RESEARCH ARTICLE

Inverse Correlation between Cancer Size and Abdominal Obesity in Colorectal Cancer Cases

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Abstract

Background: Correlation between colorectal cancer (CRC) and abdominal obesity has been established, but there is a paucity of data on non-obese CRC patients. The aim of this study was to establish the characteristics of CRCs that occur in such patients. Materials and Methods: Consecutive CRC patients without cachexia were included. Unintended body weight loss, T4- or M1-staged CRCs, extensive lymph node involvement, or synchronous malignancy were classified as cachectic conditions. Abdominal fat volumes were measured using a multidetector CT unit with a software (Rapidia, INFINITT, Seoul, Korea). Results: Of the newly-diagnosed CRC patients, 258 non-cachectic and 88 cachectic patients were analyzed. The cancer size (p<0.001) and T stage (p<0.001) were inversely correlated with body mass index (BMI), visceral fat and subcutaneous fat volumes. Cancer size was the only independent factor related to BMI (p=0.016), visceral fat volume (p=0.002), and subcutaneous fat volume (p=0.027). In non-cachectic patients, a significant inverse correlation was found only between the cancer size and visceral fat volume (p=0.017). Conclusions: Non-obese CRC patients tend to have larger CRC lesions than their obese counterparts even under non-cachectic conditions. Such an inverse correlation between cancer size and visceral fat volume suggests that considerable CRCs are not correlated with abdominal obesity.

Keywords: Obesity - abdominal fat - colorectal cancer - size

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Introduction

Metabolic syndrome and obesity are important risk factors for colorectal cancer (CRC), and a link between the degree of excessive body weight and an increased risk of CRC has been reported (Bardou et al., 2013; Watanabe et al., 2007). A higher body mass index (BMI) is associated with an increased risk of CRC with waist and hip circumferences also being used to assess the overall risk (Aleksandrova et al., 2013; Frezza et al., 2006). Angiogenic factors, insulin resistance, and adipokines secreted by visceral fat have been proposed as biological mechanisms underlying obesity-related carcinogenesis (Sung et al., 2011; Lysaght et al., 2011). These factors are thought to accelerate cell growth and increase the risk of CRC development.

For a given BMI, Asians tend to have a higher percentage of body fat, especially with regard to abdominal obesity (Goh et al., 2013). Indexes of abdominal obesity are more sensitive for estimating the overall risk of CRC than are indexes of overall obesity (Nagata et al., 2014). Therefore, radiographic measurement of abdominal fat is considered one of the optimal methods for assessing the obesity-related risk of developing CRC. Indeed, accounting for both BMI and visceral fat volume may be the best approach to assess CRC risk, but the evidence for CRC risk in Asians without obesity is not clear at present. There is a paucity of data in CRC patients without metabolic syndrome and abdominal obesity. A more in-depth understanding of the link between the type of CRC and the degree of abdominal obesity may be helpful in preventing CRC, and may provide further guidance with respect to the colonoscopy surveillance interval recommendations according to abdominal fat content.

With the increased use of CRC screening colonoscopies, an incidental diagnosis of CRC in non-obese subject without cachexia is not an uncommon occurrence. Nevertheless, there is a paucity of CRC data in non-obese patients that cannot be explained by the slow adenoma-carcinoma sequence. The aim of the present study was to determine the characteristics of CRCs found in non-obese patients by measuring the volume of abdominal fat using multidetector computed tomography (CT) scan. In order to establish the characteristics of CRC in non-obese patients, we further analyzed the correlation between the clinicopathologic characteristics of the CRC and the fat

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volumes after excluding patients with cachexia.

Materials and Methods

Study patients

Consecutive Korean adults who were evaluated by physicians at our center for the resection of CRC between August 2005 and May 2015 were enrolled in this cross sectional study. Inclusion criteria included being non-cachectic at presentation, agreement and consent for genetic analysis for microsatellite instability (MSI), CT scan, and positron emission tomography (PET) imaging data prior to surgery. The patients were excluded if; *(i)* the subject had a genetic predisposition for developing CRC including familial adenomatous polyposis or Lynch's syndrome (hereditary nonpolyposis colorectal cancer), *(ii)* neoadjuvant chemo- or radiotherapy was performed before the operation, or *(iii)* CRC was resected endoscopically. Possible cachectic condition was considered when; *(i)* there was unintended, progressive body weight loss within the 6 months prior to presentation, *(ii)* there was any co-existing disease(s) that may lead to cachexia, or *(iii)* there was extensive (>10) lymph node invasion, M1 stage, or T4 stage.

This study was approved by Institutional Review Board (IRB) of Konkuk University School of Medicine (KUH1010510), and all patients provided informed consent before the analysis. After the IRB approval, the study was registered in the Korean Clinical Trial Registry at ClinicalTrials.gov ID KCT0000935 (https://cris.nih.go.kr). The authors had access to the study data and had reviewed and approved the final manuscript.

Measurement of obesity-related factors

Obesity was evaluated using three factors; (i) BMI, (ii) visceral fat volume and (iii) subcutaneous fat volume in this study. BMI was recorded to assess for general obesity (BMI ≥25 kg/m^2).

Abdominal obesity was measured on CT images obtained by a multidetector CT unit (either Light Speed Pro 16 or Light Speed VCT XT, GE Healthcare, Milwaukee, WI, USA) at our center prior to the surgical resection. CT image data sets were analyzed using a CT software (Rapidia, INFINITT, Seoul, Korea). After selecting a representative slice at the level of the umbilicus for analysis of the abdominal fat volume, the visceral and subcutaneous fat tissue boundaries were defined using a tracing method (Figure 1). The subcutaneous adipose tissue area was defined as fat areas external to the back muscles, while the visceral adipose tissue area was defined as intraperitoneal fat bound by fascia or peritoneum. The subcutaneous fat volume was itself calculated by deducting visceral fat volume from total abdominal fat volume.

Preoperative evaluations

After CT scan, the maximum standardized uptake value (SUVmax) was measured using a GEMINIPET/CT scanner (Philips Medical Systems, Cleveland, OH, USA) as described (Chung et al., 2013). SUVmax was defined as maximum tumor concentration of fludeoxyglucose (FDG) for the quantitative determination of FDG-PET/CT activity. In addition, serum carcinoembryonic antigen (CEA) was measured before surgery.

Postoperative evaluations

Cancer staging was performed according to the 7th edition of TMN stating for CRC. If the gland-forming area exceeded 95% of the high-power field, well-differentiated adenocarcinoma was diagnosed, whereas poorly-differentiated adenocarcinoma was diagnosed if glands composed less than 50% of the field. When different cancer cell types were noticed, the diagnosis was based on the predominant cell type. Lymphovascular invasion was defined as either venous, lymphatic or perineural invasion.

The size of CRC was defined as the maximum diameter of the cancer. The volume of CRC was measured by multiplying the height, width, and depth of the cancer. The location of CRC was classified as either *(i)* proximal colon (cecum to splenic flexure), *(ii)* distal colon (descending colon to sigmoid colon) or rectum (rectosigmoid junction to anal sphincter). The shape of CRC was categorized into ulcerofungating, ulceroinfiltrating and fungating appearances of the resected specimen. With the aid of ABI 3100 Genetic Analyzer (Applied Biosystems, Foster City, CA, USA), DNA preparation was also performed for MSI analysis (Lee et al., 2010).

After 6 months of CRC resection, patients were referred for a follow-up CT scan and blood tests including serum CEA titer. If there was a lesion suspicious of CRC recurrence, additional evaluations were performed, including PET scan and/or liver magnetic resonance imaging.

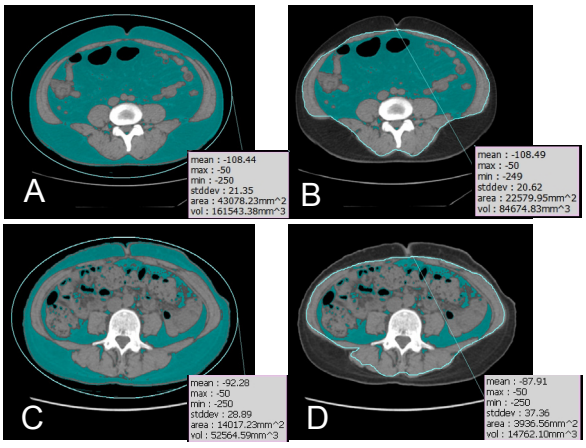

Figure 1. Abdominal fat Measurements in an Obese (BMI 26.3 kg/m^2) TisN0M0 Staged CRC Patient and in Non-obese (BMI 19.4 kg/m^2) T2N0M0 CRC Patient. **(A)** Dark area indicates total abdominal fat tissue, and the numerical at the bottom indicates the volume of total abdominal fat (161,543.3 mm^3) in this obese CRC patient. **(B)** Dark area indicates visceral fat tissue, and the numerical at the bottom indicates the volume of visceral fat (84,674.8 mm^3). The volume of subcutaneous fat (76,868.5 mm^3) is calculated by deducting the volume of visceral fat from the volume of total abdominal fat. **(C)** The volume of total abdominal fat (dark area) is 52,564.6 mm3 as exhibited at the bottom of the box in this non-obese CRC patient. **(D)** The volume of visceral fat (dark area) is 14,762.1 mm^3 as shown in the box, and thus the volume of subcutaneous fat is 37,802.5 mm^3

Statistical analysis

Correlation analysis was performed between obesity-related factors and characteristics of CRC. Continuous variables with symmetric distribution were compared by t-test and presented as mean ± standard deviation (SD). In cases of asymmetric distribution, continuous variables were compared using the Kruskal-Wallis test and presented as median values with ranges. For categorical variables, the differences were compared using chi-square test. Linear regression analyses were performed to verify whether the significant variables were independently correlated with obesity-related factors. A p-value less than 0.05 was considered statistically significant.

Results

Characteristics of the patients

Of the 544 newly-diagnosed CRC patients, a total of 258 non-cachectic Korean CRC patients were analyzed. Of the 269 excluded patients due to the possibility of underlying cachexia, 88 were analyzed for the comparison (Figure 2). There were significant differences between the 258 non-cachectic and 88 cachectic patients with regard to the cancer size, volume, location, cell type, shape, CEA titer, TNM stages, lymphovascular invasion, and prognosis (Table 1). All of the three obesity-related factors (BMI, visceral fat, and subcutaneous fat volumes) were significantly decreased in the cachectic group than those of the non-cachectic group.

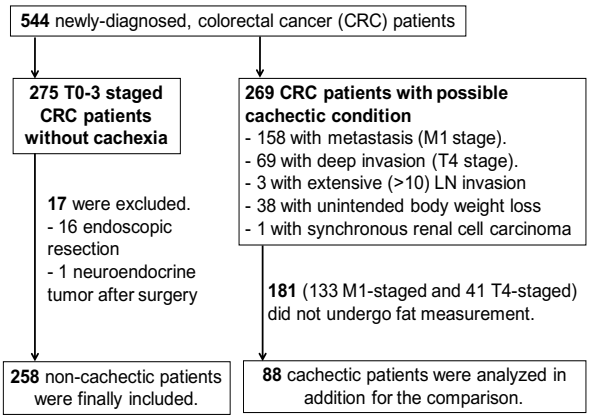

Figure 2. Study Flow of the Retrospective Analysis of Prospectively Collected Data. Of the 544 Korean CRC patients who were evaluated at our center before the surgical resection, 258 non-cachectic patients were finally included. Of the 269 CRC patients with possible cachectic condition, 88 were analyzed additionally as a cachectic CRC patients for the comparison

Correlations between the obesity-related factors

BMI, visceral fat volume, and subcutaneous fat volume exhibited a symmetrical distribution. Statistically significant correlations were found between BMI, visceral fat volume, and subcutaneous fat volume (Table 2).

Table 1. Characteristics of the CRC Patients

Variables	All CRC patients (n=346)	Non-cachectic vs. cachectic patients		p-value
		Without cachexia (n=258)	With cachexia (n=88)*	
Age (years old, mean ± SD)	63.5 ± 11.0	63.8 ± 11.2	62.3 ± 10.6	0.354
Gender (male : female)	186 : 160	133 : 125	52:36:00	0.245
Location of CRC (proximal colon : distal colon : rectum)	81 : 158 : 107	59 : 108 : 91	22:50:16	0.008
Size (mm, mean ± SD)	47.0 ± 22.6	43.5 ± 21.9	57.3 ± 21.8	<0.001
Volume (cm3, median with ranges)	21.2 (0.1-672.0)	15.5 (0.1 – 672.0)	46.6 (0.1-289.6)	<0.001
Cell type (WD : MD : PD : mucinous adenocarcinoma)	4 : 73 : 0 : 11	12 : 232 : 6 : 8	4 : 73 : 0 : 11	0.005
Shape (ulcerofungating: ulceroinfiltrating : fungating appearance)	228 : 67 : 51	169:41:48	59:26:03	<0.001
SUVmax on positron emission tomography (mean ± SD)	11.8 (0-38.6)	11.1 (0 – 38.6)	13.8 (4.0 - 20.4)	0.253
Microsatellite instability (present, %)	66 (19.1%)	45 (17.4%)	21 (23.9%)	0.345
Serum carcinoembryonic antigen (ng/ml, median with ranges)	3.3 (0.2-601.3)	2.9 (0.2 – 72.5)	8.7 (1.0-601.3)	<0.001
T stage (T0 : T1: T2 : T3 : T4)	2 : 34 : 42 : 223 : 45	2 : 33 : 42 : 181 : 0	0 : 1 : 0 : 42 : 45	<0.001
N stage (N0 : N1 : N2)	187 : 83 : 76	173 : 63 : 22	14:20:54	<0.001
M stage (M0 : M1)	287:59:00	258:00:00	29:59:00	<0.001
Lymphovascular invasion (present, %)	142 (41.0%)	79 (30.6%)	63 (71.6%)	<0.001
Body mass index (kg/m2, mean ± SD)	23.7 ± 3.1	24.0 ± 3.2	22.7 ± 2.9	<0.001
Visceral fat volume (cc, mean ± SD)	39672.6 ± 20756.5	41607.0 ± 20815.6	34001.3 ± 19618.6	0.003
Subcutaneous fat volume (cc, mean ± SD)	50106.5 ± 22905.0	52727.9 ± 23372.7	42420.7 ± 19662.3	<0.001
Duration of follow-up (months, median with ranges)	13.7 (1 - 42)	13.6 (1 – 42)	13.7 (2 - 28)	0.094
Prognosis (no event : recurrence without death : CRC-related death : CRC-unrelated death)	312 : 14 : 8 : 1	251 : 6 : 0 : 1	72 : 8 : 8 : 0	<0.001

CRC, colorectal cancer; SD, standard deviation; WD, well differentiated; MD, moderately differentiated; PD, poorly differentiated; SUVmax, maximum standardized uptake value. *Of the 269 excluded CRC patients due to possible confounding by co-existing cachectic condition, fat volume measurement was performed in 88 patients (25 M1-staged patients, 18 T4- staged patients, 3 with >10 LN involvements, 38 with unintended body weight loss, and 1 with renal cell carcinoma).

Table 2. Correlation between CRC and Obesity-Related Factors

All patients (n=346)	Body mass index		Visceral fat volume		Subcutaneous fat volume	
	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value
Age	-0.004	0.941	0.17	0.001*	-0.074	0.168
Gender	0.027	0.621	0.007	0.89	0.112	0.038
Location of CRC	0.08	0.137	0.019	0.729	-0.058	0.285
Size of CRC	-0.25	<0.001*	-0.191	<0.001*	-0.244	<0.001*
Volume of CRC	-0.18	0.001*	-0.075	0.163	-0.177	0.001*
Cell type of CRC	-0.022	0.69	-0.069	0.2	-0.082	0.126
Shape of CRC	0.025	0.639	-0.006	0.91	0.015	0.78
T stage	-0.205	<0.001*	-0.203	<0.001*	-0.218	<0.001*
N stage	-0.147	0.006	-0.053	0.321	-0.121	0.025
M stage	-0.166	0.002*	-0.106	0.049	-0.188	<0.001*
Lymphovascular invasion	-0.01	0.065	-0.051	0.344	-0.085	0.117
SUVmax	-0.049	0.369	-0.034	0.525	0.017	0.752
Microsatellite instability	0.087	0.114	0.048	0.382	0.128	0.02
Carcinoembryonic antigen	-0.188	<0.001*	-0.168	0.002*	-0.045	0.406
Body mass index	-	-	0.637	<0.001*	0.565	<0.001*
Visceral fat volume	0.637	<0.001*	-	-	0.478	<0.001*
Subcutaneous fat volume	0.565	<0.001*	0.478	<0.001*	-	-
Non-cachectic patients (n=258)	Body mass index		Visceral fat volume		Subcutaneous fat volume	
	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value
Age	-0.066	0.29	0.12	0.055	-0.14	0.024
Size of CRC	-0.184	0.003**	-0.19	0.002**	-0.178	0.004**
Volume of CRC	-0.168	0.007	-0.156	0.012	-0.149	0.016
T stage	-0.179	0.004**	-0.18	0.004**	-0.212	0.001**
N stage	-0.056	0.373	-0.003	0.965	-0.023	0.719
Lymphovascular invasion	-0.054	0.385	0.015	0.805	-0.032	0.614
Carcinoembryonic antigen	-0.125	0.045	-0.011	0.863	-0.156	0.012

CRC, colorectal cancer; SUVmax, maximum standardized uptake value. *After multiple testing correction, statistical significance was considered as p<0.0029 (p<0.05 divided by the number of variables). **After multiple testing correction, statistical significance was considered as p<0.005 (p<0.05 divided by 10 variables). All of the three obesity-related factors showed significant correlations. The correlation coefficient value between the BMI and visceral fat was 0.560 (p<0.001), BMI and subcutaneous fat was 0.540 (p<0.001), and visceral fat and subcutaneous was 0.532 (p<0.001)

Table 3. Significant Variables Correlated with Obesity-Related Factors

All CRC patients (n=346)	Body mass index		Visceral fat volume		Subcutaneous fat volume	
	Unstandardized coefficients		Unstandardized coefficients		Unstandardized coefficients	
	B (SE)	p-value	B (SE)	p-value	B (SE)	p-value
Size of CRC	-0.027 (0.011)	0.016	-230.118 (74.649)	0.002	-183.977 (82.858)	0.027
Volume of CRC	0.001 (0.004)	0.919	37.739 (24.614)	0.126	-1.451 (27.321)	0.958
T stage	-0.186 (0.247)	0.452	-2562.370 (1662.126)	0.124	-2353.569 (1844.902)	0.203
N stage	-0.061 (0.240)	0.799	1844.874 (1611.436)	0.253	1374.216 (1788.638)	0.443
M stage	0.487 (0.534)	0.363	-1380.742 (3587.657)	0.701	-11793.589 (3982.175)	0.003
Carcinoembryonic antigen titer	-0.007 (0.003)	0.012	-44.937 (19.730)	0.023	12.229 (21.900)	0.577
Age	0.001 (0.015)	0.971	349.339 (98.743)	0.001	-134.233 (109.601)	0.222
Non-cachectic patients (n=258)	Body mass index		Visceral fat volume		Subcutaneous fat volume	
	Unstandardized coefficients		Unstandardized coefficients		Unstandardized coefficients	
	B (SE)	p-value	B (SE)	p-value	B (SE)	p-value
Size of CRC	-0.009 (0.014)	0.534	-217.631 (90.406)	0.017	-38.873 (101.697)	0.703
T stage	-0.403 (0.312)	0.198	-2141.303 (2058.029)	0.299	-3966.207 (2315.059)	0.088

CRC, colorectal cancer; SE, standard error. Linear regression analyses were performed using only the significant variables on the correlation analyses after the multiple testing corrections as summarized in Table 2

Correlations between CRC and BMI

The size (p<0.001) and volume (p=0.001) of CRC, T stage (p<0.001), M stage (p=0.002) and serum CEA titer (p<0.001) were inversely correlated with general obesity as reflected by BMI. There was no correlation between BMI and other characteristics including age, gender, location, cell type, shape, lymphovascular invasion, SUVmax, and MSI findings. Of these correlated variables, the size of CRC (p=0.016) and serum CEA titer (p=0.012) were independent risk factors for BMI. Using the linear regression analysis, neither the cancer volume, T stage, nor M stage showed an independent correlation with BMI (Table 3).

Correlations between CRC and abdominal fat

The visceral fat volume was inversely correlated with the cancer size (p<0.001), T stage (p<0.001), and serum CEA titer (p=0.002). Furthermore, a positive correlation was found between visceral fat volume and old age (p=0.001). Similarly, subcutaneous fat volume was inversely correlated with the cancer size (p<0.001), cancer volume (p=0.001), T stage (p<0.001), and M stage (p<0.001).

Of these significant variables, the size of CRC

(p=0.002), serum CEA titer (p=0.023), and age (p=0.001) were independently correlated with visceral fat volume. Elderly patients had a larger amount of overall visceral fat volume (Table 3). For the subcutaneous fat volume, the cancer size (p=0.027) and M stage (p=0.003) were independent risk factors.

Significant findings in non-cachectic conditions

To exclude any possible effect of cachexia, 258 non-cachectic patients were further analyzed after excluding 88 cachectic patients. In non-cachectic patients, the cancer size and T stage were inversely correlated with all three obesity-related factors (Table 2). Nevertheless, none of these variables were independently correlated with BMI or subcutaneous fat volume on linear regression analysis after multiple testing corrections (Table 3). Significant difference was found only with the cancer size when categorizing obesity by visceral fat volume (p=0.017). Distinct from that of visceral fat volume, BMI (p=0.534) or subcutaneous fat volume (p=0.703) showed no difference.

Follow-up findings after surgical resection

Recurrence of CRC and cancer-related death were significantly higher in the cachectic group (15.9%) than the non-cachectic group (2.3%). All of the 8 CRC-related deaths were found among the cachectic patients (Table 1). In non-cachectic patients, CEA titers were higher in CRC patients with recurrence (median of 3.7 ng/ml ranging from 0.9 to 56.8 ng/ml) than those without recurrence (median of 2.9 ng/ml ranging from 0.2 to 72.5 ng/ml). Furthermore, recurrence was more common in CRC patients with lymphovascular invasion (5/79, 6.3%) than those without lymphovascular invasion (1/179, 0.6%). None of the obesity-related factors were associated with recurrence of CRC. There were no differences between the six patients with CRC recurrence and the other 252 patients without recurrence with respect to the mean ± SD values of BMI (23.1 ± 3.6 kg/m^2 *vs*. 24.0 ± 3.2 kg/m2, p=0.503), visceral fat volume (47889.4 ± 20796.2 cc *vs*. 45157.5 ± 20834.3, p=0.456), and subcutaneous fat volume (41893.4 ± 14635.9 cc *vs*. 52985.9 ± 23499.0 cc, p=0.251).

Discussion

The present study found that visceral fat volume and BMI were inversely correlated with the size of cancer in non-cachectic CRC patients. Non-obese CRC patients tend to have larger CRC lesions than their obese counterparts. The inverse correlation between the cancer size and obesity suggests that considerable CRCs occurring in Koreans are not correlated with abdominal obesity as reflected by visceral fat volumes. To the best of our knowledge, this is the first study to show an inverse correlation between the cancer size and visceral abdominal fat volume. Because it is hard to collect non-cachectic CRC patients without abdominal obesity in countries where obesity is common, most CRC studies focused on the adenoma-carcinoma sequence related to obesity.

The present findings suggest that large-sized CRCs in non-obese patients may originate from faster, aggressive oncogenic pathways than occurs in obese patients whose cancers may progress along the slow adenoma-carcinoma sequence. On the contrary, small CRCs were more common among obese patients than their non-obese counterparts in this study. Given that the adenoma-carcinoma sequence is a slow process, this finding suggests that the CRCs found in obese patients may be driven by this slow carcinogenesis pathway. This would allow for the detection of CRC lesions at an earlier stage, i.e. when they are smaller. There are several lines of evidence supporting this hypothesis. It has been shown elsewhere that metabolic syndrome and obesity are significant risk factors for colorectal adenomas, which is the precancerous lesion of CRC based on the slow adenoma-carcinoma sequence (Kim et al., 2009; Kim et al., 2010; Kim et al., 2012; Hong et al., 2012). Moreover, a recent study exhibited that higher visceral fat volume indicates lower lymph node metastasis rate and better survival (Park et al., 2015). Together with these studies, our findings suggest that larger CRCs are inversely correlated with obesity, and that considerable CRCs occurring in Koreans are not correlated with abdominal obesity. Therefore, when designing CRC screening protocols, it should be considered that large CRCs tend to occur in non-obese patients without abdominal obesity, as reflected by a normal visceral fat volume.

In the present study, we sought the characteristics of CRCs that tend to occur in non-obese patients without cachexia. Our findings are based on strict inclusion criteria, after having excluded CRC patients with advanced stage or any other conditions that may induce body weight loss. The volumes of visceral fat and subcutaneous fat were measured using a multidetector CT scan in each patient together with the recorded BMI, and it was possible to analyze the significance of abdominal obesity and general obesity simultaneously. Interestingly, all of the obesity-related factors analyzed in this study were inversely correlated with the size of CRC lesions. Moreover, obese patients with abdominal fat showed the smallest overall CRC size. Our data confirm that visceral fat volume is more tightly associated with CRC risk than is BMI, and supports that visceral fat volume may be an optimal method for assessing obesity-related risk (Frezza et al., 2006; Lee et al., 2016). The later study showed that visceral obesity was positively related to a higher prevalence of gallbladder polyp irrespective of BMI or waist circumference.

Previous studies revealed that correlations between obesity and CRC risk varies in female (Kaneko et al., 2014; Chacko L et al., 2015), and there was a significant difference between premenopausal and postmenopausal women (Kim et al., 2007; Song et al., 2008). However, neither gender nor age itself were significantly associated with the clinicopathological factors of CRC in this study. Age was no longer significant on regression analysis, although the elderly tended to have more visceral fat volume. This may have contributed to the significant correlation we observed in this study between obesity and CRC-related factors, irrespective of gender or age.

Another limitation of this study is that no correlation

was observed between abdominal obesity and overall prognosis. This may be attributable to a relatively short-term follow-up period after the surgery. Although a recent Western study showed that visceral fat volume is related to lower rates of survival (Rickles AS et al., 2013), their findings could not be replicated in our population because more than half (50.7%) of their 219 CRC patients had visceral obesity. In that study, stage II CRC patients with visceral obesity were at higher risk for poor outcomes, but viscerally obese patients had a longer time to recurrence in stage III cancer. These contradictory findings between stage II and stage III CRCs indicate a possible selection bias induced by a large number of CRC patients with abdominal obesity.

In conclusion, obese patients tend to have smaller CRC lesions than their non-obese counterparts. The present findings suggest that abdominal obesity may contribute to the slow pathway of CRC development via the adenoma-carcinoma sequence, enabling the detection of early-staged, smaller CRCs. Furthermore, these data suggest that larger CRC lesions in non-obese patients are associated with the faster pathway than the adenoma-carcinoma sequence. Taken together, our findings suggest that considerable CRCs occurring in Koreans are not correlated with abdominal obesity as reflected by visceral fat volume. Therefore, care must be taken in non-obese subjects without abdominal obesity when designing CRC screening protocols in Koreans.

Acknowledgements

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