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Relationship between Abdominal Fat Area Measured by Screening Abdominal Fat CT and Metabolic Syndrome in Asymptomatic Korean Individuals
무증상 한국인에서 복부지방 CT와 대사증후군의 관계

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Purpose: The purpose of this study was to investigate the relationship between abdominal fat as assessed by abdominal fat CT and metabolic syndrome (MS), especially in asymptomatic Korean individuals.
Materials and Methods: Retrospectively, a medical record analysis was performed in a total of 111 patients with screening abdominal fat CT. The data such as visceral fat (VF), subcutaneous fat (SF) and VF/SF were elicited by abdominal fat CT, and we analyzed the relationship of VF, SF, and VF/SF with MS and cardiovascular risk factors.
Results: In males, VF and SF had a positive correlation with many cardiovascular risk factors and MS, but VF was superior to SF. In females, VF, but not SF, had a positive correlation with some cardiovascular risk factors and MS. The cut-off values of VF and SF to predict MS, which were calculated by drawing receiver operating characteristic curves, were as follows: the cut-off value of VF in men: 136.50 cm^2, the cut-off value of SF in men: 159.50 cm^2, and the cut-off value of VF in women: 134.50 cm^2.
Conclusion: In conclusion, VF accumulation was the best predictor of MS and it had a positive correlation with cardiovascular risk factors in both sexes. SF also had a significant association with MS, especially in men, although it was not superior to VF.

Index terms
Visceral Fat
Subcutaneous Fat
Multidetector Computed Tomography
Metabolic Syndrome

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INTRODUCTION

Metabolic syndrome (MS) is a cluster of conditions, including physical and biochemical abnormalities that are associated with an increased risk of cardiovascular complications and type 2 diabetes (1-4). An increase in the prevalence of MS due to modified socioenvironmental and behavioral changes has been recognized as a national public health problem, not only in Korea, but also worldwide (5, 6). Central obesity is known as one of the main causes of insulin resistance and MS. Waist circumference and body mass index (BMI) are used as indicators of central obesity, and they are included in the diagnostic criteria for MS (1-4).

Abdominal fat CT is an optimal technique for the accurate assessment of abdominal fat, as well as the distribution of subcutaneous fat (SF) and visceral fat (VF) (7). Waist circumference is an index that can increase, regardless of SF or VF accumulation, and these 2 types of fat have different physiological characteristics (8-11). Compared to SF, VF contributes to the development of MS and cardiovascular diseases. Although the exact molecular mechanisms are unclear, it could be due to the anatomical location and higher lipolytic characteristic of VF (10, 11). VF is located proximally to the portal venous system and it can lead to direct drainage of metabolites and free fatty acids into the liver, resulting in insulin resistance (10, 11).

Several studies have been conducted to assess the relationship of VF and SF with MS, using abdominal fat CT (12-16). It seems clear that VF accumulation is associated with MS, but there are minor differences between SF and MS. Sandeep et al. (12) reported that visceral adipose tissue, but not subcutaneous adipose tissue, is associated with MS. However, Pickhardt et al. (13) concluded that VF was the best predictor of MS only in women, while VF was a poorer predictor than SF in men. Also, there have been several studies to determine the cut-off value of VF for predicting MS (15, 16), but there is no consensus on the meaningful cut-off value of VF and SF for predicting MS.

Among these studies, only a few studies have specifically targeted Korean individuals (14-16). Therefore, this study was conducted to investigate the relationship of VF and SF, as assessed by abdominal fat CT, with MS, especially in asymptomatic Korean individuals. We also investigated the specific cut-off values of fat indicators for predicting MS.

MATERIALS AND METHODS

Subjects

Our retrospective study included 111 asymptomatic participants (15 females and 96 males) who visited our healthcare center from January 2014 to December 2015 for comprehensive health screening. All participants underwent unenhanced CT for measuring abdominal fat and had no existing cardiovascular disease and previous cardiovascular event. Our Institutional Review Board (IRB) approved this study, and from the outset of the study, the requirement for obtaining informed consent was waived because of the overall retrospective analysis.

Clinical and Laboratory Measurements

Participants received anthropometric measurements by trained nurses. Height and weight were measured using automatic measuring devices. The BMI was calculated by dividing the weight by the square of the height (BMI = kg/m^2). Waist circumference was measured in the standing position by placing a tape measure horizontally in between the lower part of the costal bone and the highest part of the pelvic iliac crest. Blood pressure (BP) was measured after at least 10 minutes of rest using an automatic BP measurement device. If systolic blood pressure (SBP) was greater than 140 mm Hg or diastolic blood pressure (DBP) was greater than 90 mm Hg, measurement of BP was repeated. We recorded the average value of the SBP and DBP measurements. It was performed according to the Hypertension Detection and Follow-up Program protocol (a coordinating center in a clinical trial).

After at least 8 hours of fasting, fasting blood glucose, total cholesterol, triglyceride (TG), and high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) levels were checked using an auto-analyzer.

Metabolic Syndrome

Various diagnostic criteria for MS have been proposed by different organizations (1-4). However, there is no internationally agreed definition of MS. We used the American Heart Association and the National Heart, Lung, and Blood Institute (AHA/NHLBI) criteria for the diagnosis of MS (4), which are not inferior to the other definitions, including those modified by the World Health Organization (WHO), National Cholesterol Education Program Third Adult Treatment Panel (NCEP-ATP III), and International Diabetes Federation (IDF), as all reflected insulin resistance and the risk of coronary heart disease in Koreans (17).

According to the AHA/NHLBI guidelines, MS can be diagnosed when three of the following conditions are met: 1) waist circumference ≥ 90 cm (males) or ≥ 80 cm (females), 2) TG ≥ 150 mg/dL or medicated to treat this condition, 3) HDL-C < 40 mg/dL (male), < 50 mg/dL (female) or medicated to treat this condition, 4) SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg or medicated to treat hypertension, and 5) fasting glucose ≥ 100 mg/dL or medicated to treat diabetes.

The criteria for abdominal obesity were revised by the Western Pacific Regional Office of WHO, the Asia-Pacific perspective (≥ 90 cm in men and ≥ 80 cm in women for Asian patients) (18).

Abdominal Fat CT

SF and VF were assessed using a 64-slice multidetector CT (GE Healthcare, LightSpeed VCT, Milwaukee, WI, USA) with a tube voltage of 120 kVp, 5.0 mAs, 2.5 mm slide thickness, and 0.5 sec CT gantry rotation time protocol. In one slice at the periumbilical level, SF and VF were automatically quantified using AW version 4.5 (GE Healthcare, Milwaukee, WI, USA). The CT values of adipose tissue were set within attenuating regions as -50 to -250 Hounsfield unit using the histogram method (Fig. 1A). Three areas were obtained by drawing lines along the abdominal

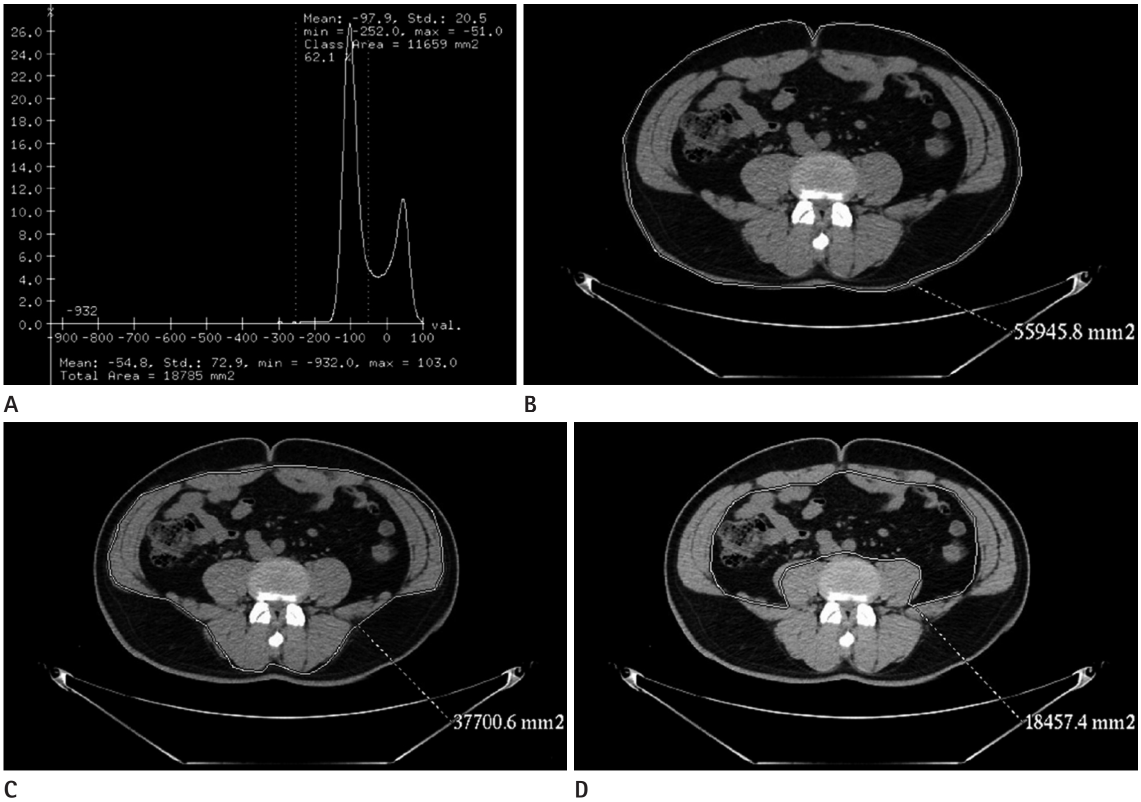

Fig. 1. Measurement of visceral and subcutaneous fat using a 64-slice multidetector CT with AW version 4.5.
A. Class areas are calculated based on the **(D)** attenuating region as -50 to -250 Hounsfield unit using the histogram method. The calculated area is 122.32 cm^2 and this is the value of visceral fat.
B–D. Three areas are obtained by drawing lines along the abdominal skin **(B)**, the outer line of the abdominal muscles **(C)** and the inner line of the abdominal muscles and psoas muscles **(D)**.

skin (Fig. 1B), the outer line (Fig. 1C) of the abdominal muscles and the inner line (Fig. 1D) of the abdominal muscles and psoas muscles. SF is an area obtained by subtracting the area of Fig. 1B from the area of Fig. 1C. VF is an area obtained by drawing a line along the inner line of the abdominal muscles and psoas muscles. We then calculated the value of VF/SF.

Statistical Analysis

IBM SPSS 23.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. A *p* value of less than 0.05 was considered statistically significant.

Pearson correlation analysis was used to determine the correlation between parameters of abdominal fat measured by abdominal fat CT and anthropometrically measured cardiovascular risk factors including waist circumference, BMI, BP, TG, HDL cholesterol.

Analysis of covariance was used to test the relationship between MS and indicators of abdominal fat, including VF, SF, VF/SF, waist circumference and BMI.

A receiver operating characteristic (ROC) curve analysis was performed, and the area under the curve (AUC) was analyzed to evaluate the usefulness of VF, SF, and VF/SF as diagnostic criteria for MS and to separately determine their cut-off values. The upper left points on the ROC curves were determined as the cut-off values, which maximized the sensitivity and specificity.

RESULTS

Among the 111 subjects, 96 participants were male and 15 participants were female. The mean ages of male and female participants were 46.20 ± 11.45 years and 48.20 ± 14.78 years, respectively. Furthermore, 30.2% (29 participants) of males and 26.7% (4 participants) of females had a positive diagnosis of MS. The mean areas of VF and SF in males were 150.28 ± 69.00 cm^2 and 175.78 ± 60.09 cm^2, respectively. The mean areas of VF and SF in females were 119.93 ± 84.59 cm^2 and 197.47 ± 104.73 cm^2, respectively. Other demographic and biochemical characteristics of the participants are presented in Table 1.

In males, VF had a significant positive correlation with waist circumference, BMI, BP, TG and it had a negative correlation with HDL cholesterol. SF also had a significant positive correlation with waist circumference, BMI, BP, and LDL cholesterol, and it had a negative correlation with HDL cholesterol. VF/SF had a positive correlation with only a few risk factors (fasting glucose and TG). In females, VF had a positive correlation with waist circumference, BMI, SBP, and fasting glucose and it had a negative correlation with HDL cholesterol. SF had a positive correlation only with waist circumference and BMI, and it had a negative correlation with HDL cholesterol. VF/SF did not show any significant correlation with anthropometrically measured cardiovascular risk factors (Tables 2, 3).

In males, the areas of VF and SF, waist circumference and BMI were significantly higher in the MS group compared with the non-MS group ($p < 0.001$ for all correlations). The VF/SF ratio was higher in the MS group, but without any statistical significance. In females, only the area of VF was significantly higher in the MS group compared with the non-MS group ($p = 0.048$). The area of SF, VF/SF ratio, waist circumference and BMI were higher in the MS group, but without any statistical significance (Table 4).

To evaluate the usefulness of VF, SF and VF/SF as positive predictive factors of MS and to determine the cut-off values, we drew ROC curves and calculated the AUC of VF, SF and the VF/SF ratio, respectively (Table 5, Figs. 2, 3). The cut-off value was set to the upper left point on the ROC curve, which maximizes both specificity and sensitivity. In males, the AUC of VF was 0.762 and the result was statistically significant ($p < 0.001$). The cut-off value of VF was 136.50 cm^2, and we could assume that if VF was higher than 136.50 cm^2, the male patient had a high probability of developing MS. The AUC of SF was 0.681 and the result was statistically significant ($p < 0.01$). The cut-off value of SF was 159.50 cm^2, and we could assume that if SF was higher than 159.90 cm^2, the male patient had a high probability of developing MS. The AUC of the VF/SF ratio was 0.601, which was not statistically significant. In females, the AUC of VF was 0.909 and the result was statistically significant ($p < 0.05$). The cut-off value of VF was

Table 1. Baseline Characteristics

Variable	Male	Female
Total	96 (100.0)	15 (100.0)
Age	46.20 ± 11.45	48.20 ± 14.78
MS		
Yes	29 (30.2)	4 (26.7)
No	67 (69.8)	11 (73.3)
VF (cm^2)	150.28 ± 69.00	119.93 ± 84.59
SF (cm^2)	175.78 ± 60.09	197.47 ± 104.73
VF/SF	0.92 ± 0.45	0.63 ± 0.40
Waist circumference (cm)	86.21 ± 7.58	78.40 ± 14.76
BMI (kg/m^2)	25.63 ± 2.99	24.53 ± 4.93
SBP (mm Hg)	126.53 ± 12.62	121.20 ± 16.27
DBP (mm Hg)	77.85 ± 9.19	71.93 ± 10.97
Fasting glucose (mg/dL)	98.73 ± 15.74	89.80 ± 8.65
Total cholesterol	195.52 ± 33.68	176.53 ± 40.20
Triglycerides (mg/dL)	154.67 ± 99.39	107.00 ± 65.88
HDL cholesterol (mg/dL)	49.54 ± 11.86	56.20 ± 17.59
LDL cholesterol (mg/dL)	120.09 ± 29.81	101.20 ± 34.10

Values are *n* (%) or mean ± standard deviation.
BMI = body mass index, DBP = diastolic blood pressure, HDL = high-density lipoprotein, LDL = low-density lipoprotein, MS = metabolic syndrome, SBP = systolic blood pressure, SF = subcutaneous fat, VF = visceral fat

Table 2. Pearson Correlation Coefficients between Indicators of Fat Measured by Abdominal Fat CT and MS, Cardiovascular Risk Factors in Men

Cardiovascular Risk Factors	VF		SF		VF/SF	
	r	*p*	*r*	*p*	*r*	*p*
Waist circumference	0.57	< 0.001	0.76	< 0.001	-0.04	0.702
BMI	0.49	< 0.001	0.68	< 0.001	-0.03	0.800
SBP	0.41	< 0.001	0.31	0.002	0.15	0.158
DBP	0.43	< 0.001	0.22	0.028	0.22	0.031
Fasting glucose	0.29	0.004	-0.11	0.277	0.34	< 0.001
Total cholesterol	-0.03	0.735	0.16	0.110	-0.12	0.231
Triglycerides	0.24	0.019	0.00	0.994	0.22	0.031
HDL cholesterol	-0.31	0.002	-0.13	0.195	-0.19	0.058
LDL cholesterol	0.00	0.987	0.23	0.027	-0.12	0.234

BMI = body mass index, DBP = diastolic blood pressure, HDL = high-density lipoprotein, LDL = low-density lipoprotein, MS = metabolic syndrome, SBP = systolic blood pressure, SF = subcutaneous fat, VF = visceral fat

134.50 cm^2, and we could assume that if VF was higher than 134.50 cm^2, the female patient had a high probability of developing MS. The AUC values of SF and the VF/SF ratio were 0.773 and 0.750, which were not statistically significant. As a result, VF could be evaluated as being useful for predicting MS in both sexes, but SF only affected males.

DISCUSSION

The purpose of our study was to assess the cross-sectional correlation of abdominal VF and SF with MS in a Korean population. Our principal findings can be summarized in the following 3 points: first, VF accumulation was the best predictor of MS and it had a positive correlation with cardiovascular risk factors in both sexes. SF also had a significant association with MS, especially in men, although it was not superior to VF. Second, the VF/SF ratio was not significantly associated with MS in either sex. Third, the calculated cut-off values of VF and SF to predict MS were as follows: the cut-off value of VF in men: 136.50 cm^2, the cut-off value of SF in men: 159.50 cm^2, and the cut-off value of VF in women: 134.50 cm^2.

There are various definitions of MS, but central obesity is widely recognized as a key factor of MS (1-4). Until now, waist

Table 5. Calculated Cut-Off Value of Indicators of Fat Measured by Abdominal Fat CT and AUC

Sex	Variable	Cut-Off Value	AUC	*p*-Value
Male	VF (cm^2)	136.50	0.762	< 0.001
	SF (cm^2)	159.50	0.681	0.005
	VF/SF		0.601	0.116
Female	VF (cm^2)	134.50	0.909	0.019
	SF (cm^2)		0.773	0.117
	VF/SF		0.750	0.151

AUC = area under the curve, SF = subcutaneous fat, VF = visceral fat

Table 3. Pearson Correlation Coefficients between Indicators of Fat Measured by Abdominal Fat CT and MS, Cardiovascular Risk Factors in Women

Cardiovascular Risk Factors	VF		SF		VF/SF	
	r	*p*	*r*	*p*	*r*	*p*
Waist circumference	0.85	< 0.001	0.87	< 0.001	0.28	0.304
BMI	0.75	< 0.001	0.92	< 0.001	0.15	0.593
SBP	0.55	0.032	0.48	0.068	0.21	0.454
DBP	0.33	0.225	0.15	0.602	0.27	0.326
Fasting glucose	0.55	0.034	0.39	0.152	0.30	0.280
Total cholesterol	-0.20	0.475	-0.35	0.196	0.01	0.971
Triglycerides	0.47	0.080	0.21	0.456	0.36	0.185
HDL cholesterol	-0.84	< 0.001	-0.67	0.006	-0.46	0.086
LDL cholesterol	-0.08	0.783	-0.07	0.813	0.11	0.687

BMI = body mass index, DBP = diastolic blood pressure, HDL = high-density lipoprotein, LDL = low-density lipoprotein, MS = metabolic syndrome, SBP = systolic blood pressure, SF = subcutaneous fat, VF = visceral fat

Table 4. Relationships between Indicators of Fat and MS

Sex	Variable	MS: Yes	MS: No	*p*-Value
		Mean ± Standard Deviation	Mean ± Standard Deviation	
Male	VF (cm^2)	195.38 ± 83.36	130.76 ± 51.22	< 0.001
	SF (cm^2)	201.28 ± 63.92	164.75 ± 55.27	< 0.001
	VF/SF	1.03 ± 0.44	0.88 ± 0.45	0.919
	Waist circumference (cm)	92.14 ± 8.29	83.64 ± 5.61	< 0.001
	BMI (kg/m^2)	28.08 ± 3.05	24.56 ± 2.27	< 0.001
Female	VF (cm^2)	217.00 ± 88.46	84.64 ± 50.30	0.048
	SF (cm^2)	275.50 ± 143.24	169.09 ± 76.68	0.350
	VF/SF	0.88 ± 0.50	0.54 ± 0.34	0.573
	Waist circumference (cm)	94.00 ± 16.02	72.73 ± 9.77	0.116
	BMI (kg/m^2)	29.25 ± 4.93	22.81 ± 3.82	0.189

BMI = body mass index, MS = metabolic syndrome, SF = subcutaneous fat, VF = visceral fat

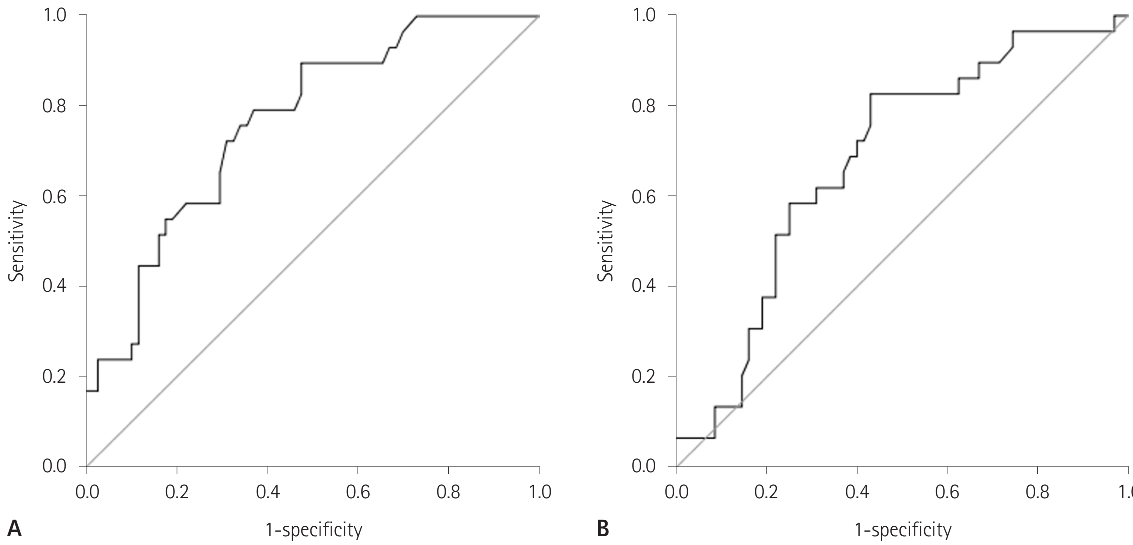

Fig. 2. ROC curves of VF **(A)** and SF **(B)** for predicting metabolic syndromes in men.
A. The AUC of VF was 0.762 and the result was statistically significant ($p < 0.001$).
B. The AUC of SF was 0.681 and the result was statistically significant ($p < 0.01$).
AUC = area under the curve, ROC = receiver operating characteristic, SF = subcutaneous fat, VF = visceral fat

circumference has been considered as the diagnostic criterion for MS and it can increase regardless of SF or VF accumulation. These 2 types of fat have different physiological characteristics; therefore, it is worthwhile to know what kind of fat contributes to MS. In fact, VF contributes to the development of MS and cardiovascular diseases, probably due to its anatomical proximity to the portal venous system and higher lipolytic characteristic (10, 11). It can lead to direct drainage of metabolites and free fatty acids into the liver, resulting in insulin resistance. On the other hand, small adipocytes in SF play the role of buffers that are involved in uptake of free fatty acids and TGs. But if they lose their functions, SF accumulation also contributes to insulin resistance (10, 11).

Several studies assessing the relationships between abdominal fat CT and metabolic diseases as cardiovascular risk factors have been reported worldwide (12-16); however, only a few of these studies were conducted in a Korean population (14-16). Also, minimal differences have been demonstrated between the kind of abdominal fat and the specific metabolic disease. Pickhardt et al. (13) reported that VF was the best predictor of MS in women and SF was the best predictor of MS in men, among the American population. Sandeep et al. (12) reported that VF, but not SF, is associated with cardiovascular risk factors and MS in non-diabetic Asian Indians. Also, Kim et al. (14) reported that increased SF is negatively correlated with the prevalence of MS in Korean population.

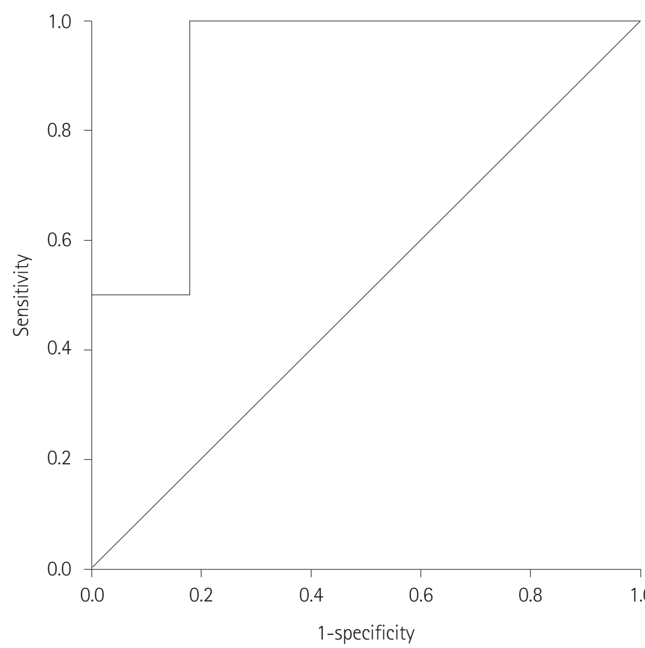

Fig. 3. A ROC curve of VF for predicting metabolic syndrome in women. The AUC of VF was 0.909, and the result was statistically significant ($p < 0.05$).
AUC = area under the curve, ROC = receiver operating characteristic, VF = visceral fat

Our result that VF is associated with MS and cardiovascular risk factors provides support to the results that have been previously reported. However, our current study results are partially consistent with those of the study by Pickhardt et al. (13), because VF was consistently the best predictor in both sexes in our study. Additionally, in contrast with the results of the study by Kim et al. (14), our results revealed that SF was a positive predictive indicator in men, but it was not superior to VF. There are some discrepancies between our study and other studies; however, our study is valuable as it was conducted in a Korean population. Also, further investigation should be performed to confirm the relationship between abdominal fat, especially SF, and MS.

To date, there have been some difficulties while trying to explain the results of abdominal fat CT to patients due to lack of specific cut-off values for positively predicting MS. We observed that VF could be evaluated as being useful for predicting MS in both sexes, while SF only affected males. Additionally, we calculated the cut-off values of VF and SF to predict MS and they were as follows: cut-off value of VF in men: 136.50 cm^2, cut-off value of SF in men: 159.50 cm^2, cut-off value of VF in women: 134.50 cm^2. If VF and SF values are higher than the cut-off values for the respective case, we can assume that the male or female patient has a higher probability of developing MS.

However, there are limitations to our study. First, the overall study population was small, especially the female population. Om comparing with the study by Kim et al. (15), the cut-off value of VF for predicting MS in men was 136 cm^2, which is very similar to that in our study. However, in women, the cut-off value of VF for predicting MS was 95 cm^2, which is somewhat lower compared with that in our study. This discrepancy could be due to the small population of females; therefore, a large cohort study should be conducted to determine which findings were accurate. Second, it is not certain that our local population represents the entire Korean population well. Third, there is radiation exposure to each patient when obtaining the VF and SF values by abdominal fat CT, although it is minimal. To avoid unnecessary radiation exposure, further investigations should be conducted to determine whether abdominal fat CT is better for predicting metabolic diseases and cardiovascular risk factors as compared with other anthropometric values, such as waist circumference or BMI.

In conclusion, VF accumulation was positively associated with MS and cardiovascular risk factors. SF accumulation also showed a positive association with MS in men, but it was not superior to VF. The calculated cut-off values of VF and SF to predict MS were as follows: the cut-off value of VF in men: 136.50 cm^2, the cut-off value of SF in men: 159.50 cm^2, and the cut-off value of VF in women: 134.50 cm^2.

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무증상 한국인에서 복부지방 CT와 대사증후군의 관계

박대웅 · 박노혁* · 박지연 · 김선정

목적: 이 연구의 목적은 무증상 한국인에서 복부지방 CT를 활용한 복부지방의 평가와 대사증후군과의 관계를 살펴보기 위함이다.

대상과 방법: 검진 복부지방 CT를 찍은 무증상의 111명의 한국인을 대상으로 연구가 진행되었으며 내장지방, 피하지방, 내장지방/피하지방의 비율과 대사증후군 및 심혈관계 질환 위험인자들과의 분석을 실시하였다.

결과: 남자에서는 내장지방과 피하지방이 모두 대사증후군, 많은 심혈관계 질환 위험인자들과 유의한 정적 상관관계를 보였고 내장지방이 피하지방보다 관련성의 강도가 강하였다. 여자에서는 내장지방만이 대사증후군과 몇몇의 심혈관계 질환 위험인자들과 유의한 정적 상관관계를 보였다. Receiver operating characteristic 곡선을 이용한 내장지방과 피하지방의 대사증후군 예측값은 다음과 같다. 내장지방은 남자: 136.50 cm^2, 피하지방은 남자: 159.50 cm^2, 내장지방은 여자: 134.50 cm^2이다.

결론: 내장지방의 축적은 남자와 여자에서 모두 대사증후군과 심혈관계 질환 위험인자들을 예측하는 지표이다. 피하지방은 남자에서만 대사증후군 및 심혈관계 질환의 위험인자들과 유의한 정적 상관관계를 보였으나 내장지방보다는 열등한 지표이다.

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