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Changes in Abdominal Obesity Affect the Risk of Metachronous Advanced Colorectal Neoplasia Development after Polypectomy

Yoon Suk Jung, Nam Hee Kim, Jung Ho Park, Dong Il Park, and Chong Il Sohn

Division of Gastroenterology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea.

Purpose: The impact of changes in body mass index and waist circumference on the development of metachronous colorectal neoplasia (CRN) after polypectomy has rarely been examined. We evaluated the association between changes in overall/abdominal obesity and metachronous CRN risk.

Materials and Methods: We studied patients who underwent ≥1 adenoma removal and surveillance colonoscopy. Patients were classified into the following four groups based on the changes in overall obesity from index to follow-up colonoscopy: non-obesity persisted (group 1), obesity to non-obesity (group 2), non-obesity to obesity (group 3), and obesity persisted (group 4). Patients were also divided into another four groups based on similar changes in abdominal obesity (groups 5–8).

Results: The number of patients in groups 1, 2, 3, and 4 was 5074, 457, 643, and 3538, respectively, and that in groups 5, 6, 7, and 8 was 4229, 538, 656, and 2189, respectively. Group 4 had a significantly higher risk of metachronous CRN compared to groups 1 and 2. However, metachronous advanced CRN (ACRN) risk was not different among groups 1, 2, 3, and 4. Metachronous CRN risk in group 8 (abdominal obesity persisted) was higher than that in groups 5 (non-abdominal obesity persisted) and 7 (non-abdominal obesity to abdominal obesity), and tended to be higher than that in group 6 (abdominal obesity to non-abdominal obesity). Additionally, group 8 had a significantly higher risk of metachronous ACRN compared to groups 5, 6, and 7.

Conclusion: Changes in obesity affected the metachronous CRN risk. In particular, changes in abdominal obesity affected the metachronous ACRN risk.

Key Words: Metachronous advanced colorectal neoplasia, waist circumference, obesity

INTRODUCTION

Overall obesity, measured based on the body mass index (BMI), is an important risk factor for colorectal neoplasia (CRN) including colorectal cancer (CRC) and its precursor, colorectal adenoma.[1,2] Abdominal obesity, measured based on the waist circumference (WC), is a stronger risk factor for CRN.[3-7] Many cross-sectional studies have shown a positive association between overall/abdominal obesity and the prevalence of CRN.[2,8] However, it is difficult to clarify the causal relationship between obesity and CRN development from the results of cross-sectional studies.

Given that obesity is an important risk factor for CRN, it can be hypothesized that obesity may also be associated with a risk of metachronous CRN development after polypectomy. In fact, some longitudinal studies have reported that obesity at baseline (time of index colonoscopy) is associated with an increased risk of metachronous CRN development after adenoma removal.[9-12] However, some obese patients at baseline may have decreased BMI and/or WC, and conversely, some non-obese patients at baseline may have increased BMI and/or WC

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Corresponding author: Yoon Suk Jung, MD, PhD, Division of Gastroenterology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, 29 Saemunan-ro, Jongno-gu, Seoul 03181, Korea.
Tel: 82-2-2001-8577, Fax: 82-2-2001-2049, E-mail: ys810.jung@samsung.com

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during the follow-up period. These changes in BMI and WC may affect the patients' risk of developing metachronous CRN after polypectomy. For example, a reduction in BMI or WC may reduce the risk of metachronous CRN. However, there have been few studies on this topic. To better understand the relationship between obesity and the risk of metachronous CRN, the association between these two variables should be evaluated based on the changes in BMI and WC between index colonoscopy and follow-up colonoscopy, rather than only BMI and WC at index colonoscopy. Nevertheless, most previous studies only examined the association between obesity status at baseline and the risk of metachronous CRN without performing dynamic assessments of changes in BMI and WC over time.[9-12]

Therefore, in this study, we aimed to evaluate the association of changes in overall obesity (BMI) and abdominal obesity (WC) with the risk of metachronous CRN in asymptomatic examinees who underwent adenoma removal.

MATERIALS AND METHODS

Study population

The study population comprised asymptomatic adults who underwent colonoscopy as part of a health examination at Kangbuk Samsung Hospital Total Healthcare Center in South Korea between 2010 and 2017. The characteristic of our cohort has been described in detail in previous studies.[13] We retrospectively analyzed the data obtained from this prospectively established cohort.

Patients who had ≥1 adenoma detected on an index colonoscopy performed between 2010 and 2014 and underwent follow-up colonoscopy at an interval of ≥1 years until December 2017 were included in the study.[13] All of the patients underwent a single follow-up colonoscopy at once, and all polyps were endoscopically removed during index colonoscopy.

Data were stratified into four groups based on the changes in overall obesity between index colonoscopy and follow-up colonoscopy: groups 1, 2, 3, and 4 were defined as "non-overall obesity at the time of index colonoscopy→non-overall obesity at the time of follow-up colonoscopy," "overall obesity→non-overall obesity," "non-overall obesity→overall obesity," and "overall obesity→overall obesity," respectively. Data were also stratified into another four groups according to changes in abdominal obesity: groups 5, 6, 7, and 8 were defined as "non-abdominal obesity→non-abdominal obesity," "abdominal obesity→non-abdominal obesity," "non-abdominal obesity→abdominal obesity," and "abdominal obesity→abdominal obesity," respectively.

Patients with a history of CRC or colorectal surgery, those diagnosed with CRC during index colonoscopy, those with a history of inflammatory bowel disease (IBD), and those with poor bowel preparation were excluded. Poor bowel preparation was defined as "large amounts of solid fecal matter observed in the bowel precluding a satisfactory study, unacceptable preparation, or a condition in which <90% of the mucosa could be adequately visualized."[14]

This study was approved by the Institutional Review Board of Kangbuk Samsung Hospital (KBSMC 2017-11-01). The requirement for informed consent was waived, as only de-identified data were retrospectively accessed.

Measurements and definitions

Data on health-related behaviors and medical history were collected through a self-administered questionnaire. Family history of CRC was defined as the presence of CRC in at least one first-degree relative of any age. Self-reported regular use of nonsteroidal anti-inflammatory drugs (NSAIDs) during the previous month was assessed. In addition, the weekly frequency of moderate or vigorous physical activity was assessed, and regular exercise was defined as ≥3 times of exercise per week.

Body weight, height, and WC were measured by trained staff. Overall obesity was defined as BMI ≥25 kg/m^2, and abdominal obesity was defined as WC ≥90 cm in men and ≥80 cm in women, which are the proposed cutoff values for Asians.[15,16]

Colonoscopic and histologic examinations

All colonoscopic examinations were performed by experienced endoscopists. Suspicious neoplastic lesions were removed via biopsy, snare polypectomy, or endoscopic mucosal resection, and histologically assessed by experienced pathologists.

Overall CRN was defined as cancer or adenoma, and advanced CRN (ACRN) was defined as cancer or advanced adenoma. Advanced adenoma was defined as the presence of one of the following features: a lesion ≥10 mm in diameter, a lesion showing a tubulovillous or villous structure, and high-grade dysplasia.[17] Low-risk adenoma (LRA) was defined as 1–2 adenomas measuring <10 mm, and high-risk adenoma (HRA) was defined as advanced adenomas or ≥3 adenomas.[17]

Statistical analysis

Baseline characteristics were compared between groups using the chi-square test and 1-way analysis of variance. The cumulative incidence of metachronous CRN was calculated using the Kaplan-Meier method, and the differences between groups were determined using the log-rank test. To compare the risk for development of metachronous CRN between groups, we also performed multivariable analysis using the Cox proportional hazards regression model after adjusting for potential confounding variables including age, sex, family history of CRC, use of NSAIDs, physical activity, baseline adenoma characteristics (LRA vs. HRA), diabetes, and hypertension. All reported p-values were two-tailed, and $p<0.05$ was considered statistically significant. SPSS software version 21 (IBM Corp., Armonk, NY, USA) was used to perform all statistical analyses.

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RESULTS

Baseline patient characteristics

A total of 12457 patients who had ≥1 adenoma at the time of index colonoscopy and underwent follow-up colonoscopy were eligible to be included in this study. Among them, 2745 patients were excluded for the following reasons: diagnosis of CRC at the time of index colonoscopy (n=9), history of CRC or colorectal surgery (n=97), history of IBD (n=35), poor bowel preparation (n=2172), follow-up colonoscopy within 1 year (n=259), and missing data of BMI and WC (n=173). Ultimately, 9712 patients were analyzed (Fig. 1). The mean age was 43.6±8.3 years, and 82.8% of the enrolled subjects were men. The mean interval between index colonoscopy and follow-up colonoscopy was 3.1±1.3 (range, 1.0–7.4) years.

When stratified into predefined risk groups based on the change in overall obesity, the patients were categorized into four groups as follows: group 1 (n=5074), group 2 (n=457), group 3 (n=643), and group 4 (n=3538). Table 1 shows the baseline characteristics of these four groups. The mean age and the proportion of men and smokers were the highest in group 2. The proportion of patients with hypertension, diabetes, and HRA was the highest in group 4.

Of 9712 patients, 7612 had WC measurements at both index and follow-up colonoscopies. The number of patients in groups 5, 6, 7, and 8 was 4229, 538, 656, and 2189, respectively. Table 2 shows the baseline characteristics of these four groups. The mean age and the proportion of smokers and patients with hypertension and HRA were the highest in group 8. The proportion of men was the highest in group 5, and the proportion of patients with diabetes and regular exercise was the highest in groups 6 and 7, respectively.

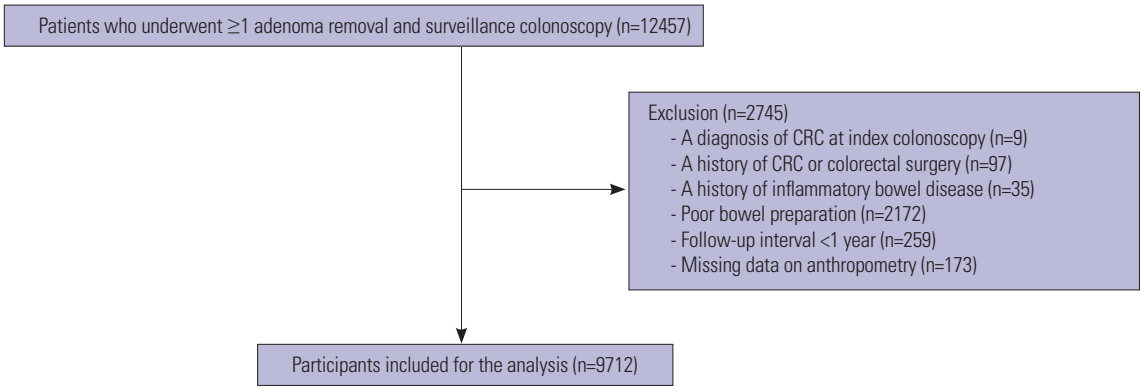

Fig. 1. Flow diagram for selection of study participants. CRC, colorectal cancer.

Table 1. Baseline Characteristics according to Change in Overall Obesity (BMI)

Variable	Group 1 Non-overall obesity →non-overall obesity	Group 2 Overall obesity →non-overall obesity	Group 3 Non-overall obesity →overall obesity	Group 4 Overall obesity →overall obesity	*p* value
No. of patients	5074	457	643	3538	
Age (yr)	43.9±8.5	44.0±7.5	42.6±7.8	43.2±8 .1	<0.001
Men	3819 (75.3)	421 (92.1)	550 (85.5)	3250 (91.9)	<0.001
Current or former smoker	2703 (53.3)	317 (69.4)	414 (64.4)	2404 (67.9)	<0.001
Family history of CRC	309 (6.1)	26 (5.7)	43 (6.7)	194 (5.5)	0.533
Use of NSAIDs	177 (3.5)	17 (3.7)	23 (3.6)	93 (2.6)	0.122
Regular exercise*	739 (14.6)	63 (13.8)	114 (17.7)	528 (14.9)	0.175
Abdominal obesity†	412 (10.2)	161 (48.6)	110 (22.8)	2011 (74.4)	<0.001
Hypertension	637 (12.6)	119 (26.0)	125 (19.4)	1004 (28.4)	<0.001
Diabetes mellitus	227 (5.5)	41 (9.0)	33 (5.1)	349 (9.9)	<0.001
Baseline adenoma characteristics					0.026
Low-risk adenoma	4304 (84.8)	378 (82.7)	547 (85.1)	2920 (82.5)	
High-risk adenoma	770 (15.2)	79 (17.3)	96 (14.9)	618 (17.5)	
Interval between index and follow-up colonoscopies (yr)	3.1±1.3	3.2±1.4	3.2±1.3	3.1±1.3	0.074

BMI, body mass index; CRC, colorectal cancer; NSAIDs, nonsteroidal anti-inflammatory drugs.
Data are presented as number (%) or mean±standard deviation. Overall obesity was defined as BMI ≥25 kg/m^2.
*Moderate or vigorous physical activity ≥3 times per week, †Missing data in 2099 patients.

Table 2. Baseline Characteristics according to Change in Abdominal Obesity (WC)

Variable	Group 5 Non-abdominal obesity →non-abdominal obesity	Group 6 Abdominal obesity →non-abdominal obesity	Group 7 Non-abdominal obesity →abdominal obesity	Group 8 Abdominal obesity →abdominal obesity	*p* value
No. of patients	4229	538	656	2189	
Age (yr)	43.9±8.5	43.9±8.0	44.4±9.0	44.5±9.1	0.022
Men	3553 (84.0)	429 (79.6)	521 (79.4)	1769 (80.8)	<0.001
Current or former smoker	2455 (58.1)	321 (59.7)	391 (59.6)	1339 (61.2)	0.116
Family history of CRC	246 (5.8)	30 (5.6)	40 (6.1)	138 (6.3)	0.854
Use of NSAIDs	126 (3.0)	12 (2.2)	26 (4.0)	61 (2.8)	0.316
Regular exercise*	661 (15.6)	77 (14.3)	114 (17.4)	287 (13.1)	0.014
Overall obesity (BMI ≥25 kg/m^2)	594 (14.0)	332 (61.7)	278 (42.4)	1873 (85.6)	<0.001
Hypertension	622 (14.7)	130 (24.2)	133 (20.3)	639 (29.2)	<0.001
Diabetes mellitus	250 (5.9)	61 (11.3)	46 (7.0)	217 (9.9)	<0.001
Baseline adenoma characteristics					0.012
Low-risk adenoma	3548 (83.9)	454 (84.4)	536 (81.7)	1770 (80.9)	
High-risk adenoma	681 (16.1)	84 (15.6)	120 (18.3)	419 (19.1)	
Interval between index and follow-up colonoscopies (years)	3.1±1.3	3.1±1.2	3.1±1.3	3.0±1.3	0.212

WC, waist circumference; CRC, colorectal cancer; NSAIDs, nonsteroidal anti-inflammatory drugs; BMI, body mass index.
Data are presented as number (%) or mean±standard deviation. Abdominal obesity was defined as WC ≥90 cm in men and ≥80 cm in women.
*Moderate or vigorous physical activity ≥3 times per week.

Table 3. Multivariable Analysis for the Relationship between Change in Overall Obesity and the Risk of Metachronous CRN

	3-year cumulative incidence rate (%)	5-year cumulative incidence rate (%)	Adjusted HR (95% CI)	*p* value	Adjusted HR (95% CI)	*p* value	Adjusted HR (95% CI)	*p* value
Metachronous CRN								
Group 1	19.7	55.0	1 (reference)					
Group 2	22.4	49.9	0.87 (0.74–1.03)	0.096	1 (reference)			
Group 3	19.4	54.6	1.00 (0.87–1.15)	0.990	1.15 (0.94–1.40)	0.183	1 (reference)	
Group 4	23.0	60.9	1.11 (1.03–1.19)	0.006	1.27 (1.08–1.49)	0.004	1.11 (0.96–1.28)	0.162
Metachronous advanced CRN								
Group 1	1.4	5.2	1 (reference)					
Group 2	2.2	4.0	1.04 (0.58–1.86)	0.892	1 (reference)			
Group 3	1.7	4.0	1.08 (0.64–1.83)	0.774	1.04 (0.50–2.16)	0.922	1 (reference)	
Group 4	1.8	6.2	1.12 (0.84–1.49)	0.434	1.08 (0.60–1.93)	0.806	1.04 (0.61–1.77)	0.893

HR, hazard ratio; CI, confidence interval; CRN, colorectal neoplasia; group 1, non-overall obesity→non-overall obesity; group 2, overall obesity→non-overall obesity; group 3, non-overall obesity→overall obesity; group 4, overall obesity→overall obesity.
Values were adjusted for age, sex, smoking status, family history of colorectal cancer, use of nonsteroidal anti-inflammatory drugs, physical activity, hypertension, diabetes, and baseline adenoma characteristics (low- vs. high-risk adenoma).

Risk of metachronous neoplasia based on change in overall obesity

During the follow-up period, metachronous CRN developed in 1669 (32.9%), 167 (36.5%), 221 (34.4%), and 1385 (39.1%) patients in groups 1, 2, 3, and 4, respectively; and metachronous ACRN developed in 114 (2.2%), 13 (2.8%), 16 (2.5%), and 94 (2.7%) in the four groups, respectively. Table 3 shows the results of multivariable Cox regression analyses comparing the risk of metachronous CRN among the four groups based on change in BMI. The risk of metachronous CRN in group 4 was higher compared to group 1 [adjusted hazard ratio (aHR), 1.11; 95% confidence interval (CI), 1.03–1.19] and group 2 (aHR, 1.27; 95% CI, 1.08–1.49). In contrast to the results of metachronous CRN risk, the risk of metachronous ACRN was not significantly different among groups 1, 2, 3, and 4.

Risk of metachronous neoplasia based on change in abdominal obesity

During the follow-up period, metachronous CRN developed in 1445 (34.2%), 179 (33.3%), 235 (35.8%), and 888 (40.6%) patients in groups 5, 6, 7, and 8, respectively; and metachronous ACRN developed in 98 (2.2%), 7 (1.3%), 10 (1.5%), and 79 (3.6%) in the four groups, respectively. The risk of metachronous CRN among the four groups based on WC change was

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compared in Table 4. The risk of metachronous CRN in group 8 was significantly higher compared to group 5 (aHR, 1.19; 95% CI, 1.10–1.30) and group 7 (aHR, 1.18; 95% CI, 1.02–1.36). Moreover, the risk in group 8 tended to be higher than that in group 6 (aHR, 1.17; 95% CI, 1.00–1.37).

The results of metachronous ACRN risk were similar to those of metachronous CRN risk. The cumulative risk of metachronous ACRN was higher in group 8 than in groups 5, 6, and 7 (p<0.001, p=0.006, and p=0.003. respectively), whereas the risk was not significantly different among groups 5, 6, and 7 (Fig. 2). Even after adjusting for confounders, the risk of metachronous ACRN in group 8 was significantly higher compared to group 5 (aHR, 1.53; 95% CI, 1.12–2.09), group 6 (aHR, 2.57; 95% CI, 1.18–5.59), and group 7 (aHR, 2.35; 95% CI, 1.21–4.54) (Table 4).

Table 5 shows the results adjusted for both BMI change and WC change. The significant association of BMI change with the risk of metachronous CRN disappeared after adjusting for WC change. However, the association between WC change and the risk of metachronous CRN significantly persisted even after adjusting for BMI change [groups 5 and 7 vs. group 8; aHR (95% CI), 0.84 (0.74–0.95) and 0.86 (0.74–0.998), respectively]. In addition, the association between WC change and the risk of metachronous ACRN did not attenuate and remained significant even after adjusting for BMI change [groups 5, 6, and 7 vs. group 8; aHR (95% CI), 0.49 (0.31–0.78), 0.32 (0.14–0.72), and 0.37 (0.19–0.75), respectively].

DISCUSSION

In this large-scale study, we found that patients with overall obesity at both index and follow-up colonoscopies had a higher risk of metachronous CRN compared to patients who changed status from "overall obesity" to "non-overall obesity," as well as patients without overall obesity at both index and follow-up colonoscopies. However, there was no significant association between the overall change in obesity and the risk of metachronous ACRN. Meanwhile, patients with abdominal obesity at both index and follow-up colonoscopies had a higher risk of metachronous CRN compared to patients without abdominal obesity at both index and follow-up colonoscopies, and they also tended to have a higher risk of metachronous CRN compared to patients who changed status from "abdominal obesity" to "non-abdominal obesity." More importantly, patients with abdominal obesity at both index and follow-up

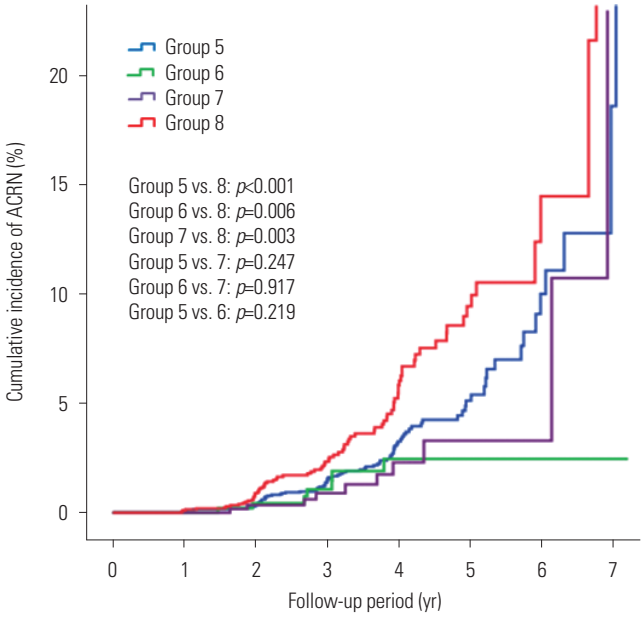

Fig. 2. Cumulative incidence of metachronous advanced colorectal neoplasia (ACRN) based on changes in abdominal obesity between index colonoscopy and follow-up colonoscopy. Group 5, non-abdominal obesity persisted; group 6, changed from abdominal obesity to non-abdominal obesity; group 7, changed from non-abdominal obesity to abdominal obesity; group 8, abdominal obesity persisted.

Table 4. Multivariable Analysis for the Relationship between Change in Abdominal Obesity and the Risk of Metachronous CRN

	3-year cumulative incidence rate (%)	5-year cumulative incidence rate (%)	Adjusted HR (95% CI)	*p* value	Adjusted HR (95% CI)	*p* value	Adjusted HR (95% CI)	*p* value
Metachronous CRN								
Group 5	20.3	58.2	1 (reference)					
Group 6	18.2	58.4	1.02 (0.87–1.19)	0.807	1 (reference)			
Group 7	22.5	54.6	1.02 (0.88–1.17)	0.837	1.00 (0.82–1.21)		1 (reference)	
Group 8	25.6	65.2	1.19 (1.10–1.30)	<0.001	1.17 (1.00–1.37)	0.057	1.18 (1.02–1.36)	0.028
Metachronous advanced CRN								
Group 5	1.5	5.1	1 (reference)					
Group 6	1.1	2.5	0.59 (0.28–1.29)	0.186	1 (reference)			
Group 7	0.9	3.3	0.65 (0.34–1.25)	0.200	1.10 (0.42–2.89)	0.851	1 (reference)	
Group 8	2.3	9.4	1.53 (1.12–2.09)	0.008	2.57 (1.18–5.59)	0.017	2.35 (1.21–4.54)	0.011

HR, hazard ratio; CI, confidence interval; CRN, colorectal neoplasia; group 5, non-abdominal obesity→non-abdominal obesity; group 6, abdominal obesity→non-abdominal obesity; group 7, non-abdominal obesity→abdominal obesity; group 8, abdominal obesity→abdominal obesity.
Values were adjusted for age, sex, smoking status, family history of colorectal cancer, use of nonsteroidal anti-inflammatory drugs, physical activity, hypertension, diabetes, and baseline adenoma characteristics (low- vs. high-risk adenoma).

Table 5. Multivariable Analysis with Adjustments for Both BMI Change and WC Change

	Metachronous CRN		Metachronous advanced CRN	
	Adjusted HR (95% CI)	*p* value	Adjusted HR (95% CI)	*p* value
Change in overall obesity (BMI)				
Group 1	1.01 (0.90–1.14)	0.877	1.49 (0.93–2.39)	0.098
Group 2	0.89 (0.74–1.08)	0.250	1.60 (0.79–3.25)	0.195
Group 3	0.92 (0.77–1.10)	0.345	1.18 (0.59–2.36)	0.648
Group 4	1 (reference)		1 (reference)	
Change in abdominal obesity (WC)				
Group 5	0.84 (0.74–0.95)	0.004	0.49 (0.31–0.78)	0.002
Group 6	0.87 (0.74–1.03)	0.110	0.32 (0.14–0.72)	0.006
Group 7	0.86 (0.74–0.998)	0.048	0.37 (0.19–0.75)	0.005
Group 8	1 (reference)		1 (reference)	

CRN, colorectal neoplasia; HR, hazard ratio; CI, confidence interval; BMI, body mass index; WC, waist circumference.
Values were adjusted for change in overall obesity (4 groups), change in abdominal obesity (4 groups), age, sex, smoking status, family history of colorectal cancer, use of nonsteroidal anti-inflammatory drugs, physical activity, hypertension, diabetes, and baseline adenoma characteristics (low- vs. high-risk adenoma).

colonoscopies had a higher risk of metachronous ACRN compared to patients who changed status from "abdominal obesity" to "non-abdominal obesity," as well as patients without abdominal obesity at both index and follow-up colonoscopies. Our results indicate that the risk of metachronous CRN after polypectomy was affected by the changes in overall and abdominal obesity between index and follow-up colonoscopies. Furthermore, changes in abdominal obesity affected the risk of metachronous ACRN.

Most previous studies assessed the risk of recurrence of CRN based solely on the baseline obesity status at index colonoscopy, without considering the changes in BMI or WC.[9-12] However, obese patients at index colonoscopy may have lost weight during the follow-up period, and may have become non-obese at follow-up colonoscopy; similarly, some non-obese patients at index colonoscopy may have gained weight and become obese at follow-up colonoscopy. In fact, in our study, the proportion of these patients was 4.7% and 6.6% for overall obesity and 7.1% and 8.6% for abdominal obesity, respectively.

To date, only a few studies have examined the relationship between weight change and the risk of metachronous CRN development after adenoma removal,[18-20] with inconsistent results. Laiyemo, et al.[18] studied a total of 1826 patients who underwent removal of ≥1 adenoma, and reported that weight loss or gain over 4 years did not affect the development of metachronous adenoma. Their study did not support weight loss alone as an effective intervention for reducing adenoma recurrence.[18] In contrast, a Japanese study demonstrated that the incidence of colorectal adenoma after 1 year in the weight-reduction group was significantly lower than that in the non-reduction group.[19] Our preceding study also showed that among the 2176 patients with adenomas at baseline, the risk of metachronous adenoma significantly increased with increasing weight-change quartiles over 2.2 years.[20] However, the interval of surveillance colonoscopies in these two studies showing positive results was too short to assess metachronous CRN development. Discrepancies in the results of the relationship between weight change and metachronous CRN risk may suggest that the development of metachronous CRN may not be attributable to weight change (BMI, overall obesity) alone.

There are even fewer studies assessing the impact of WC change on the risk of metachronous CRN. In fact, only one study on this topic has been published to date. Similar to our results, a recent study reported a positive association between the change in WC and the risk of metachronous adenoma in patients with baseline adenoma over a median period of 43 months.[21] In that study, an increase in WC was associated with the risk of metachronous adenoma [HR, 1.04 (per 1 cm); 95% CI, 1.01–1.07].[21] The study also showed that an increase in BMI was associated with the risk of metachronous adenoma [HR, 1.33 (per 1 kg/m^2); 95% CI, 1.18–1.49].[21] However, the previous study was limited by the small number of patients with baseline adenoma (n=654). In addition, the baseline adenoma characteristics, which are the most important risk factors for metachronous CRN, were not adjusted for in the study; and the association between the change in WC/BMI and the risk for metachronous ACRN, which is an indicator for determining the surveillance interval, was not analyzed. Unlike this previous study, our study did not show significant results for both metachronous CRN and ACRN when we analyzed the changes in WC and BMI as continuous variables. Instead, our study showed significant results when we analyzed WC and BMI as categorical variables based on the criteria for obesity. Our study, which included a relatively large number of patients and considered baseline adenoma characteristics, may provide more reliable information. Our results may suggest that minor changes in WC and BMI within the normal range may not affect the incidence of metachronous CRN/ACRN.

An interesting finding of our study is that the patients who changed status from "overall obesity" to "non-overall obesity"

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had a lower risk of metachronous CRN compared to patients with overall obesity at both index and follow-up colonoscopies. This suggests that the impact of obesity on CRN development may be reversible. A more remarkable finding is that the patients who changed status from "abdominal obesity" to "non-abdominal obesity" had a lower risk of metachronous ACRN compared to those with abdominal obesity at both index and follow-up colonoscopies. These results strongly suggest that reducing abdominal obesity may help prevent CRC. In addition, when deciding the postpolypectomy surveillance interval, the abdominal obesity status as well as the adenoma characteristics of the patients may have to be considered. The interval may need to be shortened in patients with persistent abdominal obesity.

However, there was no difference in the risk of metachronous CRN and ACRN between non-obesity persisted group vs. non-obesity to obesity group (group 3 vs. group 1 and group 7 vs. group 5). Although it is difficult to clearly explain the reason behind these results, the duration of obesity may have affected the development of metachronous neoplasia. Although the dynamic changes in WC and BMI during the follow-up period were not investigated, the obesity duration of patients in groups 3 and 7 may have been short. To better understand the relationship between obesity and metachronous neoplasia, long-term follow-up studies considering dynamic changes in WC and BMI should be performed.

In the present study, the association between the overall obesity change and the risk of metachronous CRN disappeared after adjusting for abdominal obesity change, whereas the association between change in abdominal obesity and the risk of metachronous CRN significantly remained even after adjusting for overall obesity change. Furthermore, the risk of metachronous ACRN was affected by changes in abdominal obesity but not by changes in overall obesity, and the association of abdominal obesity change with the risk of metachronous ACRN significantly persisted even after adjusting for overall obesity change. These results indicate that changes in abdominal obesity are associated with the risk of metachronous CRN and ACRN, independent of changes in overall obesity. Changes in abdominal obesity may be more strongly predictive of metachronous ACRN development than changes in overall obesity. Based on our findings, changes in abdominal obesity (WC), rather than changes in overall obesity (BMI), may need to be considered in determining the interval of surveillance colonoscopy. Our findings were in line with the results of an existing literature which revealed that WC is a stronger risk factor than BMI for ACRN and CRC.[3-5,7] Compared with subcutaneous adipose tissue, visceral adipose tissue has been reported to be a better indicator of metabolic disturbances including insulin resistance and systemic inflammation.[22-24] The better capability of WC, compared with BMI, to capture the visceral adipose tissue may be the reason behind the stronger association between changes in WC and metachronous CRN.

This study is the first to demonstrate that changes in abdominal obesity may affect the risk of metachronous ACRN development, independent of changes in overall obesity. Nevertheless, our study had several limitations. First, dietary habits such as red meat consumption, which are positively associated with both CRN risk and abdominal obesity, were not considered. Second, given the high percentage of patients with LRAs at index colonoscopy, the interval between index and follow-up colonoscopies was not sufficient. Third, although we excluded the patients with poor bowel preparation, we did not use a validated scale for bowel preparation quality. Accordingly, we did not assess the degree of bowel cleansing in detail. Fourth, we did not consider diabetes and smoking status at the time of follow-up colonoscopy. Metabolic and smoking status may have changed during the follow-up period, and these may have affected the risk of metachronous CRN. Lastly, most of our cohort consisted of relatively healthy young men, which may have led to a selection bias.

In conclusion, the changes in obesity affected the risk of metachronous CRN development after polypectomy. In particular, the changes in abdominal obesity had an impact on the risk of metachronous ACRN development. These findings suggest that patients with persistent abdominal obesity may need to undergo more intensive surveillance colonoscopy, and that reducing abdominal obesity may help prevent CRC.

AUTHOR CONTRIBUTIONS

Conceptualization: Yoon Suk Jung. Data curation: all authors. Formal analysis: Yoon Suk Jung. Investigation: Yoon Suk Jung and Nam Hee Kim. Methodology: Yoon Suk Jung. Project administration: Yoon Suk Jung. Resources: Yoon Suk Jung. Software: Yoon Suk Jung. Supervision: Yoon Suk Jung. Validation: Yoon Suk Jung. Visualization: Yoon Suk Jung. Writing—original draft: Yoon Suk Jung. Writing—review & editing: Yoon Suk Jung. Approval of final manuscript: all authors.

ORCID iDs

Yoon Suk Jung https://orcid.org/0000-0002-1963-7170
Nam Hee Kim https://orcid.org/0000-0002-2686-9754
Jung Ho Park https://orcid.org/0000-0002-8367-4371
Dong Il Park https://orcid.org/0000-0003-2307-8575
Chong Il Sohn https://orcid.org/0000-0002-9748-8537

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