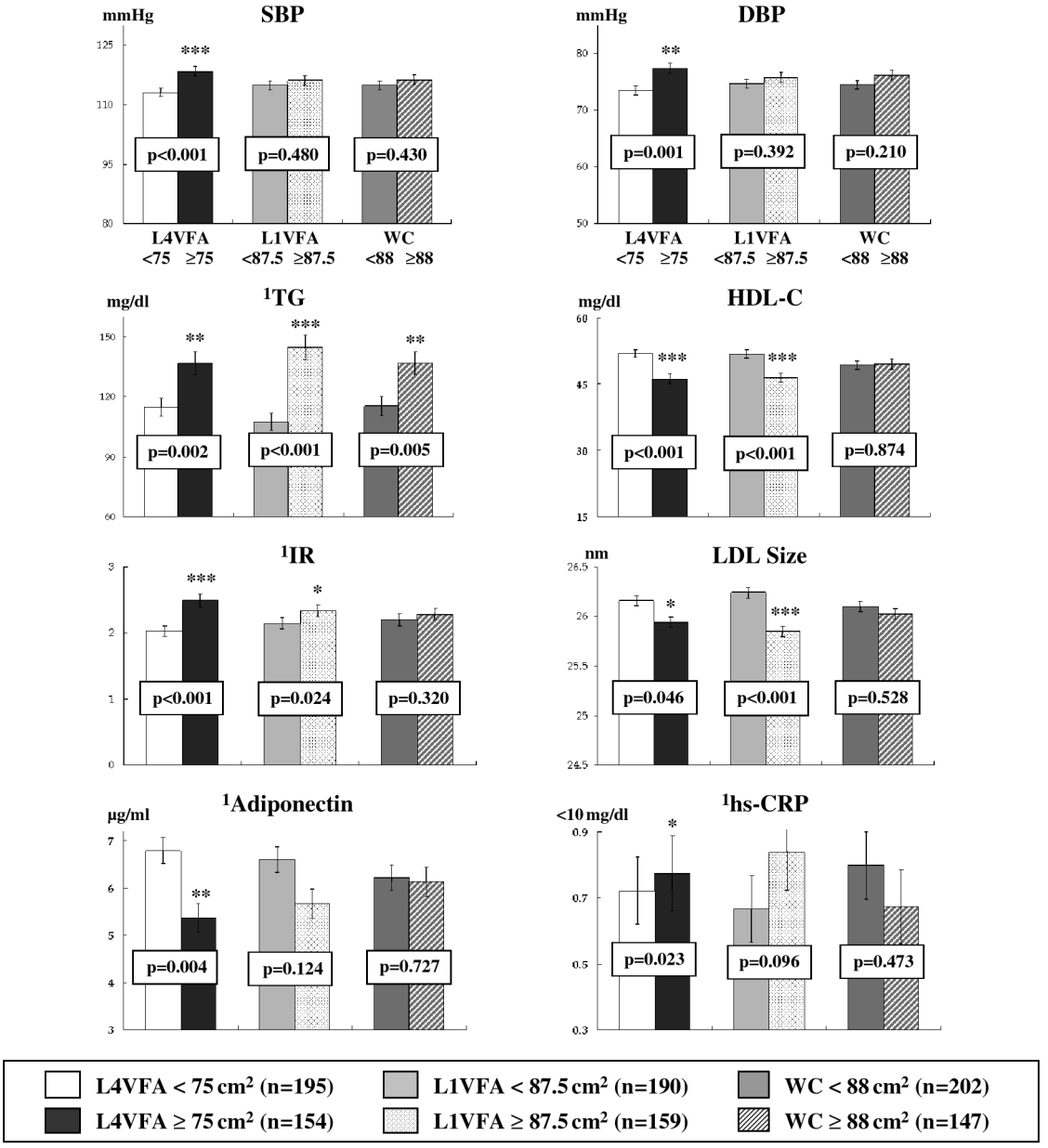

Fig 2. Adjusted mean values of metabolic syndrome (MetS) risk-related variables according to each cut-point of visceral fat area (VFA) and the corresponding waist circumference (WC) in premenopausal women. Adjusted means, [1]Tested by log-transformed; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; IR, insulin resistance = {fasting insulin (µIU/ml) × fasting glucose (mmol/L)}/22.5; LDL, low-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; L1, 1st lumbar; L4, 4th lumbar. ***p<0.001, **p<0.01, *p<0.05 significantly different from the normal group in each category tested by a general linear model followed by Bonferroni test adjusted for age, body mass index, and smoking status.

and in the subjects with MetS RFs ≥3 it was 77.5 cm^2 (sensitivity=0.85, specificity=0.64). The area under the ROC curve (AUC) was 0.68±0.03 (p<0.001) for MetS RF ≥2 and 0.77±0.04 (p<0.001) for MetS RF ≥3. Analysis of the ROC curve of VFA at the L1 level showed that the largest mean value of sensitivity and specificity detected in both the subjects with MetS RF ≥2 (sensitivity=0.66, specificity=0.67) and those with MetS RFs ≥3 (sensitivity=0.79, specificity=0.59) was 87.5 cm^2. The AUC was 0.72±0.03 (p<0.001) for MetS RFs ≥2 and 0.70±0.05 (p<0.001) for MetS RFs ≥3. Therefore, 75 cm^2 of VFA measured at L4 and 87.5 cm^2 at L1 were the optimal cut-off thresholds for determining the risk of MetS in premenopausal women.

Estimation of WC Corresponding to the VFA

The WC corresponding to the optimal cut-off point of VFA was estimated by regression equation for the relationship between the WC and VFA. WC correlated positively with VFA at the L4 level (r=0.54, p<0.001) and at L1 the level (r=0.63, p<0.001). WC was found to be more correlated with SFA at both the L1 (r=0.759, p<0.001) and L4 level (r=0.625, p<0.001) than with the respective VFA. The WC corresponding to 75 cm^2 of VFA at L4 was 88.0 cm (L4VFA=1.8217 (waist)–85.216) and that corresponding

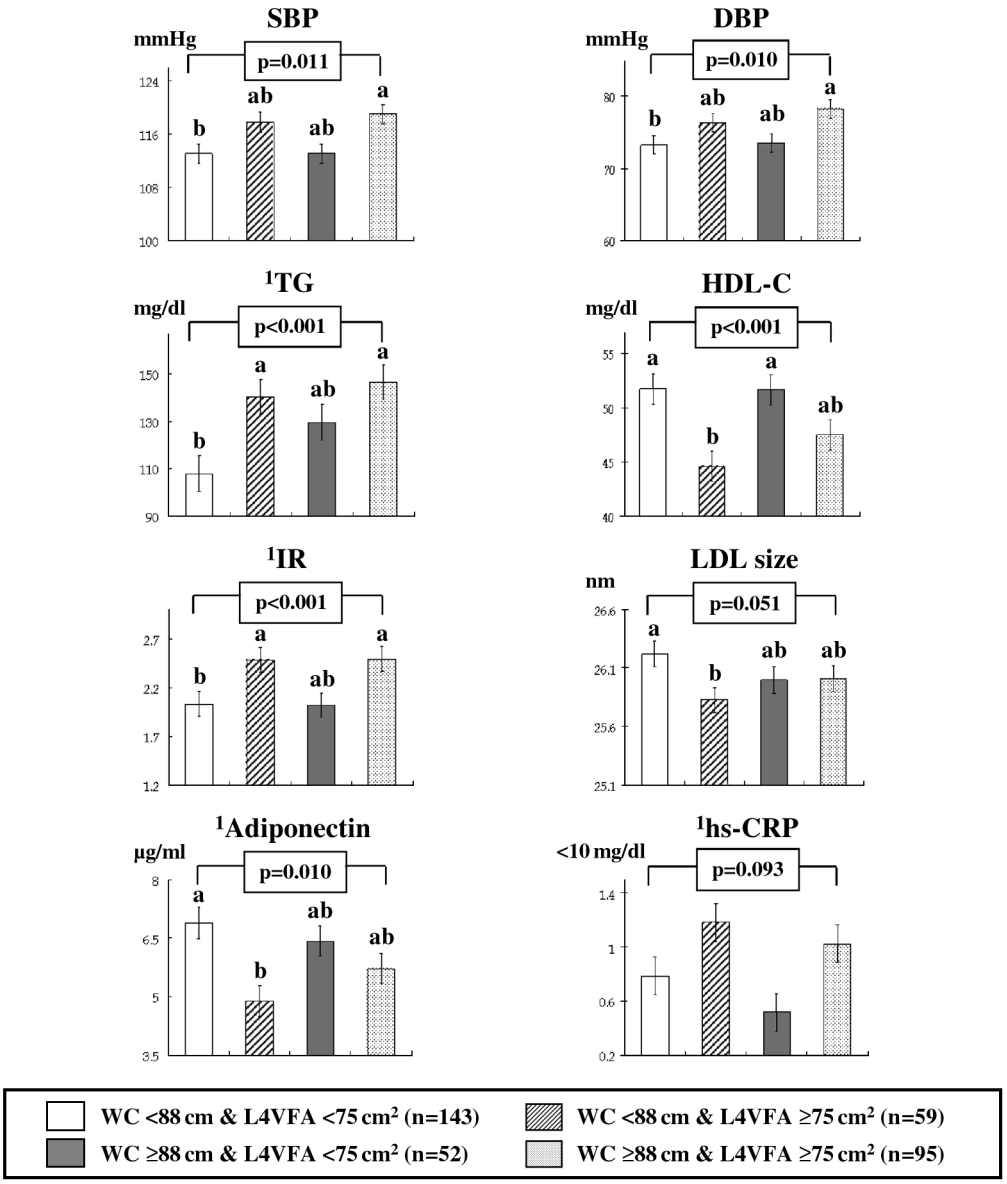

Fig 3. Adjusted mean values of metabolic syndrome (MetS) risk-related variables according to the cut-off point of visceral fat area (VFA) 75 cm^2 and waist circumference (WC) 88 cm. Adjusted means, [1]Tested by log-transformed; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; IR, insulin resistance = {fasting insulin (μIU/ml) × fasting glucose (mmol/L)}/22.5; LDL, low-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; L1, 1st lumbar; L4, 4th lumbar. Different letters indicate significant difference at $p<0.05$ based on a general linear model with Bonferroni method adjusted for age, body mass index, and smoking status.

to 87.5 cm^2 of VFA at L1 was 87.4 cm (L1VFA=2.9056 (waist)−166.39). Because the position for measuring WC was more correct at L4 than at L1, we finally selected 88 cm WC for our examination of the relationship with VFA.

Comparison of the Cut-off Points of VFA and WC Derived From VFA for MetS Risk-Related Variables

To determine whether the WC derived from the mean cut-off point of VFA can be used as a cut-off point reflecting the risk of MetS, we subdivided subjects into 2 groups according to each of 3 categories: the cut-point of VFA at L4 (L4VFA<75, ≥75 cm^2) and at L1 (L1VFA<87.5, ≥87.5 cm^2), and the WC (WC<88, ≥88 cm). Fig 2 shows the mean values of the MetS components and other-related variables adjusted for age, BMI, and smoking status according to these categories. Interestingly, we found significant differences in all the variables related to MetS risk when subdivided by the L4VFA cut-off point (75 cm^2), BP ($p<0.001$), TG ($p=0.002$), HDL-C ($p<0.001$), HOMA-IR ($p<0.001$), LDL size ($p=0.046$), adiponectin ($p=0.004$) and CRP ($p=0.023$). We also observed significant differences in TG ($p<0.001$), HDL-C ($p<0.001$), HOMA-IR ($p=0.024$), and LDL particle size ($p<0.001$) between the subgroups when divided by the L1VFA cut-off point (87.5 cm^2). On the other hand, when sub divided by the WC<88, ≥88 cm, the groups showed a significant difference only in the TG level ($p=0.005$) after adjustment for age, BMI and smoking status.

Contribution of VFA at L4 to MetS Risk Variables When Subdivided by WC

To investigate the contribution of VFA on MetS risk more precisely, we subdivided the study population into 4 groups according to WC (88 cm) and the cut-off point at L4VF (75 cm^2): (1) lower WC – lower VFA (WC <88 cm & L4VF <75 cm^2, n=143), (2) lower WC–higher VFA (WC <88 cm & L4VF ≥75 cm^2, n=59), (3) higher WC – lower VFA (WC ≥88 cm & L4VF <75 cm^2, n=52), and (4) higher WC – lower VFA (WC ≥88 cm & L4VF ≥75 cm^2, n=95) (Fig 3). Interestingly, among the 4 groups subjects with a lower WC – higher VFA showed a similar status in MetS components (elevated BP, high TG, low HDL-C, and high HOMA-IR index) and lower plasma adiponectin to those with a higher WC – higher VFA. Even though the differences in CRP among the 4 groups were not statistically significant (p=0.093), subjects with a lower WC – higher VFA had a high CRP concentration as did subjects with a higher WC – higher VFA.

Discussion

The present study results demonstrate that visceral adiposity is a major determinant of evaluating the risk of MetS in premenopausal women. Our subjects with a VFA ≥75 cm^2 showed distinctive features of MetS, together with higher levels of CRP and lower levels of adiponectin, when compared with those in the less than 75 cm^2 of VFA group, after adjusting for age, BMI and smoking status. However, when subjects were subdivided by WC=88 cm, corresponding to 75 cm^2 of VFA, we could not observe distinguishable features of MetS between these 2 subgroups. Interestingly, subjects with a lower WC (<88 cm) and higher VFA (≥75 cm^2) presented a similar pattern of MetS components as those with a higher WC (≥88 cm) and higher VFA (ie, elevated BP, high TG, low HDL-C, and high HOMA-IR index) and also showed a similarly lower plasma adiponectin level. This suggests that subjects with a smaller WC who were not diagnosed as MetS by the IDF criteria, but who have a higher VFA, have more possibility of a disturbed metabolic profile that can lead to type 2 diabetes and CVD.

Previous studies already reported that visceral fat is a more relevant index of incremental MetS risk than subcutaneous fat or WC[5,18,19] In particular, the VFA in the lower abdomen (L4–L5 level) is considered ideal for assessing the obesity-related metabolic risk[1,18,20] In our study, VFA in both the lower (L4 level) and upper (L1 level) abdomen was a major influential independent factor on the initial phase of MetS. VFA at the L1 level significantly correlated with lipid levels, HOMA-IR and adiponectin, as did VFA at L4 level, which may be explained by the greater deposition of more metabolically active visceral adipocytes in the omental and mesenteric depots located in the upper abdomen[21,22] Recently, Kuk et al reported that VFA at the L1–L2 level is much more strongly associated with MetS than that measured at the L4–L5 level[20] In this aspect, our results are important confirmation that the VFA in both the upper and lower abdomen should be considered when assessing metabolic derangements, particularly in premenopausal women.

Only a few studies have determined the critical cut point of VFA for MetS-related disorders[23–25] In the present study, 75 cm^2 of VFA at L4 and 87.5 cm^2 at L1 level were the optimal cut-off thresholds for discrimination of MetS risk. Shigematsu et al also reported similar results to ours; their cut-off values for obesity-related metabolic disorders in Japanese obese women were 80 cm^2 in the premenopausal and 110 cm^2 in the postmenopausal[24] Those results indicate that in premenopausal women relatively small amount of VFA has a detrimental effect on MetS risk.

On the other hand, we could not find a discriminative effect of a cut-off point of WC 88 cm on metabolic abnormalities. It might be that measurement of WC includes not only abdominal VFA but also the SFA. Adipose tissue in young adults particularly, is mainly subcutaneous rather than visceral[5] Our study subjects (premenopausal) also showed a higher correlation of WC with SFA (r=0.648, p<0.001) than with VFA (r=0.544, p<0.001). The concern that WC is not a good predictor of visceral fat has been addressed in several studies[26–28] Schreiner et al reported that WC predicted more of the variance in SFA than in intra-abdominal fat area in middle-aged subjects[26] and Bonora et al reported that VFA should be measured through direct methods, such as MRI and CT, whereas SFA can be estimated from simple anthropometric measurements[27] Recently, from the data of the Framingham Heart study, Fox et al concluded that only VFA provides information above and beyond easily obtainable clinical anthropometric measurements and gives a more complete understanding of metabolic risk[28] These findings denote that WC as a surrogate measure for the VFA could underestimate the contribution of visceral fat on health outcome. However, the limitation of CT measurement has to be considered, as it may not be feasible for use in the general population because of exposure to radiation, complex methodology, and expense.

The underlying pathophysiological development of MetS is still debatable (IR vs visceral obesity);[6,7,29] however, there is mounting evidence that abdominal visceral fat is an important link between the many features of MetS![17,23,30,31] Our result also showed that visceral fat accumulation was associated with a heightened dyslipidemic, insulin resistant and pro-inflammatory state. Currently, the endocrine function of visceral adipose tissue is emphasized, besides the altered non-esterified fatty acid metabolism, when depicting the pathophysiology of the MetS.[30,32,33] Elevated CRP and decreased adiponectin levels in viscerally obese subjects confirm adipose tissue as a remarkable endocrine organ releasing numerous cytokines[30,33] This is also partly supported by a recent report of macrophage infiltration in adipose tissue, which could contribute to an inflammatory state in obesity[34] Furthermore, low adiponectin levels observed in the viscerally obese are a plausible explanation of adiponectin as a key factor responsible for the atherogenic and diabetogenic profile[35,36]

Two recent large-scale studies found that the IDF criteria requiring WC as an obligatory factor could fail to identify those with metabolic disturbances and at increased mortality risk[15,37] A cross-sectional study, using national data from Korea NHANES, indicated that the discrepant group who satisfied the revised NCEP criteria, but not the IDF criteria, had more metabolic abnormalities and an unfavorable lifestyle despite a smaller WC[15] In addition, a prospective study that analyzed the all-cause and CVD death rates according to WC categories in 20,789 non-Hispanic white men found that one-third of men with a lower WC had multiple RF and a high risk of mortality, whereas one-fourth of men with an elevated WC had less than 2 metabolic RF and relatively lowered risk of mortality[37] Our findings also strengthen those concerns by showing that the amount of intra-abdominal visceral fat, regardless of WC, was more

associated with adverse MetS risk variables. When adjusted for age, BMI and smoking status, the lower WC–higher VFA group (WC <88 cm & L4VF ≥75 cm^2) were more likely to have an unfavorable metabolic profile, such as small LDL particle size, reflecting a high TG-low HDL state, elevated HOMA-IR, even with normal glucose level and low adiponectin level. Conversely, subjects with a higher WC–lower VFA (WC ≥88 cm & L4VF <75 cm^2) did not show a heightened MetS risk. These findings are compatible with the notion that the location of visceral fat rather than the body fat itself can be a hazard to health! They also reinforce the recommendation that visceral adiposity should be taken into account when interpreting the health risks, not solely depending on measurement of WC.

In conclusion, this study clarified that visceral fat rather than WC itself is a major determinant of the risk of MetS in premenopausal Korean women. As WC has its limitations as a crude anthropometric indicator of visceral adiposity, solely depending on WC measurement for evaluating MetS risk should be reconsidered. In addition, the present study highlights the need for cut-off points of sex, age, and menopause-specific WC and VFA to optimally discriminate individuals with both MetS and the related increase in CVD risk from healthy ones. Moreover, our results show that subjects with a lower WC–higher VFA, even though they were not diagnosed for MetS by the IDF criteria, have more possibility of the adverse metabolic profile that leads to type 2 diabetes and CVD. From this perspective, more population-based clinical research is needed to identify high-risk subjects who do not have central obesity but show clustering of metabolic RF.

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