Visceral adiposity index and longitudinal risk of incident metabolic syndrome: Korean genome and epidemiology study (KoGES)

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Abstract. Available data is insufficient to identify the influence of visceral adiposity assessed by visceral adiposity index (VAI) on incident MetS. This study was to evaluate the association of VAI with incident MetS. In a cohort of Korean genome epidemiology study, 5,807 free of MetS were followed-up for 10 years. They were subdivided into 3 tertile groups according to VAI score. Cox proportional hazard model was used to evaluate the hazard ratios (HRs) and 95% confidential interval (CI) [adjusted HRs (95% CI)] for MetS according to VAI tertiles. Subgroup analyses were conducted for VAI and waist circumference (WC). Receiver operating characteristic (ROC) and area under curve (AUC) analyses were conducted to compare the discriminative ability for Mets among indices. The risk for MetS increased proportionally to VAI tertiles in all participants, which was similarly observed in both men and women. Subgroup analysis indicated that group with high VAI and low WC had the increased risk for MetS (all participants: 2.76 [2.48–3.07], men: 2.77 [2.40–3.19] and women: 2.55 [2.16–3.00]), compared with groups with low VAI and low WC. Group with low VAI and high WC generally had the higher adjusted HRs for MetS than group with the high VAI and low WC. In AUC analyses, WC had the highest discriminative ability for Mets. In conclusion, elevated VAI was significantly associated with the increased long-term risk of MetS. VAI is a useful supplementary to classic anthropometric indices in screening high risk group of MetS.

Key words: Visceral adiposity index, Metabolic syndrome, Obesity

OBESITY has been established as a risk factor for cancer, cardiovascular disease (CVD), dyslipidemia, insulin resistance and metabolic syndrome [1, 2]. It has been recognized that increased adiposity mediates the causative relationship between obesity and cardiometabolic diseases. In particular, visceral adiposity is an important determinant of cardiometabolic risk associated with obesity [3]. Despite classic indices like body mass index (BMI) and waist circumference (WC) have been commonly used to describe the degree of obesity, each index showed some limitation in indicating visceral adiposity [4-8].

In the last decade, Amato et al. has developed Visceral Adipose Index (VAI), a mathematical model evaluated by clinical and anthropometric measurements to allow inexpensive and precise assessment of visceral adiposity [9]. This index showed the strong correlation with the amount of visceral adipose tissue measured by magnetic resonance imaging, suggesting the clinical usefulness as a surrogate marker for visceral adipose dysfunction [9]. Previous observations have demonstrated the significant association of VAI with cardiovascular and cerebrovascular event [9, 10], type 2 diabetes mellitus (T2DM) and hypertension [11-13]. However, the long term risk of cardiometabolic disease according to VAI levels has been still less well described.
Metabolic syndrome (MetS) is a clustering of at least three of the five medical conditions including abdominal obesity, high blood pressure (BP), high blood glucose, high triglycerides (TG) and low high density lipoprotein-cholesterol (HDL-C) levels [14]. The development of MetS is induced by increase in visceral adiposity, aggravation of IR and elevation of BP, which profoundly increases the risk of cardiometabolic diseases. Thus, it is postulated that MetS mediates the significant association between high VAI and increased risk of cardiometabolic diseases. However, evidence is still less clear regarding the long-term risk of MetS according to VAI score.

To evaluate the influence of visceral adiposity assessed by VAI score on the development of MetS, we examined the risk of MetS across VAI score in Koreans. Considering the discrepancy between real visceral adiposity and WC, we conducted analysis in individuals with normal WC.

Research Design and Methods

Study population

All subjects were participants of the Korean Genome and Epidemiology Study (KoGES) Ansan and Ansung Study, which is a population-based, epidemiology study of rural and urban community in South Korea. Detailed methods and study population of the present study described in the previous study [15]. The baseline survey of KoGES Ansan and Ansung study was completed in 2001–2002, and follow-up survey were conducted every two years. Initially, a total of 10,038 participants aged 40 to 69 participated in the study. A total of 5,108 participants were recruited by cluster-sampling method stratified by age, sex, and residential district in Ansung community and 5,012 subjects selected by random sampling method in Ansan. Of these 10,038 participants, 617 had missing values in lipid profile, waist circumference, body mass index (BMI). 2,988 participants had baseline MetS. During a 10 years follow-up period, 636 were excluded because follow-up loss or incomplete follow-up data. Finally, 5,807 participants were enrolled in the present study. All subjects participated in the study voluntarily, and informed consent was obtained in all cases. Ethics approvals for the study protocol and analysis of the data were obtained from the institutional review board of Kangbuk Samsung Hospital.

Clinical and biochemical measurements

Study data included a medical history and sociodemographic information provided by a self-administered questionnaire, anthropometric measurements and laboratory biochemical measurements. All study participants were also asked to respond to a health-related behavior questionnaire, which included the topics of alcohol consumption, smoking and exercise. Physical activity divided two categories; regular exercise (≥90 minutes exercise per week, at least moderate intensity) or inactive group. Diabetes mellitus (DM) was defined as fasting serum glucose level of at least 126 mg/dL, or serum HbA1c level of at least 6.5%, or 2 h-glucose level at least 200 mg/dL, or participant have ever been diagnosed with DM [16]. Hypertension was defined in the participants who have ever been diagnosed as hypertension, or had measured blood pressure (BP) ≥140/90 mmHg at initial examinations. BP was measured both arm in sitting position after participants had been in a relaxed state for at least 10 min. The arithmetic mean value of the BP was used to define the systolic and diastolic BP. Waist circumference (WC), height and weight were also measured in all participants. Body mass index (BMI) was also calculated (kg/m²).

After fasting overnight for 12 hours, the plasma concentrations of glucose, total cholesterol, TG and HDL-C were measured enzymatically using a HITACHI Automatic Analyzer 7600 (Hitachi, Tokyo, Japan). In the baseline and follow-up examinations, the study participants also underwent oral glucose tolerance test (OGTT). The HbA1C level was measured by high-performance liquid chromatography (VARIANT II; Bio-Rad Laboratories, Hercules, CA). VAI was calculated by following equation [9];

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\text{Men: } VAI = \frac{(WC/(39.68 + (1.88 \times BMI))) \times (TG/0.81)}{(1.52/HDL-C)} \\
\text{Women: } VAI = \frac{(WC/(36.58 + (1.89 \times BMI))) \times (TG/0.81)}{(1.52/HDL-C)}
\]

(TG and HDL-C were expressed in mmol/L)

The presence of metabolic syndrome (MetS) was made according to the joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention [14]. Elevated BP was defined as a systolic or diastolic BP ≥130/85 mmHg; elevated fasting serum glucose level was defined as ≥100 mg/dL; high serum triglyceride levels were defined as ≥150 mg/dL; low HDL-C levels were defined as <40 mg/dL in men and <50 mg in women. The presence of visceral obesity was defined as the criteria of the Korean Society of the Study of Obesity (waist circumference ≥90 cm for men and ≥85 cm for women) [17]. MetS was defined as the presence of three or more of the above components in baseline and follow-up examinations.

Statistical analysis

All participants were categorized into tertile groups according to the VAI. Data are presented as means ±
standard deviation within study groups for continuous variables and as proportions for categorical variables. The linear trends of variables between study groups were calculated by linear regression model in continuous variables and Cochran-Armitage trend test in categorical variables.

The unadjusted and multivariate-adjusted hazard ratios (HRs) and their 95% confidence intervals (HRs [95% CI]) for each group were estimated with the use of the Cox proportional hazards model. The selected covariates in multivariate-adjusted model are age, sex, area, regular exercise, systolic blood pressure, smoking, alcohol intake, total cholesterol, DM, (sex excluded in gender subgroup analysis). The incidence cases of MetS and incidence density (incidence cases per 1,000 person-years) was calculated in each study groups. Additionally, subgroup analyses were performed in participants without abdominal obesity (WC <90 cm for men and <85 cm for women) and high TG (≥150 mg/dL) and low HDL-C (<40 mg/dL in men and <50 mg in women).

Receiver operating characteristic (ROC) curve and area under curve (AUC) analyses were also performed to assess the discriminative ability of VAI, WC, BMI, HDL-C and TG for the incident MetS. DeLong method was used to compare the differences in AUC between VAI and other parameters with p-values.

All statistical analyses were performed using R 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria) and a value of \( p < 0.05 \) was considered statistically significant in all analyses.

### Result

A total of 5,807 participants were enrolled in the study (2,931 men and 2,876 women). The overall incidence of MetS was 29.8% (\( n = 1,728 \)), and mean age of the study population was 50.8 ± 8.7. The baseline clinical characteristics of study population are presented in Table 1. While man is predominant in 1st VAI tertile group, preponderance of women is identified in 2nd and 3rd VAI tertile groups. Except mean values of age and proportion of smoker, other clinical characteristics showed the statisti-

| Characteristics          | VAI (−1.33) (\( n = 1,936 \)) | VAI (1.33–2.05) (\( n = 1,936 \)) | VAI (2.05–) (\( n = 1,935 \)) | \( p \) for Trend |
|-------------------------|--------------------------------|---------------------------------|-------------------------------|------------------|
| Male Sex (\( n, \% \))         | 1,152 (59.5%)                  | 906 (46.8%)                    | 873 (45.1%)                  | <0.001           |
| Age (year)               | 51.1 ± 9.0                     | 50.7 ± 8.6                     | 50.8 ± 8.5                   | 0.294            |
| Fasting Glucose (mg/dL)  | 84.3 ± 13.3                    | 84.1 ± 16.4                    | 83.0 ± 13.6                  | 0.005            |
| Total cholesterol (mg/dL)| 186.4 ± 33.6                   | 186.6 ± 34.2                   | 190.9 ± 35.8                 | <0.001           |
| HDL-cholesterol (mg/dL)  | 54.3 ± 10.2                    | 46.4 ± 7.6                     | 40.6 ± 7.3                   | <0.001           |
| HDL-cholesterol (mmol/L) | 1.4 ± 0.3                      | 1.2 ± 0.2                      | 1.1 ± 0.2                    | <0.001           |
| Triglyceride (mg/dL)     | 86.3 ± 20.7                    | 118.1 ± 25.2                   | 193.1 ± 106.8                | <0.001           |
| Triglyceride (mmol/L)    | 1.0 ± 0.2                      | 1.3 ± 0.3                      | 2.2 ± 1.2                    | <0.001           |
| SBP (mmHg)               | 116.8 ± 17.3                   | 117.6 ± 16.7                   | 115.1 ± 15.4                 | 0.002            |
| DBP (mmHg)               | 77.7 ± 11.0                    | 78.1 ± 10.7                    | 76.6 ± 10.1                  | 0.001            |
| BMI (Kg/m\(^2\))        | 22.9 ± 2.9                     | 23.9 ± 2.8                     | 24.3 ± 2.6                   | <0.001           |
| Waist Circumference (cm) | 77.2 ± 7.5                     | 80.0 ± 7.6                     | 81.6 ± 6.9                   | <0.001           |
| VAI                      | 1.0 ± 0.2                      | 1.7 ± 0.2                      | 3.2 ± 1.9                    | <0.001           |
| Current smoker (%)       | 28.6%                          | 24.7%                          | 27.3%                        | 0.351            |
| Average alcohol use (g/day)| 10.9 ± 22.3                  | 8.4 ± 19.8                     | 9.3 ± 22.2                   | 0.020            |
| Regular exercise (%)     | 44.2%                          | 39.4%                          | 35.4%                        | <0.001           |
| Hypertension (%)         | 20.2%                          | 21.7%                          | 13.8%                        | <0.001           |
| Diabetes mellitus (%)    | 6.0%                           | 5.6%                           | 3.5%                         | <0.001           |
| Incidence of MetS [\( n, \% \)] | 314 (16.2%)                 | 594 (30.7%)                    | 820 (42.4%)                  | <0.001           |

Values are mean (±SD); HDL, high density lipoprotein cholesterol; BMI, body mass index; VAI, Visceral Adiposity Index; SBP, systolic blood pressure; DBP, diastolic blood pressure, MetS, Metabolic syndrome.

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cally significant difference in their mean values (p for trend <0.05) among VAI tertile groups. In metabolic components, groups with higher VAI tertile tended to have the higher mean values of baseline HDL-C, triglyceride and waist circumference.

The unadjusted and multivariate-adjusted HRs 95% and their confidence intervals (CI) were presented in Table 2. The adjusted HRs for MetS increased proportionally to VAI score across study groups in all study participants (2nd tertile: 1.50 [1.12–2.01] and 3rd tertile: 1.50 [1.12–2.01]), men (2nd tertile: 1.27 [0.90–1.79] and 3rd tertile: 2.49 [1.82–3.40]) and women (2nd tertile: 1.77 [1.01–3.11] and 3rd tertile: 3.51 [2.08–5.92]).

In ROC and AUC analyses (Table 5), compared to VAI (all participants: 0.660 [0.646–0.675], men: 0.670 [0.650–0.691] and women: 0.658 [0.637–0.680]), WC had the highest discriminative ability for incident MetS (all participants: 0.712 [0.698–0.726], men: 0.709 [0.689–0.728] and women: 0.725 [0.705–0.744]). BMI, TG and HDL-C were not superior to VAI in discriminating incident MetS.

**Discussion**

In a cohort of general Korea population without MetS, the risk of MetS increased proportionally to VAI score in both men and women. Our baseline data may be an explanation for this finding. In our baseline analysis, groups with elevated VAI score had the worse metabolic profile in triglyceride, HDL-C, and waist circumference. Thus, it is inferred that elevated visceral adiposity assessed by VAI has good correlation with metabolic derangement, resulting in the increased long term risk of MetS. Similar findings were observed in a study for Peruvians where VAI

| Table 2 Hazard ratios (HRs) and 95% confidence intervals (CI) for the incidence of Metabolic syndrome according to the tertile of visceral adiposity index |
|-----------------|-----------------|-----------------|
| Characteristics | Tertile 1        | Tertile 2        | Tertile 3        |
| Range of VAI    | VAI (–1.33)      | VAI (1.33–2.05)  | VAI (2.05–)      |
| Unadjusted HR   | 1.00 (Reference) | 2.08 (1.81–2.38) | 3.24 (2.85–3.69) |
| Adjusted HR     | 1.00 (Reference) | 2.11 (1.83–2.42) | 3.75 (3.28–4.29) |
| Incidence cases | 314             | 594             | 820             |
| Incidence density | 20.9           | 42.0           | 62.2           |

Men (n = 2,931)

| Characteristics | Tertile 1        | Tertile 2        | Tertile 3        |
| Range of VAI    | VAI (–1.22)      | VAI (1.22–1.93)  | VAI (1.93–)      |
| Unadjusted HR   | 1.00 (Reference) | 2.05 (1.70–2.47) | 3.41 (2.85–4.08) |
| Adjusted HR     | 1.00 (Reference) | 2.00 (1.66–2.42) | 3.83 (3.19–4.60) |
| Incidence cases | 165             | 315             | 442             |
| Incidence density | 22.2           | 44.5           | 68.7           |

Women (n = 2,876)

| Characteristics | Tertile 1        | Tertile 2        | Tertile 3        |
| Range of VAI    | VAI (–1.45)      | VAI (1.45–2.15)  | VAI (2.15–)      |
| Unadjusted HR   | 1.00 (Reference) | 2.22 (1.82–2.73) | 3.45 (2.84–4.18) |
| Adjusted HR     | 1.00 (Reference) | 2.08 (1.70–2.55) | 3.42 (2.81–4.15) |
| Incidence cases | 140             | 277             | 389             |
| Incidence density | 18.3           | 39.1           | 58.1           |

Adjusted for age, sex, area, regular exercise, systolic blood pressure, smoking, alcohol intake, total cholesterol, diabetes mellitus, (sex excluded in gender subgroup analysis) 
Incidence density: incidence cases per 1,000 person-year
### Table 3  Hazard ratios (HRs) and 95% confidence intervals (CI) for the incidence of metabolic syndrome according to subgroups stratified by visceral adiposity index and waist circumference (WC)

| Characteristics | Group 1 | Group 2 | Group 3 | Group 4 |
|-----------------|---------|---------|---------|---------|
| All participants (n = 5,807) | (n = 3,464) | (n = 1,667) | (n = 408) | (n = 258) |
| Unadjusted HR | 1.00 (Reference) | 2.41 (2.17–2.68) | 3.20 (2.74–3.74) | 3.42 (2.84–4.11) |
| Adjusted HR | 1.00 (Reference) | 2.76 (2.48–3.07) | 3.14 (2.68–3.69) | 4.50 (3.71–5.46) |
| Incidence cases | 705 | 685 | 203 | 135 |
| Incidence density | 26.5 | 59.3 | 77.1 | 82.5 |
| Men (n = 2,931) | (n = 1,812) | (n = 908) | (n = 142) | (n = 69) |
| Unadjusted HR | 1.00 (Reference) | 2.44 (2.12–2.80) | 3.26 (2.56–4.16) | 5.17 (3.74–7.14) |
| Adjusted HR | 1.00 (Reference) | 2.77 (2.40–3.19) | 3.44 (2.70–4.38) | 6.52 (4.69–9.05) |
| Incidence cases | 401 | 401 | 79 | 41 |
| Incidence density | 29.4 | 65.9 | 87.6 | 116.7 |
| Women (n = 2,876) | (n = 1,637) | (n = 784) | (n = 281) | (n = 174) |
| Unadjusted HR | 1.00 (Reference) | 2.52 (2.14–2.96) | 3.22 (2.61–3.98) | 3.88 (3.07–4.89) |
| Adjusted HR | 1.00 (Reference) | 2.55 (2.40–3.19) | 2.62 (2.12–3.26) | 3.90 (3.06–4.96) |
| Incidence cases | 293 | 295 | 124 | 94 |
| Incidence density | 22.8 | 53.3 | 66.9 | 81.0 |

Adjusted for age, sex, area, regular exercise, systolic blood pressure, smoking, alcohol intake, total cholesterol, diabetes mellitus, (sex excluded in gender subgroup analysis)

### Table 4  Hazard ratios (HRs) and 95% confidence intervals (CI) for the incidence of Metabolic syndrome according to the tertile of visceral adiposity index in participants without abdominal obesity, high TG and low HDL-cholesterol level

| Characteristics | Tertile 1 | Tertile 2 | Tertile 3 |
|-----------------|----------|----------|----------|
| All participants (n = 2,157) | VAI (<0.97) | VAI (0.97–1.29) | VAI (1.29–) |
| Unadjusted HR | 1.00 (Reference) | 1.51 (1.13–2.02) | 2.98 (2.29–3.88) |
| Adjusted HR | 1.00 (Reference) | 1.50 (1.12–2.01) | 2.93 (2.24–3.83) |
| Incidence cases | 77 | 112 | 202 |
| Incidence density | 13.4 | 20.0 | 38.6 |

Men (n = 1,336)

| Range of VAI | VAI (<0.93) | VAI (0.94–1.25) | VAI (1.25–) |
| Unadjusted HR | 1.00 (Reference) | 1.29 (0.91–1.81) | 2.43 (1.78–3.31) |
| Adjusted HR | 1.00 (Reference) | 1.27 (0.90–1.79) | 2.49 (1.82–3.40) |
| Incidence cases | 58 | 75 | 131 |
| Incidence density | 16.9 | 21.8 | 40.3 |

Women (n = 821)

| Range of VAI | VAI (<1.03) | VAI (1.03–1.38) | VAI (1.38–) |
| Unadjusted HR | 1.00 (Reference) | 2.09 (1.20–3.65) | 4.75 (2.87–7.88) |
| Adjusted HR | 1.00 (Reference) | 1.77 (1.01–3.11) | 3.51 (2.08–5.92) |
| Incidence cases | 19 | 36 | 72 |
| Incidence density | 8.3 | 16.9 | 36.1 |

Adjusted for age, sex, area, regular exercise, systolic blood pressure, smoking, alcohol intake, total cholesterol, diabetes mellitus, (sex excluded in gender subgroup analysis)

Incidence density: incidence cases per 1,000 person-year
had positive correlation with fasting glucose, TG, SBP and DBP [18]. However, available data is still scarce in Asians, and ethnic difference was reported regarding the predictive ability of specific adiposity index on cardiometabolic risk among previous studies [19-21]. Our results showed the markedly increased long-term risk of MetS in East Asians (Koreans) with elevated VAI, providing additional insight to the association between VAI and cardiometabolic risk. Our baseline data indicates that the substantial proportion of study subjects in each group had the normal range of baseline metabolic profiles. All tertile groups of VAI showed the normal range of mean values in baseline measurements including fasting glucose <90 mg/dL, SBP/DBP <120/85 mmHg, BMI <25 kg/m² and WC <85 cm. The development of MetS in individuals with normal metabolic profiles requires the aggravation of metabolic condition during follow-up. Thus, it is postulated that the elevated VAI has an adverse impact on metabolic milieu as well as development of MetS. Given the influence of worse metabolic profiles on cardiometabolic disease, our results may suggest a mechanism for studies demonstrating the increased cardiovascular event and metabolic derangement on elevated VAI scores.

WC is commonly used in assessing the degree of abdominal obesity. WC is recognized to be better than BMI in predicting cardiometabolic disease associated with obesity. Since WC well correlates with visceral adiposity as a metabolic component, it is plausible that elevated WC links to the high risk of MetS. Thus, in order to identify the independent influence of VAI on the metabolic derangement, it seems necessary to evaluate the risk of MetS in individuals with normal WC. In our analysis, it is of note that elevated VAI was significantly associated with the increased risk of MetS even in individuals with normal WC. Imaging modalities like computed tomography or MRI are most reliable technical tools in quantifying visceral fat mass [22], but expensiveness and inconvenience of exams enabled WC to be most commonly used indicator in assessing visceral adiposity. However, considering the evident limitation in WC [8], exclusive reliance on WC may lead to a subset of people at the increased risk of MetS being missed. In our results, individuals with high VAI and normal WC had the more than 2.5 times higher risk of MetS compared to individuals with normal VAI and normal WC. This finding links to a hypothesis that VAI can be potentially effective tool supplementary to WC in predicting cardiometabolic risk. Nonetheless, the predictability of VAI on MetS should be interpreted with caution. Our AUC analyses didn’t show the superiority of VAI to WC in predicting MetS, presenting the higher AUC in WC than VAI. Similar finding was observed in a study that compared the association of anthropometric indices with visceral fat mass assessed by computed tomography [23]. In that study, AUC analysis indicated that predictability for visceral fat area >100 cm² was lower in VAI (0.751 [0.703–0.800]) than WC (0.832 [0.791–0.873]) [23]. These results suggest that VAI is not superior to WC in assessing cardiometabolic risk in Koreans. The clinical significance of VAI should be confined to the effective supplementary to WC.

Since formula of VAI includes the components of MetS like WC, TG and HDL-C [9], individuals with elevated VAI may be close to the diagnostic criteria of MetS. In practice, our baseline data presented that 2nd and 3rd tertile groups had the higher levels in mean WC and TG and lower level in mean HDL-C than 1st tertile group. Thus, it can be understood that the risk of MetS increased in individuals with metabolic components closer to diagnostic criteria of MetS. To minimize the influence of baseline levels in WC, TG and HDL-C on results, we evaluated the risk of MetS according to VAI in individuals with normal range of WC, TG and HDL-C. In this analysis, we found that VAI was significantly associated with increased risk of MetS even in individuals with normal range of WC, TG and HDL-C. Although our AUC analysis didn’t show the superiority of VAI over WC and BMI in predicting MetS, VAI had the stronger predictive ability for MetS than TG and HDL-C.

### Table 5 Comparison of area under the curve (AUC) for the prediction of MetS according to the VAI, WC, WHtR, BMI, TG, HDL-C

| Variables | All participants | Men | Women |
|-----------|------------------|-----|-------|
|           | AUC (95% CI)     | p-value | AUC (95% CI) | p-value | AUC (95% CI) | p-value |
| VAI       | 0.660 (0.646–0.675) | Reference | 0.670 (0.650–0.691) | Reference | 0.658 (0.637–0.680) | Reference |
| WC        | 0.712 (0.698–0.726) | <0.001 | 0.709 (0.689–0.728) | 0.003 | 0.725 (0.705–0.744) | <0.001 |
| BMI       | 0.657 (0.642–0.672) | 0.711 | 0.660 (0.639–0.680) | 0.438 | 0.659 (0.638–0.681) | 0.982 |
| HDL-C     | 0.594 (0.578–0.610) | <0.001 | 0.598 (0.576–0.620) | <0.001 | 0.583 (0.560–0.606) | <0.001 |
| TG        | 0.639 (0.623–0.654) | <0.001 | 0.646 (0.625–0.668) | <0.001 | 0.630 (0.608–0.653) | <0.001 |

DeLong method was used to compare the differences in AUC between VAI and other parameters with p-values.
These results suggest that VAI is useful to screen the high risk group for MetS in non-obese population with normal TG and HDL-C. As a reliable indicator of visceral adiposity, it is speculated that elevated VAI may trigger pathophysiological processes associated with MetS, independently of other metabolic milieu. Further studies should identify whether elevated VAI longitudinally links to the increased risk of cardiometabolic disease through MetS.

The strengths of the study are the population-based longitudinal design with 10 years’ follow-up and the relatively appropriate number of subjects with identifiable medical records, which enable us to conduct subgroup analyses for gender, BMI, WC and lipid profiles. Our results expand the clinical usefulness of VAI to identifying the individuals with the higher risk for MetS. Nonetheless, the limitation of the study should be acknowledged.

First, our findings should be viewed in point of study conducted for only Koreans. As aforementioned, influence of visceral adiposity on cardiometabolic risk can differ among ethnics [19-21]. Thus, our results are not likely to be generalized into other ethnics and regions.

Second, our results can’t provide the reliable mechanisms underlying adverse influence of visceral adiposity on metabolic derangement and MetS. Despite the suggested theories and hypotheses it should be recognized that our results was obtained from epidemiological observation.

In conclusion, our results demonstrated that elevated visceral adiposity assessed by VAI score increased the long-term risk of MetS in general Korean population. The impact of VAI was identically identified in individuals with normal levels of WC, TG and HDL-C. These findings suggest that elevation of VAI may increase the risk of MetS even in metabolically healthy non-obese subjects, indicating the clinical usefulness of VAI, supplementary to classic anthropometric indices in screening high risk group of MetS.

**Author Contribution**

Ju Young Jung coordinated the study, analyzed the data and wrote the manuscript as a first author. Jae-Hong Ryoo participated in conducting study and writing manuscript. Chang-Mo Oh played role in analyzing data and verifying the results. Joong-Myung Choi and Pil-Wook Chung participated in English editing and reviewing manuscript. Hyun Pyo Hong conducted additional statistical analysis and writing manuscript in process of revising manuscript.

Sung Keun Park is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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