

Body Mass Index as a Predictor of Advanced Colorectal Neoplasia

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Background: Colorectal cancer (CRC) is the third frequent cancer in Korea. There are several risk factors including male sex, older age, smoking and family history of colon cancer. Recently, obesity is thought to be a risk factor for CRC and advanced colon polyps. Therefore, we designed a cross-sectional study to determine the association between BMI and advanced colorectal neoplasia.

Methods: A total of 256 patients with advanced colorectal neoplasia who were diagnosed using colonoscopy between May, 2004 and December, 2011 were included in this study. Advanced colorectal neoplasia was defined large (≥ 1 cm) adenoma or adenocarcinoma. We compared these patients to a control group consisting of 217 subjects with normal colonoscopic findings recruited during the same period.

Results: Of the 256 patients, there were 132 (51.6%) men, and the mean age was 56.4 ± 12.3 years. The rate of males, alcohol drinker and current smokers was significantly higher in the advanced colorectal neoplasia compared to control group. In the subgroup analysis, the mean age and body mass index (BMI, kg/m^2) of advanced colorectal neoplasia were higher than control group in the female subjects. However, there were no significant differences between two groups in the male subjects. Multiple logistic regression analysis identified overweight (BMI 23.0–24.9 kg/m^2 , odds ratios [OR]=2.022) and obesity (BMI ≥ 25 kg/m^2 , OR=2.383) as independent risk factors for advanced colorectal neoplasia.

Conclusions: We suggest that BMI should be considered as an independent risk factor for advanced colorectal neoplasia, and people with high BMI should be recommended to undergo colonoscopy screening earlier than scheduled. (*J Cancer Prev* 2013;18:144–148)

Key Words: Body mass index, Adenomatous polyps, Colorectal neoplasms

INTRODUCTION

According to the Korean Central Cancer Registry, the prevalence of colorectal cancer (CRC) was 25,860 (12.8%), placing itself as the third frequent cancer in 2010.¹ This data showed that colon cancer was diagnosed in 62.5 and 40.8 per 100,000 of men and women, respectively. CRC has become a second and third cancer in men and women. In addition, this rate has shown a significant increase since

1999, compared with other cancers such as stomach cancer (men: -0.5% , women: -0.4%) and hepatocellular carcinoma (men: -2.1% , women: -1.6%).^{2,3} Western diet, life style and increased obesity are suggested as causes of increased CRC prevalence. Risk factors such as alcohol intake, smoking, low fiber-high lipid diet, high consumption of red meat, low level of physical activity and obesity have been suggested in many studies.^{4,5} Recently, obesity has become a major concern as a risk factor for CRC.

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In addition, colorectal adenoma is known as a precancerous lesion. Advanced adenomas, which are obvious precancerous lesions, commonly develop into adenocarcinomas during 5-10 years through adenoma-carcinoma sequence.^{6,7} BMI is not only known as a major risk factor for colorectal adenoma but also for cancer.⁸⁻¹⁰ The association between obesity and colorectal neoplasm has been studied and shown various results according to sex and the location of polyp in other countries.¹¹⁻¹³ However, there are not enough data about the relation between obesity and advanced colorectal neoplasia in the Korean population. Therefore, this study was conducted to elucidate the association between BMI and advanced colorectal neoplasia, and show whether other risk factors were associated with advanced colorectal neoplasia, such as age, sex, alcohol intake, and smoking.

MATERIALS AND METHODS

1. Study subjects

Four hundred and seventy-three subjects who underwent colonoscopy at Seoul National University Bundang Hospital in Korea, between May, 2004 and December, 2011 were enrolled in this cross-sectional study. One hundred and fifty-eight subjects with colorectal adenoma larger than 1 cm and 98 subjects with CRC were included in this study. Two hundred and seventeen subjects who had normal screening colonoscopic findings without colorectal adenoma or cancer in the same period were enrolled as a control group.

2. Data collection

We reviewed the participants' age, gender, smoking habits and alcohol intake from their medical records. Current smoker was defined as a subject who had been smoking at least one cigarette per day for the previous 12 months and an ex-smoker was defined as a subject who had ceased smoking at least 12 months before enrollment and a never smoker was defined as a subject who had never smoked before. Alcohol consumption was defined as drinking over 140 g of alcohol per week. These data were obtained based on self-reporting. All participants were measured for height and weight by nurses. BMI was defined as body weight (kg) divided by the square of height (m²) (weight [kg]/[height (m)]²). We classified subjects into three groups according to the WHO Asia-Pacific classification for obesity: normal, <23.0 kg/m²; overweight 23.0-24.9 kg/m²; and obese, ≥25.0 kg/m². The study protocol was approved by the Ethical Committee at Seoul National University Bundang Hospital.

3. Statistical analysis

We analyzed three groups; advanced adenoma group, CRC group and control groups. One-way ANOVA analysis was selected to compare age, height, body weight and BMI among the three groups; chi-squared analysis was used to determine the significances of differences in sex, alcohol intake and smoking among the three groups. Binary logistic regression analysis was used to determine whether BMI was an independent risk factor for advanced colorectal neoplasia after adjusting for age, sex, smoking and alcohol intake. Statistical analysis was obtained by SPSS for 19.0

Table 1. Clinical characteristics of all included subjects

Variables	Control groups	Non-advanced colorectal neoplasia	Advanced colorectal neoplasia	P-value
Number of subjects	217	79	256	
Age (year)	50.3±11.7	56.59±9.99	61.50±10.26	<0.001
Male	54 (24.9%)	43 (54.4%)	190 (74.2%)	<0.001
Alcohol intake	28 (13.0%)	11 (13.9%)	86 (33.6%)	<0.001
Current smoker	21 (9.8%)	10 (12.7%)	81 (31.6%)	<0.001
Height (cm)	162.3±7.6	164.50±8.54	165.08±8.06	<0.001
Weight (kg)	60.1±10.7	62.70±12.72	66.18±9.67	<0.001
BMI (kg/m ²)	22.8±3.0	23.46±2.83	24.23±2.60	<0.001

BMI, body mass index.

(SPSS, Chicago, IL, USA). A P-value of less than 0.05 was considered statistically significant.

RESULTS

1. Clinical characteristics of all included subjects

Total 473 subjects, 244 men (51.6%) and 229 women (48.4%), were included. The mean age of all subjects was 56.4 ± 12.3 years. The mean age of advanced colorectal neoplasia group was higher than that of control group. The rate of male, alcohol drinker and current smoker were higher in the advanced colorectal neoplasia group compared to control group. Moreover, BMI was higher in the colorectal neoplasia group than control group. Comparison of clinical characteristics among the advanced colorectal neoplasia, non-advanced colorectal neoplasia and control groups are presented in Table 1.

2. Clinical characteristics of subjects according to gender

In the gender subgroup analysis, there were no significant differences in BMI between the control group and advanced colorectal neoplasia group in male subjects (Table 2). However, BMI of advanced colorectal neoplasia group was significantly higher than that of control group in female subjects (Table 2). BMI was also significantly different among advanced adenoma, CRC and control groups in female, but was not a significant difference among three groups in male.

3. Risk factors for advanced colorectal neoplasia

Multivariate logistic analysis identified age, female gender, current smoking and BMI as independent risk factors for colorectal adenoma and carcinoma (Table 3). The risk of advanced colorectal neoplasia increased with age. Moreover, overweight (OR=2.022) and obesity (OR=2.383) were correlated with advanced colorectal neoplasia. On the other hand, alcohol intake was not significantly different in those groups.

DISCUSSION

In this study, we showed that BMI is associated with an increased risk of advanced colorectal neoplasia. Several studies have suggested that lifestyle factors, such as smoking, alcohol intake, physical inactivity, and high-

Table 3. Multivariate logistic regression analysis of variables for advanced colorectal neoplasia

Variables	P-value	Odds ratio	95% CI
Age (year)	<0.001		
40-59	<0.001	8.429	2.765-25.697
60-69	<0.001	38.948	12.049-125.894
≥70	<0.001	62.076	16.815-229.172
Sex (female)	<0.001	5.948	3.493-10.130
Current smoker	0.005	2.787	1.357-5.726
Body mass index (kg/m ²)	0.009		
23-24.9	0.023	2.022	1.102-3.712
≥25	0.004	2.383	1.322-4.295

Table 2. Clinical characteristics of the subjects in the control and advanced colorectal neoplasia groups according to gender

Variables	Total subjects			Male subjects			Female subjects		
	Control	Advanced colorectal neoplasia	P-value	Control	Advanced colorectal neoplasia	P-value	Control	Advanced colorectal neoplasia	P-value
Number	217	256		54	190		163	66	
Age (year)	50.3±11.7	61.5±10.3	<0.001	47.0±11.5	62.0±10.3	<0.001	51.3±11.6	60.1±10.2	<0.001
Alcohol intake	28 (13.0%)	86 (33.6%)	<0.001	20 (37.7%)	84 (44.2%)	0.225	8 (4.9%)	2 (3.0%)	1.000
Current smoker	21 (9.8%)	81 (31.6%)	<0.001	17 (32.1%)	77 (40.5%)	0.172	4 (2.5%)	4 (6.1%)	0.214
Height (cm)	162.3±7.6	165.1±8.1	<0.001	170.8±7.0	168.5±5.7	0.014	159.3±5.6	155.6±5.8	<0.001
Weight (kg)	60.1±10.7	66.2±9.7	<0.001	70.2±10.6	68.9±8.7	0.374	56.8±8.6	58.5±7.9	0.104
BMI (kg/m ²)	22.8±3.0	24.3±2.6	<0.001	24.0±2.8	24.3±2.4	0.485	22.4±3.0	24.2±3.0	<0.001

BMI, body mass index.

fat/low-fiber diet may contribute to this increased risk of CRC.^{4,5} Increased body weight and obesity are now recognized as environmental factors that can contribute to the development of CRC.^{4,5}

A recent meta-analysis study has shown that being obese confers an approximately 1.334 fold increased risk of developing CRC relative to being normal weight.⁸ Analyses stratified by the anatomical site suggested that higher BMI levels cause an equal increasing risk for both colon cancer and rectal cancer.⁸ Another systematic review and meta-analysis of 221 datasets (141 articles) demonstrated that each 5 kg/m² increase in BMI is associated with a 24% increased incidence of both colon and rectal cancer in men, and a 9% higher incidence of colon cancer in women.⁴

Okabayashi et al.⁹ suggested that increasing BMI is associated with an increased risk of colorectal adenoma. Their multivariate meta-analysis confirmed a positive association between higher BMI categories and the prevalence of colorectal adenoma (BMI: 25-30 vs. BMI < 25; OR=1.21 BMI ≥ 30 vs. BMI < 25; OR=1.32), and revealed a dose-response relationship.

Our study suggests that BMI increases the risk of advanced colorectal neoplasia independent of other risk factors (age, sex, alcohol intake, current smoking). According to Anderson et al.,¹⁴ the risk and prevalence of significant colorectal neoplasia increased as BMI increased in women in their study (OR=4.26; 95% CI [confidence interval]=2.00-9.11). There was no such relationship in the male population. These results suggest the hypothesis that BMI is a significant risk factor for colorectal adenoma in females. In this study, we showed that BMI is related with the prevalence of colorectal neoplasia in the female group (Table 3). This result is similar to a previous study.¹⁴ However, another study demonstrated that there were no significant differences in adenoma prevalence between sexes.⁹

Pre-menopausal females had a higher risk of adenoma (OR=2.48; 95% CI=0.56-11.05) when compared with post-menopausal females (OR=1.06; 95% CI=0.77-1.45).^{9,15} However, men have been shown to have a higher association between BMI and CRC compared to women, although the findings of this meta-analysis did not de-

monstrate any significance of male gender in colorectal adenoma formation in relation to BMI.^{9,16}

BMI is a definite risk factor for colorectal cancer and has a major role in pre-cancer stage. There are several hypotheses regarding the development of colon cancer and obesity.¹⁷ Patients with insulin resistance are able to have chronic hyperinsulinemia and increased Insulin-like growth factor (IGF) to inhibit the synthesis of Insulin-like growth factor binding protein.¹⁸ Therefore, insulin and IGF-1 are thought to be risk factors for colon cancer. Leptin, which is a kind of hormone called adipokine in adipose tissues, is also associated with colon cancer.¹⁹ In addition, obese patients have different normal flora in their colon compared with healthy people. Some studies have reported that this difference may be related with chronic inflammation in patients with colon cancer.²⁰ The correlation between alcohol intake and an increased risk of CRC has been observed in previous studies. A meta-analysis of 27 cohort and 34 case-control studies observed that, compared to never drinkers, there was a significant increase risk of CRC for moderate drinkers (2-3 drinks/day) (relative risk [RR]=1.21, 95% CI=1.13-1.28) and heavy drinkers (≥4 drinks/day) (RR=1.52, 95% CI=1.27-1.81).²¹ The RR for moderate drinkers, compared with non-occasional drinkers, was stronger for men (RR=1.24, 95% CI=1.13-1.37) than for women (RR=1.08, 95% CI=1.03-1.13). However, our study did not show this difference in the multivariate analysis, and did not provide evidence for an association between alcohol intake and advanced colorectal neoplasia.

Smoking is also another risk factor for colorectal polyps. For adenomatous polyps, the risk is particularly high for advanced adenomas.²² A meta-analysis of 42 studies observed that the pooled risk estimates for current, former, and ever smokers in comparison with never smokers were 2.14 (95% CI=1.86-2.46), 1.47 (95% CI=1.29-1.67), and 1.82 (95% CI=1.65-2.00), respectively. Also, smoking has been significantly associated with increased CRC incidence and mortality. A meta-analysis of 106 studies revealed that the risk CRC development was increased among smokers compared to those who never smoked (RR 1.18, 95% CI=1.11-1.25).²³ We also suggest that current smoking is significantly associated with advanced ade-

noma and CRC.

The current study has some potential limitations. The data of weight and height were collected from patient self-report. Moreover, regarding the history of smoking and alcohol consumption habits, we did not clearly define the amount of alcohol consumption amount and smoking in this study. Furthermore, we did not include other factors such as past medical illnesses, diet, physical activity, NSAIDs use and family medical history.

In spite of these limitations, we revealed that BMI had a correlation with the prevalence of advanced colorectal neoplasia, and was an independent risk factor for advanced colorectal neoplasia along with other factors such as age, male gender, and smoking.

Although this study involved a small population, we revealed a positive association between BMI and colorectal adenoma and CRC. In addition, the prevalence of advanced colorectal neoplasia is significantly higher in female gender and current smokers, and this prevalence increases with age. However, further studies are needed to clarify how obesity affects colorectal neoplasia development.

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