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Associations of visceral adiposity and exercise participation with C-reactive protein, insulin resistance, and endothelial dysfunction in Korean healthy adults

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Abstract

The aim of the current study was to examine the associations of visceral adiposity and exercise participation with C-reactive protein (CRP), insulin resistance, and endothelial dysfunction in Korean adults selected from the general population. We studied 160 Korean adults (aged 41.3 ± 13.0 years; n = 38 men and n = 122 women) who volunteered in a health promotion program. Subjects were divided into 2 groups based upon spontaneous exercise participation for using a cross-sectional approach. We measured anthropometric factors (body mass index [BMI], percentage body fat, waist-hip ratio [WHR], and abdominal fat area by computed tomographic scanning), blood pressure (BP), blood levels of glucose, lipids, fibrinogen, CRP, leptin, hemoglobin A_{1c}, homeostasis model assessment (HOMA), and carotid intima media thickness (IMT; via ultrasonography). Associations among the variables were assessed by Pearson partial correlation and linear regression, controlling for age and sex. Independent *t* tests were used to assess differences between exercise participants and nonparticipants. Significance was accepted at $P < .05$. As expected, the measures of adiposity (BMI, percentage body fat, WHR, abdominal fat area) were highly correlated with each other (r = .49-.86, $P < .01$). Blood levels of high-sensitivity CRP (hsCRP), leptin, and HOMA were modestly correlated with all measures of adiposity. Visceral fat area was the most important predictor of hsCRP, explaining 19.6% of the variance using stepwise linear regression analysis ($P < .01$). As visceral fat area tertiles increased from low to high, a significant stepwise increment in blood levels of CRP ($P < .001$), HOMA ($P = .005$), and left carotid IMT ($P = .035$) was observed. However, hsCRP and HOMA were not significantly different when compared across whole-body fat tertiles. Systolic BP, diastolic BP, and left carotid IMT were modestly correlated with WHR and visceral fat area ($P < .05$); but systolic BP and diastolic BP were also correlated with BMI and percentage body fat ($P < .05$). Therefore, the relative importance of central adiposity as opposed to total body fatness in endothelial dysfunction is unclear. Compared with the nonexercise group, exercise participants had significantly lower ($P < .05$) WHR, visceral fat area, ratio of visceral fat area to subcutaneous area, hsCRP, hemoglobin A_{1c}, and HOMA, with no significant differences in BMI, percentage body fat, and physical fitness. Central obesity with high visceral fat is strongly associated with blood level of hsCRP, insulin resistance, and endothelial dysfunction–related factors in healthy Korean adults. In addition, exercise participation, even in the absence of difference in physical fitness, may be protective against development of central obesity and insulin resistance in this understudied Korean population.

1. Introduction

Obesity, insulin resistance, and endothelial dysfunction are highly interrelated by multiple factors. Obesity, especially visceral fat, leads to insulin resistance and endothelial dysfunction, mainly through fat-derived metabolic products, hormones, and adipokines. Abdominal obesity due to intraabdominal adiposity drives the progression of multiple cardiometabolic risk factors independently of body mass index (BMI) through altered secretion of adipokines and exacerbation of insulin resistance [1]. Some of these adipose-derived products such as free fatty acid (FFA), tumor necrosis factor α, and interleukin 6 (IL-6) can also affect vascular function in addition to inducing insulin resistance; and these products are a potent stimulus for the production of C-reactive protein (CRP) in liver [2]. C-reactive protein is a blood biomarker for low-grade inflammation that is thought

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Table 1
Characteristics of subjects

Variables	Male (n = 38)	Female (n = 122)	All (n = 160)
Age (y)	43.00 ± 13.74	40.84 ± 12.82	41.35 ± 13.03
BMI (kg/m^2)	26.14 ± 3.19	25.12 ± 3.76	25.36 ± 3.65
Body fat (%)	22.51 ± 5.58	31.49 ± 5.29 *	29.36 ± 6.57
WHR	0.94 ± 0.06	0.88 ± 0.09 *	0.90 ± 0.08
Total abdominal fat area (cm^2)	323.99 ± 112.30	301.98 ± 115.28	306.84 ± 114.58
Subcutaneous fat area (cm^2)	191.29 ± 78.17	215.61 ± 86.93	210.24 ± 85.40
Visceral fat area (cm^2)	124.39 ± 55.27	79.60 ± 38.24 *	89.48 ± 46.27
VSR	0.61 (0.44-0.87)	0.37 (0.28-0.46) *	0.40 (0.30-0.54)
SBP (mm Hg)	124.3955.27	117.35 ± 16.73 *	119.06 ± 16.77
DBP (mm Hg)	83.03 ± 11.48	76.49 ± 11.02 *	78.05 ± 11.44
Glucose (mmol/L)	5.65 ± 2.63	4.96 ± 1.26	5.13 ± 1.71
Insulin (pmol/L)	9.91 (6.70-14.62)	9.29 (6.88-14.03)	9.35 (6.82-14.92)
HOMA	0.35 (0.21-0.51)	0.30 (0.21-0.42)	0.32 (0.21-0.43)
FFA (μEq/L)	544.84 ± 215.8	577.12 ± 234.49	569.41 ± 229.92
TC (mmol/L)	4.96 ± 1.12	4.94 ± 0.91	4.94 ± 0.96
HDL-C (mmol/L)	1.25 ± 0.28	1.48 ± 0.34 *	1.42 ± 0.34
LDL-C (mmol/L)	3.12 ± 0.95	3.18 ± 0.82	3.16 ± 0.85
TG (mmol/L)	1.86 ± 1.13	1.31 ± 0.82 *	1.44 ± 0.93
AI	2.74 (2.12-6.12)	1.71 (1.04-2.86) *	2.00 (1.22-3.38)
Fibrinogen (μmol/L)	9.14 ± 2.23	9.39 ± 2.16	9.33 ± 2.17
HbA_{1c} (%)	5.55 (5.20-5.90)	5.50 (5.30-5.85)	5.50 (5.30-5.90)
hsCRP (mg/L)	0.07 (0.04-0.16)	0.05 (0.03-0.11)	0.06 (0.03-0.12)
Leptin (ng/mL)	6.66 (4.02-11.47)	14.05 (11.32-22.58) *	13.01 (8.75-19.88)
Left carotid artery IMT (mm)	0.60 (0.50-0.80)	0.60 (0.50-0.80)	0.60 (0.50-0.80)
Right carotid artery IMT (mm)	0.60 (0.50-0.80)	0.60 (0.50-0.70)	0.60 (0.50-0.80)
PEI (%)	58.05 ± 8.28	59.21 ± 9.92	58.95 ± 9.57
Back muscular strength (kg)	88.50 ± 20.37	42.58 ± 12.99 *	53.54 ± 24.72
Sit-up (frequency)	19.62 ± 8.19	11.13 ± 7.00 *	13.08 ± 8.10
Sit and reach (cm)	2.71 ± 0.15	13.88 ± 7.22 *	11.40 ± 9.20

Values are mean and SD, or median (interquartile range) for skewed variables.
* $P < .05$ compared with the male group.

to be mechanically responsible for some of the obesity-associated comorbidities.

Visceral fat and CRP are considered important markers of insulin resistance and endothelial dysfunction by low-grade inflammation [3]. Blood CRP level is associated with cardiovascular disease (CVD) and with other inflammatory diseases, and has also been evaluated as a marker of systemic inflammation, potentially predicting risk of coronary events [4]. Insulin resistance and visceral fat are associated with low-grade inflammation [5], and visceral obesity is a hallmark of insulin resistance and type 2 diabetes mellitus. Carotid stiffness is associated with visceral obesity in patients with uncomplicated type 2 diabetes mellitus [6], but this association seems to be mediated by circulating CRP. The association of obesity, insulin resistance, and endothelial dysfunction may become a key target in the prevention of type 2 diabetes mellitus and CVD [7].

Previous studies have suggested that racial, age, or sex differences exist regarding the relationship between obesity-related health risks and body fat distribution and patterns of visceral fat accumulation [8-12]. The Asian diet is low in animal fat but high in carbohydrates. Recent studies suggest that low-carbohydrate diets are more effective than low-fat diets in inducing weight loss, suggesting that excessive carbohydrate rather than fat is the cause of obesity [13]. Gavaler and Rosenblum [14] strongly suggested that a variety of factors including hormonal status and race needs to be considered when examining the role of dietary factors and physical activity in relation to estimates of body fat mass and disease risk.

Physical activity may be associated with lower levels of inflammation through its inverse association with central obesity and increasing insulin resistance [15,16]. Subjects with the metabolic syndrome who maintain a high fitness level have markedly lower CRP concentrations as compared with those with a low fitness level [17]. Recent studies have shown that there is no relationship between change in CRP and the improvement in fitness and insulin sensitivity after exercise training [18,19].

The aim of the current study was to examine the associations of visceral adiposity and exercise participation with CRP, insulin resistance, and endothelial dysfunction in Korean adults selected from the general population.

2. Methods

2.1. Subjects

We studied 160 Korean adults (aged 41.3 ± 13.0 years; n = 38 men and n = 122 women) who visited the Fitness Center

Table 2
Subjects characteristics in exercise participants and nonparticipants

Variables	Exercise participants (n = 80)	Nonparticipants (n = 80)
Sex (male/female)	17/63	21/59
Age (y)	40.26 ± 11.92	42.44 ± 14.02
BMI (kg/m^2)	24.92 ± 3.64	25.80 ± 3.63
Body fat (%)	29.25 ± 6.23	29.46 ± 6.93
WHR	0.88 ± 0.08	0.91 ± 0.09 *
Total abdominal fat area (cm^2)	283.96 ± 94.09	334.15 ± 130.65 *
Subcutaneous fat area (cm^2)	200.62 ± 73.87	221.74 ± 96.76
Visceral fat area (cm^2)	77.02 ± 35.29	104.35 ± 53.25 *
VSR	0.38 (0.25-0.50)	0.43 (0.32-0.61) *
SBP (mm Hg)	118.13 ± 16.02	120.00 ± 17.54
DBP (mm Hg)	78.63 ± 11.22	77.47 ± 11.71
Glucose (mmol/L)	5.11 ± 1.58	5.15 ± 1.83
Insulin (pmol/L)	8.84 (6.27-13.49)	10.08 (7.71-14.44) *
HOMA	0.32 (0.17-0.41)	0.31 (0.22-0.45) *
FFA (μEq/L)	539.05 ± 209.37	599.39 ± 246.19
TC (mmol/L)	4.87 ± 0.94	5.01 ± 0.98
HDL-C (mmol/L)	1.47 ± 0.36	1.37 ± 0.33 *
LDL-C (mmol/L)	3.08 ± 0.86	3.25 ± 0.85
TG (mmol/L)	1.35 ± 0.95	1.53 ± 0.91
AI	1.82 (1.12-2.87)	2.19 (1.39-4.19)
Fibrinogen (μmol/L)	8.65 ± 1.98	10.00 ± 2.16 *
HbA_{1c} (%)	5.40 (5.20-5.60)	5.70 (5.30-6.08) *
CRP (mg/L)	0.04 (0.03-0.06)	0.08 (0.04-0.18) *
Leptin (ng/mL)	12.91 (8.67-16.65)	14.26 (10.60-24.96) *
Left carotid artery IMT (mm)	0.60 (0.50-0.80)	0.60 (0.50-0.80)
Right carotid artery IMT (mm)	0.60 (0.50-0.80)	0.60 (0.50-0.78)
PEI (%)	59.86 ± 10.21	57.91 ± 8.75
Back muscular strength (kg)	53.97 ± 22.40	53.09 ± 27.06
Sit-up (frequency)	13.63 ± 7.68	12.52 ± 8.52
Sit and reach (cm)	12.53 ± 8.50	10.23 ± 9.79

Values are mean and SD, or median (interquartile range) for skewed variables.
* $P < .05$ compared with the exercise-participant group.

at Keimyung University between March and June 2005. Sex distribution of subjects was limited because of random sampling of visitors to the fitness center. The study protocol was approved by the Institutional Review Boards of the Keimyung University. Informed consent was obtained from all the study participants. Subjects were divided into 2 groups (exercise participants, n = 80; nonparticipants, n = 80) based upon their responses to a questionnaire [20] about spontaneous exercise participation for using a cross-sectional approach. In the questionnaire, subjects were asked whether they had engaged in any sports activities (walking, jogging, running, bicycling, aerobic dance, swimming, ball games, and lower-intensity exercise) during the past 6 months and were asked if they had participated in a minimum of 3 exercise sessions weekly with exercise duration of at least 30 minutes per session at moderate intensity. Daily energy intake was estimated using Computer Aided Nutritional Analysis Program version 3.0 (The Korean Nutrition Society, Seoul, Korea) by detailed 3-day food records; there was no significant differences among groups (male, 2027.75 ± 596.70 kcal; female, 1534.93 ± 561.25 kcal; exercise participants, 1818.82 ± 742.45 kcal; nonparticipants, 1504.43 ± 415.56 kcal). Characteristics of the subjects are shown in Table 1 (sex differences) and Table 2 (exercise participants vs nonparticipants).

2.2. Anthropometric and body fat measurement

Body mass index was calculated as weight divided by height squared (kilograms per square meter); and percentage of body fat was estimated from the skinfold thickness of triceps, suprailiac crest, and thigh by the equations of Jackson et al [21] and Siri [22]. Skinfold thickness was measured using skinfold calipers (Skyndex, Fayetteville, AR) by an experienced technician. Waist circumference was measured on the midline between the lowest part of 12th rib and suprailiac crest by the World Health Organization method [23]. Waist-hip ratio (WHR) was calculated as waist circumference/hip circumference. Abdominal fat area, subcutaneous fat area, visceral fat area, and the ratio of visceral fat area to subcutaneous area (VSR) on the level of L4 through L5 were measured by computed tomographic scanning (Somatomestrit; Siemens, Munchen, Germany). Intima media thickness (IMT) of the carotid artery was measured by the B-mode imager and ultrasonography (G6OS, Siemens) by an experienced observer. Resting blood pressure (BP) was determined as the average of 3

Table 3
Relationship among measures of obesity, blood inflammatory markers, insulin resistance, endothelial dysfunction, and PEI controlled for sex and age in all subjects

	WHR	% Fat	Total	Subcut	Visceral	hsCRP	Leptin	HOMA	HbA_{1c}	Fibrinogen	AI	SBP	DBP	LC IMT	PEI
BMI	0.661 **	0.681 **	0.858 **	0.828 **	0.644 **	0.443 **	0.630 **	0.460 **	0.368 **	0.256 **	0.228 **	0.297 **	0.342 **	0.203 *	−0.017
WHR		0.417 **	0.691 **	0.637 **	0.571 **	0.432 **	0.459 **	0.302 **	0.255 *	0.190 *	0.193 *	0.296 **	0.290 **	0.272 **	−0.001
% Fat			0.682 **	0.694 **	0.435 **	0.259 **	0.685 **	0.391 **	0.210 *	0.247 **	0.003	0.198 *	0.263 **	0.148	−0.123
Total				0.951 **	0.772 **	0.404 **	0.717 **	0.398 **	0.355 **	0.234 **	0.198 *	0.263 **	0.328 **	0.253 **	−0.067
Subcut					0.538 **	0.353 *	0.689 **	0.401 **	0.315 **	0.229 **	0.136	0.247 **	0.295 **	0.159	−0.043
Visceral						0.396 **	0.568 **	0.281 **	0.345 **	0.179	0.267 **	0.208 *	0.292 **	0.365 **	−0.087
hsCRP [a]							0.226 *	0.261 **	0.372 **	0.557 **	0.139	0.204 *	0.137	0.268 **	−0.039
Leptin [a]								0.421 **	0.294 **	0.189 **	0.260 **	0.177	0.128	0.030	−0.185 *
HOMA [a]									0.400 **	0.292 **	0.422 **	0.118	0.081	0.054	−0.217 *
HbA_{1c} [a]										0.340 **	0.249 **	0.278 **	0.175	0.060	−0.040
Fibrinogen											0.096	0.058	−0.002	0.157	−0.143
AI [a]												0.117	0.113	0.028	−0.219 *
SBP													0.824 **	0.019	−0.077
DBP														0.106	0.071
LC IMT [a]															−0.002

Values are shown as Pearson correlation coefficients. LC indicates left carotid artery.

[a] Data: logarithmically transformed.

* $P < .05$.

** $P < .01$.

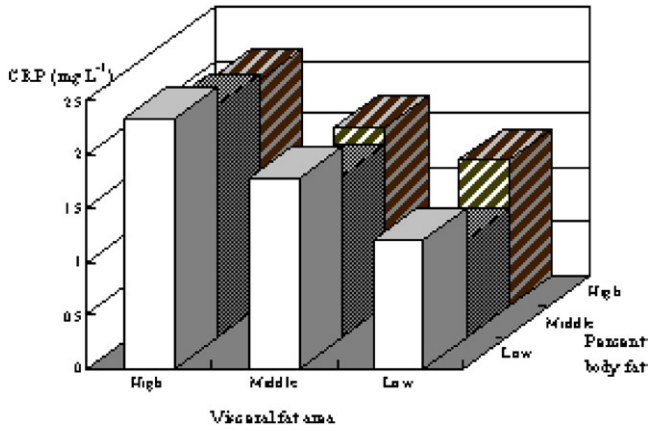

Fig. 1. Tertiles of visceral fat area and percentage body fat in relation to adjusted geometric means of hsCRP (significant main effects for visceral fat area: F = 11.373, $P < .001$; percentage body fat: $P = .732$; interaction: $P = .836$).

measures obtained on the left arm after subjects were seated quietly for 10 minutes using a random-zero sphygmomanometer (HICO, Tokyo, Japan) by an experienced technician.

2.3. Blood parameters

Blood samples were drawn from antecubital vein after an overnight fast using Vacutainer blood collection tubes (Becton Dickinson, Franklin Lakes, NJ), and serum samples were separated from whole blood by centrifugation at 1000*g* for 15 minutes after blood was allowed to clot at room temperature for 30 minutes. Plasma samples were separated from whole blood, using EDTA as an anticoagulant immediately after blood sampling, by centrifugation at 1000*g* for 15 minutes. These samples were stored at −80°C until assayed. Serum total cholesterol (TC) was determined by enzymatic methods using SICDIA L T-CHO Reagent kit (Shinyang, Seoul, Korea); and triglyceride (TG) was determined using SICDIA L TG Reagent (Shinyang), which was adjusted for free glycerol. Serum high-density lipoprotein cholesterol (HDL-C) was measured by homogeneous enzymatic colorimetric method using HDL-C plus kit (Roche, Penzberg, Germany), and low-density lipoprotein cholesterol (LDL-C) was determined using the Friedewald equation (LDL-C = TC − [HDL-C + {TG/5}]) [24]. Serum levels of glucose and FFA were determined by enzymatic methods using GLU-HK (Asan, Seoul, Korea) and NEFA-M reagent (Shinyang). Serum insulin was quantified by radioimmunoassay (Insulin IRMA; Biosource, Nivelles, Belgium). Atherogenic lipid index (AI) was obtained by the formula (TC − HDL-C)/HDL-C. Hemoglobin A_{1c} (HbA_{1c}) was determined by high-performance liquid chromatography after hemolysis (Bio-Rad, Richmond, CA). Fibrinogen levels were determined in citrated plasma using the Multifibren U method (a modification of the Clauss method [25]) on a Behring BCT analyzer (Dade Behring, Deerfield, IL). Plasma high-sensitivity CRP (hsCRP) level was measured using a commercially available latex-enhanced immunonephelometric assay on a BN II analyzer (Siemens). The detection limit of this assay is 0.03 mg/L. The intra- and interassay coefficients of variation are less than 10%. Plasma leptin level was determined by radioimmunoassay with rabbit polyclonal antibodies against highly purified recombinant human leptin (Linco Research, St Charles, MO). Insulin resistance as homeostasis model assessment (HOMA) was determined by the formula proposed by Matthews et al [26]: HOMA = fasting plasma insulin level (in micro–international units per milliliter) × fasting plasma glucose level (in millimoles per liter)/22.5.

2.4. Physical fitness

Muscular strength was measured by back muscular strength using a back muscular strength dynamometer (TKK, Tokyo, Japan). Muscular endurance was measured by a 30-second sit-up test. Flexibility was measured by a sit and reach test, and cardiopulmonary function was measured by physical efficiency index (PEI) using the Harvard step test. The PEI was calculated by the formula proposed by Brouha et al [27].

3. Statistical analysis

The anthropometric and biochemical features are presented as mean and SD, or as median (interquartile range) for skewed variables. The distributions of continuous variables were assessed for normality, and the logarithmic transformations of skewed variables (VSR, insulin, HOMA, AI, HbA_{1c}, hsCRP, leptin, carotid IMT) were used in subsequent analyses. Associations among the variables were assessed by Pearson partial correlation and linear regression analysis controlled for age and sex. Associations between geometric means of logarithmically transformed values of hsCRP, HOMA, and left carotid IMT and anthropometric variables

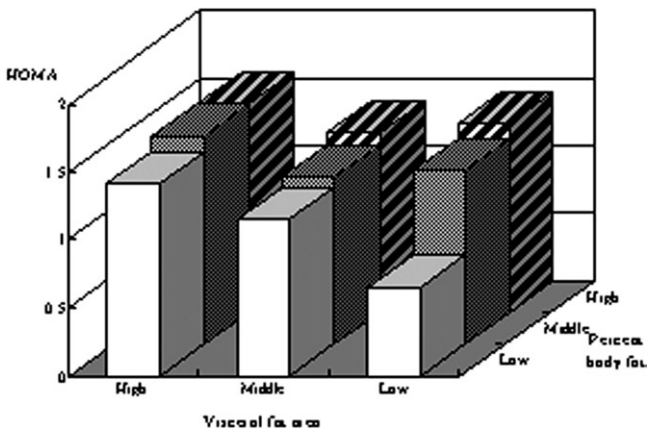

Fig. 2. Tertiles of percentage body fat and visceral fat area in relation to adjusted geometric means of HOMA (significant main effects for visceral fat area: F = 5.428, $P = .005$; percentage body fat: $P = .383$; interaction: $P = .886$).

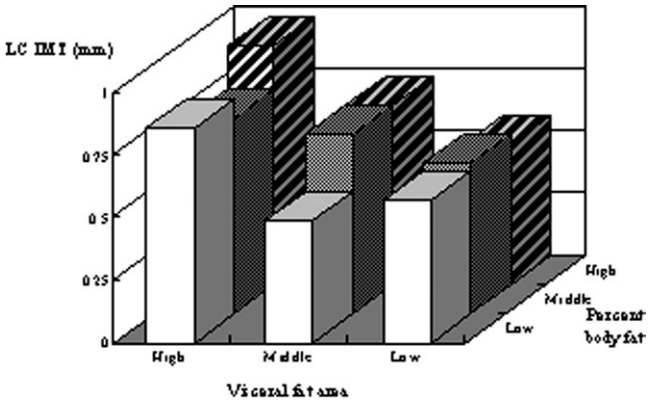

Fig. 3. Tertiles of percentage body fat and visceral fat area in relation to adjusted geometric means of left carotid IMT (significant main effects for visceral fat area: F = 3.459, P = .035; percentage body fat: P = .757; interaction: P = .756).

were assessed by stepwise linear regression and 2-way analysis of covariance with age and sex adjustment. Independent t tests were used to assess differences in anthropometric and biochemical variables between exercise participants and nonparticipants. Significance was accepted at $P < .05$.

4. Results

The characteristics of all subjects are shown in Table 1. Percentage body fat of the female group was significantly ($P < .05$) higher than that of the male group, whereas WHR, visceral fat area, and VSR of the female group were significantly ($P < .05$) lower than those of the male group. Systolic (SBP) and diastolic BP (DBP), TG, and AI were significantly ($P < .05$) lower in the female than male group, whereas HDL-C and leptin levels of the female group were significantly ($P < .05$) higher than those of the male group. Back muscular strength and sit-up of the female group were significantly ($P < .05$) lower than those of the male group, but sit and reach scores were significantly ($P < .05$) higher in the female than male group.

Compared with the nonexercise group, exercise participants had significantly lower ($P < .05$) WHR, visceral fat area, VSR, hsCRP, fibrinogen, HbA_{1c}, and HOMA despite no significant differences in BMI, percentage body fat, or physical fitness (Table 2).

As expected, the measures of adiposity (BMI, percentage body fat, WHR, abdominal fat area) were highly correlated with each other (r = .49-.86, $P < .01$) (Table 3). Blood levels of hsCRP and HOMA were modestly correlated with all measures of adiposity (Table 3).

Blood pressure and left carotid IMT were modestly correlated with WHR and visceral fat area ($P < .05$), but BP was also correlated with BMI and percentage body fat ($P < .05$) (Table 3). Blood level of fibrinogen was modestly correlated with measures of adiposity (BMI, WHR, percentage body fat, and abdominal fat area; $P < .05$) (Table 3). Leptin level was significantly ($P < .01$) correlated with measures of adiposity and was significantly correlated with hsCRP, HOMA, HbA_{1c}, fibrinogen, and SBP (Table 3). Physical efficiency index was modestly ($P < .05$) correlated with HOMA, AI, and blood leptin level (Table 3). Blood levels of hsCRP, fibrinogen, HbA_{1c}, and HOMA were significantly correlated with each other in linear regression of the total study population (Table 3).

As tertiles of visceral fat area increased from low to high, a significant stepwise increment in geometric means of logarithmically transformed values of blood levels of CRP (F = 11.373, P = .001), HOMA (F = 5.428, P = .005), and left carotid IMT (F = 3.459, P = .035) was observed. However, hsCRP, HOMA, and left carotid IMT were not significantly different when compared across the percentage of body fat tertiles (Figs. 1-3).

Visceral fat area was the most significant ($P < .01$) predictor of hsCRP and left carotid IMT, explaining 19.6% and 16.7% of the variance in stepwise linear regression analysis, respectively (Table 4).

5. Discussion

Although the men had a lower body fat percentage as compared with the women, the higher values of visceral fat area, BP, serum TG level, and AI including the lower values of HDL-C may indicate that male subjects have greater metabolic syndrome prevalence. These results may confirm the previous suggestion that the relative risk factors for men are slightly higher than those for women in the prevalence of central obesity, increased BP, and dyslipidemia [28-30].

Blood levels of hsCRP and HOMA were shown here to be modestly correlated with all measures of adiposity.

Table 4
Stepwise linear regression for hsCRP, HOMA, and left carotid artery IMT as the dependent variable and measures of obesity as independent variables in all subjects

Dependent variables	Independent variables	r^2	β Coefficients	SE	T	Sig	95% CI
hsCRP	Visceral fat area	0.196	.009	0.002	5.762	$P < .001$	0.006-0.012
HOMA	BMI	0.109	.050	0.012	4.086	$P < .001$	0.026-0.074
LC IMT	Visceral fat area	0.167	.003	0.001	4.964	$P < .001$	0.002-0.004

Independent variables: BMI, percentage body fat, WHR, total abdominal fat area, abdominal subcutaneous area, visceral fat area, VSR. CI indicates confidence interval.

Interestingly, as visceral fat area tertiles increased from low to high, a significant stepwise increment in blood levels of hsCRP, HOMA, and left carotid IMT were observed; but these variables were not significantly different when compared across whole-body fat tertiles. These results demonstrated that central obesity is strongly associated with both low-grade inflammation and insulin resistance. This finding is in line with previous studies that suggest that CRP levels could be an important factor associated with variations in insulin sensitivity [31,32] and that intraabdominal adiposity drives the progression of multiple cardiometabolic risk factors independent of BMI [1]. Hak et al [33] found that CRP was strongly related to BMI and to waist and hip circumferences separately; however, after adjustment for BMI, waist circumference was still related to CRP, whereas hip circumference was not. Therefore, they suggest that abdominal fat deposition may be the most important factor contributing to inflammation. Other previous studies have suggested that lower CRP levels, despite high levels of percentage body fat, could contribute to the favorable metabolic profile observed in metabolically healthy but obese individuals [34] and that lower CRP levels in patients with uncomplicated type 2 diabetes mellitus appear to be a marker of lower visceral fat content [6].

We found that the low-grade inflammatory status in our subjects, whose plasma CRP level was within the reference range, may also play a role in increased BP with increased serum level of TC. This finding confirms recent data showing an association between normal CRP plasma levels and arterial stiffness in healthy subjects [35] and patients with hypercholesterolemia [36].

Adipocytokines may further amplify the inflammatory cascade by stimulating hepatic CRP synthesis and altering endothelial function, resulting in vascular wall inflammation and elastin degradation [37]. C-reactive protein is considered to be an excellent marker of low-grade inflammation in the vascular wall, a well-recognized mechanism in the development of atherosclerosis [3], and may play a role in both monocyte activation and adhesion, which may be of importance during an inflammatory event [38]. Recent studies on CRP-associated endothelial dysfunction have suggested that CRP, by increasing local and systemic proteolysis, may contribute to atherosclerotic plaque vulnerability [39]. C-reactive protein elevates the level of macrophage chemoattractant protein 1 by increasing the receptor for advanced glycation end product expression, which has an important role in inflammatory processes and endothelial activation, providing it with an avenue to amplify its proatherogenic effects [40].

Central or abdominal obesity leads to insulin resistance and endothelial dysfunction through fat-derived metabolic products, hormone, and cytokines [7]. Increased levels of CRP and fibrinogen have been associated with increased CVD in the general population. Insulin resistance and obesity are important determinants of these inflammatory and fibrinolytic variables in nondiabetic [2] or type 2 diabetes mellitus subjects [41].

Obesity-associated insulin resistance and the ensuing hyperinsulinemia may promote sodium retention and sympathetic nervous system activation, and contribute to arterial stiffening [6]. Although we did not observe that obesity-associated insulin resistance may promote increased BP and carotid IMT, we found that increased blood levels of hsCRP, leptin, fibrinogen, and HOMA were associated with obesity. Moreover, a meaningful association of hsCRP with HOMA, fibrinogen, HbA_{1c}, and SBP in our results confirms an important role of CRP in the etiology of CVD with low-level chronic inflammation, insulin resistance, and endothelial dysfunction. Ridker et al [42] suggested that the addition of the measurement of CRP to screening based on lipid levels may provide an improved method of identifying women at risk for cardiovascular events. In another study in patients with uncomplicated type 2 diabetes mellitus, carotid stiffness is associated with visceral obesity; but this association seems to be mediated by circulating IL-6 and CRP [6]. Blood pressure was also correlated with BMI and percentage body fat, so the relative importance of central adiposity as opposed to total body fatness in endothelial dysfunction is unclear. However, an association of left carotid IMT with WHR and visceral fat area but not BMI and percentage body fat can be demonstrated by the higher relative risk of abdominal obesity and visceral adipose accumulation as compared with total body obesity.

An association of leptin with adiposity in our results confirms the strong relationship between BMI, waist circumference, and serum leptin levels previously reported in adults [43,44]. The association among hsCRP, leptin, and SBP demonstrates that obesity-associated cytokines may promote increased BP. The fat-derived hormone leptin promotes smooth muscle cell proliferation and angiogenesis, and high circulating levels of leptin have been associated with reduced arterial distensibility in healthy adults [45].

Our results provide evidence that adipose tissue, especially visceral fat, is an important determinant of a low-level chronic inflammatory state as reflected by a high level of hsCRP in a healthy adult population. Moreover, our results support the concept that such a low-level chronic inflammatory state may induce insulin resistance and endothelial dysfunction.

Improved fitness has favorable effects on serum lipid, BP, glucose tolerance, fibrinolysis, and endothelial function. Furthermore, the effect of physical fitness on individuals with the metabolic syndrome is more pronounced than that in subjects without metabolic abnormalities [17]. The present study showed that exercise participants had significantly lower WHR, visceral fat area, VSR, hsCRP, fibrinogen, HbA_{1c}, and HOMA than nonexercise participants. These results indicate that, although spontaneous exercise participation is not sufficient to elicit a significant improvement in physical fitness, a physically active lifestyle helps protect against the development of abdominal obesity, increased

CRP, fibrinolysis, and insulin resistance. Boreham et al [46] suggested that arterial stiffness–related benefits of exercise are most likely to accrue if exercise prescription in adults targets improvements in maximum oxygen consumption. They found that only sports-related activities, which by definition are of higher intensity than those performed in leisure time, were favorably associated with arterial stiffness, an association that was highly mediated by concomitant levels of maximum oxygen consumption.

Although our results indicate that physical fitness was independently associated with blood metabolic risk factors, body fatness and visceral fat area tend to be more strongly and consistently related to these factors. These results are consistent with previous findings that hemostatic risk factors are more favorable in physically active compared with sedentary women, but that body fat, BMI, and waist circumference are important physiological predictors of these factors [47], with body fatness being a better predictor of CVD risk factor profile than aerobic fitness in healthy men [48]. Aronson et al [17] reported that subjects with the metabolic syndrome who maintain a high cardiorespiratory fitness level have markedly lower CRP concentrations as compared with those with a low fitness level. However, we did not find this association between hsCRP and cardiorespiratory fitness level, possibly because of the fact that our subjects did not have metabolic syndrome.

We did not find a significant difference in endothelial dysfunction between exercise participants and nonparticipants; but visceral fat area, HOMA, blood levels of hsCRP, HbA_{1c}, and fibrinogen between the groups were different. We also found an inverse relationship between PEI and HOMA as well as in the atherogenic index. Physical activity most likely confers cardioprotection through multiple mechanisms such as direct effects on the cardiovascular system [49] and the association of physical activity with lower levels of inflammation [50]. Bruunsgaard [51] suggested that the beneficial health effects of physical exercise are mediated through muscle-derived IL-6, which has anti-inflammatory activities. One current concept regarding the pathophysiologic mechanism of the inflammation associated with atherosclerosis concerns the production of proinflammatory cytokines in response to stimuli from oxidized LDLs and macrophage associated with the atherosclerotic plaque [52,53]. Although no causation can be inferred from a cross-sectional study, our results suggest that the association of physical activity with lower levels of inflammation may be mediated by the association of exercise with lesser degrees of central obesity, lower HOMA, blood levels of hsCRP, HbA_{1c}, and fibrinogen; and these findings are supported by previous studies [15,54].

In summary, central obesity with high visceral fat is strongly associated with blood level of CRP, insulin resistance, and endothelial dysfunction–related factors in healthy Korean adults. In addition, exercise participation, even in the absence of differences in physical fitness, may be protective against development of central obesity, increased CRP, and insulin resistance in this understudied Korean population.

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