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Abdominal fat distribution measured using computed tomography is associated with an increased risk of colorectal adenoma in men

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Abstract

A few studies have shown inconsistent results regarding the association between the visceral fat proportion and colorectal adenomas. We aimed to investigate the association between abdominal fat distribution measured by computed tomography (CT) and colon adenoma.

A total of 336 participants underwent physical examination, blood tests, colonoscopy, and abdominal computed tomography at Chung-Ang University Hospital. The associations between the obesity indicies (body mass index, visceral fat area (VFA), subcutaneous fat area (SFA), VFA-to-SFA ratio (VFA/SFA), and colorectal adenomas were evaluated.

Of 309 subjects, 119 patients (38.5%) had colorectal adenoma. Mean age and fasting plasma glucose were higher in the patients with colorectal adenoma ($P < .05$, respectively). The mean VFA (153.3 cm^2 vs 131.4 cm^2, $P < .01$) and VFA/SFA (1.07 vs 0.92, $P < .05$) were higher in the adenoma group than in the nonadenoma group. Males had higher mean VFA and VFA/SFA ($P < .001$). The mean VFA, SFA, and VFA/SFA were not associated with the location, size, number, and advancement of colorectal adenoma. In multivariate analysis, colorectal adenoma was significantly associated with VFA rather than VFA/SFA. In addition, colorectal adenoma was significantly associated with VFA rather than VFA/SFA in the men. The VFA, SFA, and VFA/SFA were not associated with colorectal adenoma in the women.

The VFA measured by using a CT scan was positively associated with the presence of colorectal adenoma, especially in men. Furthermore, average risk men with large visceral fat volume should be examined carefully in screening colonoscopy.

Abbreviations: ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, CI = confidence interval, CRC = colorectal cancer, CRN = colorectal neoplasm, CT = computed tomography, HDL = high-density lipoprotein, hsCRP = high-sensitivity C-reactive protein, LDL = low-density lipoprotein, OR = odds ratio, SFA = subcutaneous fat area, TFA = total abdominal fat area, TG = triglyceride, VFA = visceral fat area, VFA/SFA = VFA-to-SFA ratio, WBC = white blood cell, WC = waist circumference, WHR = waist-to-hip ratio.

Keywords: colorectal adenoma, computed tomography, subcutaneous fat, visceral fat

1. Introduction

Colorectal cancer (CRC) is the third most prevalent cancer and it is the leading cause of cancer-related death in the world.[1] In addition, the incidence of CRC has increased by approximately 2 to 4 times in the past decades in many Asian countries, including China, Japan, South Korea, and Singapore.[2,3] Most CRCs develop through the adenoma–carcinoma sequence,[4] and the prevalence of colorectal adenomas is increasing in Korea.[5] Colorectal adenomatous polyps are considered precursors of CRCs, which allows for screening and prevention of CRC by using colonoscopy and polypectomy.[4,6] Screening for CRCs should be started at the age of 50 years in an asymptomatic individual in an average-risk population. However, in addition to age, factors like sex, smoking, family history, race, and obesity can affect the risk of CRC.[7,8]

So far, many epidemiological studies have shown an association between the risk of CRC and obesity measured by the body mass index (BMI), waist circumference (WC), and/or waist-to-hip ratio (WHR).[9,10] Previous studies have shown that visceral fat area (VFA) measured using computed tomography (CT) is a better predictor of colon neoplasms (CRNs) than BMI or WC,[11–14] in that VFA is directly associated with the risk of CRC. However, Asian adults generally have a lower central distribution of body weight and a smaller body size than Western adults.[15] Thus, a more accurate measurement of abdominal fat distribution in obesity other than BMI and WC may be warranted. Furthermore, the relative ratio of visceral fat to subcutaneous fat may be necessary to indicate obesity more

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accurately because of individual differences in the absolute amount of visceral adipose tissue and abdominal fat distribution. Therefore, the relative ratio of visceral fat to subcutaneous fat may indicate obesity more accurately.

In the present study, we hypothesized that the ratio of VFA to subcutaneous fat area (SFA), measured using CT might significantly correlate with the risk of colorectal adenoma. Therefore, the aim of this study was to investigate the association between abdominal fat distribution measured by CT and the incidence of colorectal adenoma.

2. Materials and methods

2.1. Study population

We reviewed the medical records of subjects aged >40 years who participated in a routine checkup program at Chung-Ang University Hospital Health Care Center between January 2013 and December 2015. For this study, 336 participants who underwent colonoscopy and abdominal CT scan, physical examinations (height, body weight, WC, BMI, and blood pressure), and blood tests (white blood cell, hemoglobin, platelet, glucose, albumin, aspartate aminotransferase, alanine aminotransferase, total bilirubin, triglyceride, total cholesterol, high-density lipoprotein [HDL] cholesterol, low-density lipoprotein [LDL] cholesterol, C-reactive protein, and high-sensitivity C-reactive protein) were considered. The exclusion criteria were a history of colonic disease (CRC, polyps, or inflammatory bowel disease), colorectal surgery, or colonoscopy, within the previous 10 years, and a family history of CRC. To avoid the potential protective effect of aspirin and statins on colorectal adenomas, patients who had been taking aspirin or a statin for ≥1 year were also excluded.

Of the 336 participants, those who could not undergo total colonoscopy (n=26) and those who could not undergo biopsy (n=1) were excluded. The remaining 309 participants were enrolled in the study (Fig. 1). The institutional review board approved the study (C2014024(1220)), and all the participants provided written informed consent for the use of personal data for this research.

2.2. Measurement of anthropometric parameters

Weight and height measurements were automated (GL-150, G-Tech International Co., Uijungbu City, South Korea; Inbody720, Biospace Co., Chun-An City, South Korea), and BMI was calculated as body-weight divided by height squared (kg/m^2). After fasting for 12 hours, a blood sample was taken, from which blood lipids and glucose levels were measured.

2.3. Colonoscopy

After bowel preparation, colonoscopy was performed by experienced endoscopists using a flexible colonoscope (CFH260AL, Olympus, Tokyo, Japan). The various drugs administered for bowel preparation were used as follows: we performed colonoscopies that reached the cecum, after bowel preparation with 4 L of CoLyte powder (Taejoon Pharm Co., Ltd, South Korea). The CoLyte powder was composed of polyethylene glycol (3350.29 g), anhydrous sodium sulfate (2.85 g), sodium hydrogen carbonate (0.84 g), sodium chloride (0.73 g), and potassium chloride (0.37 g). We examined colonoscopic features, including the size, location, number, and histological findings of polyps. Polyp size was assessed by using open colonoscope biopsy forceps (MTW-Endoskopie Manufaktur, Wesel, Germany). Adenoma size was classified into <10 and ≥10 mm, with the largest size used for multiple adenomas. The location of the colorectal adenomas was divided into 3 categories as follows: the proximal colon, including the cecum, ascending colon, and transverse colon; the distal colon, including the splenic flexure, descending colon, sigmoid colon, and rectum; and both sides of the colon. The number of adenomas was classified as either single or multiple (≥2). Histological findings were classified according to their premalignant potential as follows: Colorectal adenomas included tubular, villous, or serrated adenomas, and controls had normal colonoscopic findings and nonpolypoid, benign lesions, such as nonspecific colitis or histologically confirmed hyperplastic polyps. In addition, advanced adenomas were defined as ≥1 cm in estimated diameter, containing ≥25% villous features, and/or high-grade dysplasia.

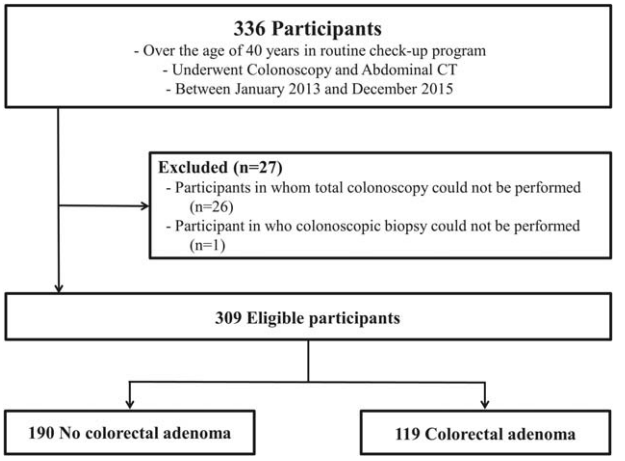

Figure 1. Study flow. A total of 336 participants were enrolled in the study. Of 309 eligible subjects, 119 patients (38.5%) had colorectal adenoma.

2.4. Measurement of abdominal adipose tissue area by using CT

Abdominal adipose tissue area was quantified by using 64-multidetector CT (Brilliance, Philips Medical Systems, Cleveland, OH). The fat area was determined by measuring the mean value of the pixels within the range of −175 to −25 Hounsfield units. Total abdominal fat area (TFA), VFA, and SFA were measured using a 10-cm CT slice scan image between the third and fourth lumbar vertebrae that was obtained during suspended respiration.

Area (cm^2) was calculated by using the Extended Brilliance Workspace version 1–4.5.2 software (Philips Healthcare, Best, the Netherlands). VFA was calculated by delineating the intra-abdominal cavity bound by parietal peritoneum or transversalis fascia, excluding the vertebral column and paraspinal muscles. SFA was calculated by subtracting VFA from TFA.

2.5. Statistical analysis

The Pearson χ^2 test or Fisher exact test for independent samples was used to assess the difference in risk factors between the subjects with and those without colorectal adenoma. For continuous variables, the data distribution was first evaluated for normality using the Shapiro–Wilk test. Normally distributed

Table 1

Baseline demographics of the subjects.

Total patients (n = 309)	
Demographics	
Age, y	48.8 ± 10.1
Male: Female	246: 63
Measurement of obesity	
Body mass index, kg/m^2	25.2 ± 3.24
Waist circumference, cm	87.7 ± 8.58
CT measurement	
VFA, cm^2	139.9 ± 68.2
SFA, cm^2	152.8 ± 64.2
VFA/SFA	0.98 ± 0.45
Measurement of metabolic markers	
Fasting plasma sugar, mg/dL	105.0 ± 23.0
HbA1c, %	5.57 ± 0.83
Total cholesterol, mg/dL	206.1 ± 36.7
HDL, mg/dL	51.4 ± 10.5
LDL, mg/dL	124.0 ± 29.4
TG, mg/dL	127.0 ± 76.3
Albumin, g/dL	4.59 ± 0.28
AST, IU/L	30.2 ± 13.4
ALT, IU/L	31.8 ± 21.8
GGT, IU/L	40.9 ± 32.8
Total bilirubin, mg/dL	1.07 ± 0.41

Values are presented as mean ± SD or absolute number (%).
ALT = alanine aminotransferase, AST = aspartate aminotransferase, CT = computed tomography, GGT = gamma glutamyltransferase, HbA1c = hemoglobin A1c, HDL = high-density lipoprotein, LDL = low-density lipoprotein, SFA = subcutaneous fat area, TG = triglyceride, VFA = visceral fat area.

Table 2

Clinical characteristics of the subjects with and without colorectal adenoma.

	Adenoma (n = 119)	Nonadenoma (n = 190)	*P*
Demographics			
Age, y	52.0 ± 9.3	46.7 ± 10.2	<.001
Male	101 (84.9%)	145 (76.3%)	.082
Measurement of obesity			
BMI, kg/m^2	25.5 ± 3.3	25.1 ± 3.2	.260
Waist circumference, cm	88.5 ± 9.0	87.2 ± 8.3	.164
VFA, cm^2	153.3 ± 67.9	131.4 ± 44.9	.006
SFA, cm^2	156.0 ± 70.0	150.8 ± 60.3	.485
VFA/SFA	1.07 ± 0.51	0.92 ± 0.41	.006
Measurement of metabolic markers			
Fasting blood sugar, mg/dL	108.6 ± 25.1	102.7 ± 21.3	.027
HbA1c, %	5.67 ± 0.96	5.50 ± 0.74	.088
Total cholesterol, mg/dL	203.7 ± 38.9	207.6 ± 35.2	.365
HDL, mg/dL	50.6 ± 11.0	51.9 ± 10.1	.298
LDL, mg/dL	120.0 ± 28.4	127.1 ± 30.0	.256
TG, mg/dL	125.6 ± 67.3	128.0 ± 81.6	.059
Albumin, g/dL	4.55 ± 0.29	4.61 ± 0.27	.042
AST, IU/L	31.6 ± 16.7	29.3 ± 10.9	.151
ALT, IU/L	31.9 ± 24.3	31.8 ± 20.2	.952
GGT, IU/L)	44.6 ± 34.8	38.7 ± 31.3	.122
Total bilirubin, mg/dL	1.05 ± 0.40	1.08 ± 0.42	.492

Values are presented as mean ± SD or absolute number (%).
ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, GGT = gamma glutamyltransferase, HbA1c = hemoglobin A1c, SD = standard deviation, SFA = subcutaneous fat area, TG = triglyceride, VFA = visceral fat area.

data were compared using Student's *t* test and nonnormally distributed data were analyzed using Mann–Whitney *U* test. To detect the dose–response relationship, we used cut points to categorize the patients into quartiles in terms of VFA, SFA, and the VFA to SFA ratio (VFA/SFA). The relationship between colorectal adenoma and obesity (obesity indexes: BMI, VFA, SFA, and VFA/SFA) was assessed based on odds ratios (ORs) with 95% confidence intervals (CIs) obtained by using the logistic regression model. The lowest quartiles of VFA, SFA, and VFA/SFA were selected as reference groups before the analysis. The significance of risk factors other than the obesity indices was examined by univariate and multivariate analyses. A *P* value of <.05 was considered statistically significant. The software package used for the statistical analysis was SPSS version 20.0 (SPSS Inc., Chicago, IL).

3. Results

3.1. Baseline demographic characteristics of the subjects

For this study, 309 subjects (male-to-female ratio, 246:63) were included. The mean age was 48.8 ± 10.1 years. The mean BMI was 25.2 ± 3.24 kg/m^2, and the mean WC was 87.7 ± 8.58 cm. The mean VFA and SFA measured by using CT scan were 139.9 ± 68.2 and 152.8 ± 64.2 cm^2, respectively. The mean VFA/SFA was 0.98 ± 0.45. The baseline characteristics of the subjects are shown in Table 1.

3.2. Clinical characteristics of the subjects with and those without colorectal adenoma

The characteristics of the subjects with and those without colorectal adenoma are compared in Table 2. Among the 309 subjects, 119 (38.5%) had colorectal adenoma. The mean age was significantly higher in the patients with colorectal adenoma than in those without it (52.0 ± 9.3 vs 46.7 ± 10.2, *P* < .001). The male-to-female ratio did not differ between the patients with and those without colorectal adenoma (101:18 vs. 145:35, *P* = .082). Of the anthropometric measurements of obesity, BMI, and WC did not differ between the groups. The mean VFA (153.3 ± 67.9 cm^2 vs 131.4 ± 44.9 cm^2, *P* = .006) and VFA/SFA (1.07 ± 0.51 vs 0.92 ± 0.41, *P* = .006) were significantly higher in the patients with colorectal adenoma that in those without colorectal adenoma, whereas the amounts of SFA did not differ between the groups. Of the various metabolic markers assayed, fasting plasma glucose concentration was higher in the patients with colorectal adenoma (108.6 ± 25.1 mg/dL vs 102.7 ± 21.3 mg/dL, *P* = .027), but albumin was lower in patients with colorectal adenoma than in those without it (4.61 ± 0.27 g/dL vs 4.55 ± 0.29 g/dL, *P* = .042).

3.3. Characteristics of colorectal adenoma according to abdominal fat distribution

In the subjects with colorectal adenoma, the mean VFA, SFA, and VFA/SFA were not associated with tumor location, number, and advancement of colorectal adenoma. The size of colorectal adenoma was not significantly associated with VFA and VFA/SFA, but significantly correlated with the number of colorectal adenoma ($r = 0.365$, $P < .001$). The characteristics of colorectal adenoma, including endoscopic and pathological features according to abdominal distribution, are summarized in Table 3.

3.4. Abdominal fat distribution according to sex-related differences

The males had higher VFA and VFA/SFA but lower SFA than the females (Table 4). In addition, their mean VFA and VFA/SFA were significantly increased with age. Positive correlations were

Table 3

Characteristics of colorectal adenoma according to abdominal fat distribution (n = 119).

	Number (%)	VFA, cm^2	*P*	SFA, cm^2	*P*	VFA/SFA	*P*
Location							
Distal	47 (39.5)	164.1 ± 62.9	.356	158.0 ± 68.3	.955	1.13 ± 0.49	.546
Proximal	45 (37.8)	144.1 ± 73.9		155.8 ± 79.6		1.02 ± 0.53	
Both	27 (22.7)	150.1 ± 65.5		152.9 ± 57.0		1.06 ± 0.51	
Size, mm							
<10	116 (97.5)	153.9 ± 68.5	.610	156.3 ± 70.5	.781	1.08 ± 0.51	.700
≥10	3 (2.5)	133.5 ± 35.1		144.8 ± 59.4		0.96 ± 0.15	
Number							
<2	73 (61.3)	150.7 ± 69.3	.550	153.4 ± 69.9	.604	1.06 ± 0.48	.371
≥2	46 (38.7)	157.7 ± 66.0		160.2 ± 66.0		1.09 ± 0.55	
Advancement							
Nonadvanced	115 (96.6)	136.8 ± 68.4	.933	156.6 ± 70.7	.615	0.96 ± 0.46	.645
Advanced	4 (3.4)	139.8 ± 25.3		138.6 ± 50.1		0.85 ± 0.41	

Values are presented as mean ± SD or absolute number (%).
SFA = subcutaneous fat area, VFA = visceral fat area.

Table 4

Abdominal fat distribution according to gender difference.

	Sex	Values	*P*	Regression coefficient of age	*P*
VFA, cm^2	Men	149.3 ± 67.1	<.001	0.233	<.001
	Women	102.9 ± 59.9			
SFA, cm^2	Men	145.8 ± 58.3	<.001	−0.044	.443
	Women	180.0 ± 77.8			
VFA/SFA	Men	1.08 ± 0.44	<.001	0.332	<.001
	Women	0.59 ± 0.29			

Values are presented as mean ± SD.
SFA = subcutaneous fat area, VFA = visceral fat area.

found between the following obesity indexes: BMI and VFA ($r = 0.678$, $P < .001$), BMI and SFA ($r = 0.724$, $P < .001$), and VFA and SFA ($r = 0.452$, $P < .001$).

3.5. Association between abdominal fat distribution and risk of colorectal adenoma

We categorized subjects into quartile according to VFA, SFA, and VFA/SFA as abdominal fat distribution. As a result, the incidence of colorectal adenoma showed increasing tendency with increasing quartiles of VFA, SFA, and VFA/SFA (*P* for trends were .001, .501, and .002, respectively, Fig. 2).

In the univariate analysis, colorectal adenoma was not associated with SFA but was associated with VFA (*P* for trend .001) and VFA/SFA for both categorical data and trend (*P* for trend .002; Table 5). In the multivariate analysis, colorectal adenoma was significantly associated with VFA rather than VFA/SFA (Table 5). The highest quartile of VFA was associated with a 2.8-fold risk of colorectal adenoma when compared with the lowest quartile.

3.6. Association between abdominal fat distribution and risk of colorectal adenoma according to sex-related differences

Data were analyzed according to sex because significant correlations were found between sex and VFA ($P < .001$), SFA ($P < .001$), and VFA/SFA ($P < .001$). In the univariate analysis, colorectal adenoma was significantly associated with VFA (*P* for trend .006) and VFA/SFA (*P* for trend .024) for both categorical data and trend in the men, but not in the women. SFA was not associated with colorectal adenoma in both the men and women.

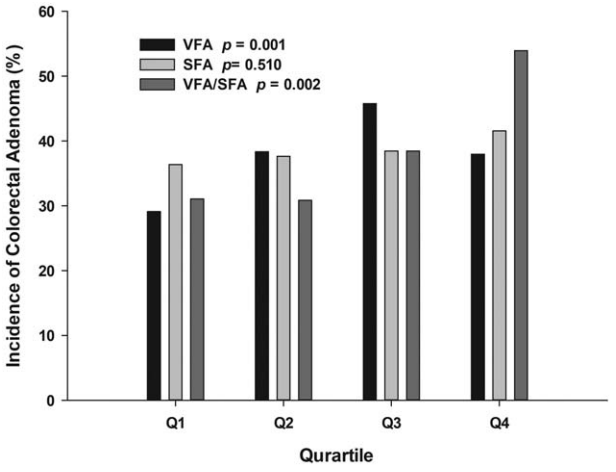

Figure 2. Incidence of colorectal adenoma according to quartiles of VFA, SFA, and VFA/SFA. When the subjects were categorized into quartile according to VFA, SFA, and VFA/SFA, the incidence of colorectal adenoma was significantly correlated with the increase of VFA and VFA/SFA rather than SFA (*P* for trends for VFA, VFA/SFA, and SFA were .001, .002, and .501, respectively). SFA = subcutaneous fat area, VFA = visceral fat area.

Table 5

Association between abdominal fat distribution and risk of colorectal adenoma.

			Unadjusted analysis		Adjusted analysis*	
	Nonadenoma (n = 190)	Adenoma (n = 119)	OR (95% CI)	P	OR (95% CI)	P
VFA, cm^2				.001		.135
Quartile I (≤92.6)	56 (29.5)	23 (19.3)	1		1	
Quartile II (92.7–131.1)	45 (23.7)	28 (23.5)	1.23 (0.61–2.47)	.559	1.35 (0.62–2.92)	.449
Quartile III (131.1–177.4)	45 (23.7)	38 (31.9)	2.23 (1.14–4.36)	.019	2.45 (1.05–5.71)	.039
Quartile IV (≥177.4)	49 (25.8)	30 (25.2)	2.60 (1.33–5.09)	.005	2.81 (1.02–7.73)	.046
SFA, cm^2				.510		.414
Quartile I (≤111.7)	49 (25.8)	28 (23.5)	1		1	
Quartile II (111.6–140.9)	48 (25.3)	29 (24.4)	1.06 (0.55–2.03)	.867	1.34 (0.65–2.85)	.407
Quartile III (140.9–185.5)	48 (25.3)	30 (25.2)	1.09 (0.57–2.10)	.787	1.70 (0.78–3.69)	.180
Quartile IV (≥185.5)	45 (23.7)	32 (26.9)	1.24 (0.65–2.38)	.509	2.30 (0.84–6.31)	.105
VFA/SFA				.002		.448
Quartile I (≤0.632)	51 (26.8)	23 (19.3)	1		1	
Quartile II (0.632–0.921)	56 (29.5)	25 (21.0)	1.24 (0.58–2.65)	.586	0.89 (0.36–2.13)	.800
Quartile III (0.921–1.202)	48 (25.3)	30 (25.2)	1.61 (0.82–3.17)	.167	1.15 (0.49–2.69)	.745
Quartile IV (≥1.202)	35 (18.4)	41 (34.5)	3.33 (1.60–6.91)	.001	1.71 (0.63–4.61)	.291

* Adjusted for age, sex, albumin, glucose, triglyceride, and waist circumference.

Values are presented as absolute number (%) or OR (95% CI).

CI = confidence interval, OR = odds ratio, SFA = subcutaneous fat area, VFA = visceral fat area.

In the multivariate analysis, colorectal adenoma was significantly associated with VFA rather than VFA/SFA in the men (Table 6). Especially the highest quartile of VFA was associated with a 2.9-fold risk of colorectal adenoma when compared with the lowest quartile. However, VFA, SFA, and VFA/SFA were not associated with colorectal adenoma in the women.

4. Discussion

This study investigated the association between abdominal fat distribution and the incidence of colorectal adenoma. Based on our results, we demonstrated that the presence of colorectal adenoma was positively associated with VFA rather than VFA/SFA. Furthermore, the presence of colorectal adenoma was significantly associated with VFA only in men. This demonstrated that abdominal visceral fat might contribute to the growth and progression of colorectal adenoma.

This study revealed an association between abdominal visceral fat and colorectal adenoma, providing the evidence of the role of visceral obesity in the development of CRN. Although many studies showed a positive association between obesity measured by using BMI and CRC,[16,17] recent studies suggested that WC and WHR, both surrogate markers of intra-abdominal fat or visceral adipose tissue, show a greater association with development of CRN than BMI.[18,19] Although the exact mechanism is not completely established, several possible mechanisms of visceral fat in colorectal carcinogenesis have been proposed. First, insulin resistance and subsequent hyperinsulinemia are involved in visceral adiposity.[20] This may increase cell proliferation and reduces cell death, which can eventually lead to carcinogenesis.[10,21] Another mechanism has

Table 6

Association between abdominal fat distribution and risk of colorectal adenoma according to gender difference.

	Men (n = 246)				Women (n = 63)			
	Nonadenoma	Adenoma	Adjusted OR (95% CI)*	P	Nonadenoma	Adenoma	Adjusted OR (95% CI)*	P
VFA, cm^2				.219				.358
Quartile I (M≤104.3, F≤58.7)	43 (29.7)	18 (18)			10 (22.2)	5 (27.8)	1	
Quartile II (M: 104.3–140.4, F: 58.7–89.5)	40 (27.6)	22 (21.8)	1.69 (0.69–4.17)	.253	13 (28.9)	3 (16.7)	0.87 (0.13–5.99)	.890
Quartile III (M:140.4–181.6, F:89.5–133.6)	32 (22.1)	30 (29.7)	2.62 (1.00–6.87)	.049	13 (28.9)	3 (16.7)	5.29 (0.49–57.7)	.172
Quartile IV (M≥181.6, F≥133.6)	30 (20.7)	31 (30.7)	2.90 (0.96–8.80)	.050	9 (20.0)	7 (38.9)	8.53 (0.34–213)	.192
SFA, cm^2				.624				.750
Quartile I (M≤107.7, F≤126.8)	39 (26.9)	22 (21.8)	1		13 (28.9)	2 (11.1)	1	
Quartile II (M:107.7–135.0,F: 126.8–167.2)	34 (23.4)	28 (27.7)	1.29 (0.58–2.85)	.528	10 (22.2)	6 (33.3)	2.06 (0.15–28.5)	.590
Quartile III (M:135.0–174.2,F:167.2–211.6)	38 (26.2)	24 (23.8)	1.43 (0.61–3.34)	.415	13 (28.9)	3 (16.7)	3.64 (0.28–47.3)	.323
Quartile IV (M≥174.2, F≥221.6)	34 (23.4)	27 (26.7)	2.15 (0.69–6.72)	.187	9 (20.0)	7 (38.9)	3.45 (0.26–48.6)	.359
VFA/SFA				.420				.845
Quartile I (M≤0.77, F≤0.42)	42 (29.0)	20 (19.8)	1		10 (22.2)	6 (33.3)	1	
Quartile II (M:0.77–0.99,F: 0.42–0.53)	36 (24.8)	24 (23.8)	1.40 (0.44–4.40)	.566	11 (24.4)	5 (27.8)	0.51 (0.10–2.52)	.409
Quartile III (M:1.0–1.32, F:0.53–0.71)	39 (26.9)	24 (23.8)	1.70 (0.57–5.50)	.335	12 (26.7)	3 (16.7)	0.55 (0.07–4.07)	.555
Quartile IV (M≥1.32, F≥0.72)	28 (19.3)	33 (32.7)	2.48 (0.74–8.28)	.139	12 (26.7)	4 (22.2)	–	1.000

* Adjusted for age, sex, albumin, glucose, triglyceride, and waist circumference.

Values are presented as absolute number (%) or OR (95% CI).

CI = confidence interval, OR = odds ratio, SFA = subcutaneous fat area, VFA = visceral fat area.

been linked to elevated serum levels of visceral fat, including interleukin 6, tumor necrosis factor alpha and adiponectin, and pro-inflammatory adipokines,[20] which may be associated with the development of colorectal adenoma. Thus, measuring visceral fat directly using CT can better predict insulin resistance than WC or BMI.[22] In general, routine use of CT is not cost-effective and has a risk of radiation exposure. However, it is important for Asian adults to measure visceral fat using CT because Asian adults generally have a smaller physique compared with Western adults, with a less central distribution of body weight.[15]

In our present study, colorectal adenoma was not associated with the location, size, number, and advancement of adenoma. However, previous studies have shown a positive correlation between the presence of visceral fat and the presence of adenomas on both sides of the colon, large adenomas, and multiple adenomas.[11,23]

Furthermore, a recent study by Nagata et al[24] showed that advanced adenomas were positively associated with higher VFA, but not with SFA. Taken together, abdominal visceral fat may influence the growth and progression of colorectal adenoma.

Among the various measurements of obesity in our present study, VFA and VFA/SFA were significantly associated with colorectal adenoma, but only VFA was independently associated with colorectal adenoma after adjusted analysis. Why VFA was the only significant factor among the obesity indexes is unclear. A previous study demonstrated that an absolute amount of visceral fat over a certain threshold is more important than the relative proportion of visceral fat in transitioning a patient into the phase of insulin resistance may be another probable mechanism.[25] However, Nagata et al[24] showed that VFA/SFA was independently associated with colorectal adenoma, but this result was observed only in men. Furthermore, abdominal subcutaneous and visceral fats have distinctly different functions with regard to insulin.[26] Further studies are needed to investigate such importance of visceral fat proportion.

In this study, only VFA was associated with colorectal adenoma in men, but not in women. Obesity is a relatively higher risk for CRC in men than in women.[10,16,27] and women generally tend to accumulate less VFA even when they gain weight more than men.[28] The difference between men and women is known to be related to estrogen levels in postmenopausal women and may be influenced by menopausal status and estrogen hormone use.[10] Our result indicated that the distribution of abdominal adipose tissue differed according to sex (higher VAT volume and lower SAT volume in the men than in the women) may explain the sex-related difference in the effects of VFA on colorectal adenoma. However, 2 large-scale studies demonstrated that VFA was independently associated with colorectal adenoma in both sexes.[11,24] Further studies are needed to investigate such risk according to sex.

Our study has several strengths. First, the data were of high quality. Colonoscopies were performed by well-trained endoscopists. Second, the volume of abdominal adipose tissue was measured using 64-multidetector CT and the result showed high validity and reproducibility.[29] Third, we assessed a healthy population to represent the general population. Accordingly, our results are applicable to clinical situations and could be used for future screening strategies.

Our study has some limitations. First, we did not assess the direct relationship between insulin resistance and the presence of colorectal adenomas despite obesity is considered a key mechanism in the development of colorectal adenoma.[10,20,21] Second, we did not evaluate the individuals' diet or lifestyles such as smoking, which could be associated with colorectal adenoma.[30]

In conclusion, VFA rather than VFA/SFA measured by using a CT scan was positively associated with the presence of colorectal adenoma, especially in men. Furthermore, average risk men with large visceral fat volume should be examined carefully in screening colonoscopy. Further large-scale studies are needed to clarify the underlying mechanism and causal relationship between abdominal visceral fat and CRN.

References

[1] Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87–108.

[2] Sung JJ, Lau JY, Goh KL, et al. Increasing incidence of colorectal cancer in Asia: implications for screening. Lancet Oncol 2005;6:871–6.

[3] Toyoda Y, Nakayama T, Ito Y, et al. Trends in colorectal cancer incidence by subsite in Osaka, Japan. Jpn J Clin Oncol 2009;39:189–91.

[4] Leslie A, Carey FA, Pratt NR, et al. The colorectal adenoma–carcinoma sequence. Br J Surg 2002;89:845–60.

[5] Kim BC, Shin A, Hong CW, et al. Association of colorectal adenoma with components of metabolic syndrome. Cancer Causes Control 2012;23: 727–35.

[6] Lieberman DA, Weiss DG, Bond JH, et al. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. N Engl J Med 2000;343:162–8.

[7] Sung JJ, Lau JY, Young GP, et al. Asia Pacific consensus recommendations for colorectal cancer screening. Gut 2008;57:1166–76.

[8] Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Gastroenterology 2008;134:1570–95.

[9] Bardou M, Barkun AN, Martel M. Obesity and colorectal cancer. Gut 2013;62:933–47.

[10] Frezza EE, Wachtel MS, Chiriva-Internati M. Influence of obesity on the risk of developing colon cancer. Gut 2006;55:285–91.

[11] Nam SY, Kim BC, Han KS, et al. Abdominal visceral adipose tissue predicts risk of colorectal adenoma in both sexes. Clin Gastroenterol Hepatol 2010;8:443–50. e1-2.

[12] Otake S, Takeda H, Suzuki Y, et al. Association of visceral fat accumulation and plasma adiponectin with colorectal adenoma: evidence for participation of insulin resistance. Clin Cancer Res 2005; 11:3642–6.

[13] Yamamoto S, Nakagawa T, Matsushita Y, et al. Visceral fat area and markers of insulin resistance in relation to colorectal neoplasia. Diabetes Care 2010;33:184–9.

[14] Oh TH, Byeon JS, Myung SJ, et al. Visceral obesity as a risk factor for colorectal neoplasm. J Gastroenterol Hepatol 2008;23:411–7.

[15] Wells JC, Treleaven P, Charoensiriwath S. Body shape by 3-D photonic scanning in Thai and UK adults: comparison of national sizing surveys. Int J Obes (Lond) 2012;36:148–54.

[16] Murphy TK, Calle EE, Rodriguez C, et al. Body mass index and colon cancer mortality in a large prospective study. Am J Epidemiol 2000;152: 847–54.

[17] Calle EE, Rodriguez C, Walker-Thurmond K, et al. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 2003;348:1625–38.

[18] Moore LL, Bradlee ML, Singer MR, et al. BMI and waist circumference as predictors of lifetime colon cancer risk in Framingham Study adults. Int J Obes Relat Metab Disord 2004;28:559–67.

[19] Giovannucci E, Ascherio A, Rimm EB, et al. Physical activity, obesity, and risk for colon cancer and adenoma in men. Ann Intern Med 1995; 122:327–34.

[20] Shoelson SE, Herrero L, Naaz A. Obesity, inflammation, and insulin resistance. Gastroenterology 2007;132:2169–80.

[21] Giovannucci E. Insulin, insulin-like growth factors and colon cancer: a review of the evidence. J Nutr 2001;131:s3109–20.

[22] Hayashi T, Boyko EJ, McNeely MJ, et al. Visceral adiposity, not abdominal subcutaneous fat area, is associated with an increase in future insulin resistance in Japanese Americans. Diabetes 2008;57:1269–75.

[23] Kang HW, Kim D, Kim HJ, et al. Visceral obesity and insulin resistance as risk factors for colorectal adenoma: a cross-sectional, case-control study. Am J Gastroenterol 2010;105:178–87.

[24] Nagata N, Sakamoto K, Arai T, et al. Visceral abdominal fat measured by computed tomography is associated with an increased risk of colorectal adenoma. Int J Cancer 2014;135: 2273–81.
[25] Freedland ES. Role of a critical visceral adipose tissue threshold (CVATT) in metabolic syndrome: implications for controlling dietary carbohydrates: a review. Nutr Metab (Lond) 2004;1:12.
[26] Giorgino F, Laviola L, Eriksson JW. Regional differences of insulin action in adipose tissue: insights from in vivo and in vitro studies. Acta Physiol Scand 2005;183:13–30.
[27] Ahmed RL, Schmitz KH, Anderson KE, et al. The metabolic syndrome and risk of incident colorectal cancer. Cancer 2006;107:28–36.
[28] Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. Endocr Rev 2000;21:697–738.
[29] Maurovich-Horvat P, Massaro J, Fox CS, et al. Comparison of anthropometric, area- and volume-based assessment of abdominal subcutaneous and visceral adipose tissue volumes using multi-detector computed tomography. Int J Obes (Lond) 2007;31:500–6.
[30] Fung T, Hu FB, Fuchs C, et al. Major dietary patterns and the risk of colorectal cancer in women. Arch Intern Med 2003;163:309–14.