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ORIGINAL PAPER

Physical activity and other lifestyle factors in relation to the prevalence of colorectal adenoma: a colonoscopy-based study in asymptomatic Koreans

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Abstract
Purpose To evaluate physical activity and other lifestyle risk factors in relation to the prevalence of colorectal adenomas in asymptomatic Koreans.
Methods A total of 1,526 asymptomatic subjects who underwent a colonoscopy were enrolled. Lifestyle factors such as physical activity and smoking data were obtained using a questionnaire. The subjects were grouped into three exposure levels by tertiles of metabolic equivalent hours per week. We evaluated the risk factors in subjects with adenomas by risk stratification (low-risk adenoma group vs. high-risk adenoma group) and by anatomic location (proximal colon, distal colon, rectum, and multiple locations). The high-risk adenoma group was defined as subjects with advanced adenomas or multiple (≥3) adenomas.
Results A total of 456 participants had colorectal adenomas, and 861 had no polyps. In multivariate analyses, higher levels of physical activity were associated with a significantly decreased risk of colorectal adenomas (OR = 0.56, 95 % CI 0.40–0.79). This inverse association was stronger for the risk of high-risk adenomas (OR = 0.39, 95 % CI 0.21–0.73) than for low-risk adenomas (OR = 0.62, 95 % CI 0.43–0.89). The negative relation of physical activity was significant for distal colon adenomas (OR = 0.54, 95 % CI 0.30–0.95) and the adenomas with multiple locations (OR = 0.39, 95 % CI 0.21–0.72).
Conclusions Increased physical activity is associated with a reduced prevalence of colorectal adenomas. The inverse association between physical activity and adenoma was stronger for the risk of advanced or multiple adenomas.

Keywords Adenoma · Colorectal neoplasm · Exercise · Physical activity · Lifestyle

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Introduction

Colorectal cancer is one of the most common cancers and remains a leading cause of cancer-related morbidity and mortality in Western countries [1]. Korea has experienced a rapid increase in the incidence of colorectal neoplasms over recent decades [2, 3]. A previous study from our group reported that the overall prevalence of adenomas was 39.4 % [4], which is similar to that in Western countries (37.5–41 %) [5–7].

One of the most important fundamental findings for colorectal cancer has been the adenoma-carcinoma sequence [8]. It has been shown that endoscopic or surgical removal of adenomas reduces the incidence of colorectal cancer [9–11]. Evaluating the risk factors for colorectal adenomas and modifying or correcting the risk factors could also be helpful for the prevention of colorectal cancer. Some lifestyle factors such as physical inactivity and obesity have been well established as risk factors for colorectal cancer [12, 13]. However, the findings from epidemiologic studies on the risk factors of adenomas are equivocal [14–18]. The results appear to be most consistent for smoking and use of nonsteroidal anti-inflammatory

drugs (NSAIDs), with an increased adenoma risk among former and current smokers [14, 15] and a decreased risk among subjects with regular use of NSAIDs [16–18]. In contrast, there is much less evidence as to whether physical activity protects against colorectal adenomas, which are thought to be precursors to most colon cancers, and the evidence that is available is inconsistent [16, 19–23]. Some studies suggested a protective effect of physical activity against colorectal adenomas or polyps [16, 19–21]. However, others showed no associations between physical activity and colorectal adenomas [22, 23]. Such diverse results may be due to several factors, including study design (cohort vs. case–control studies), the adenoma detection method (flexible sigmoidoscopy vs. colonoscopy), the study population, differences in the case definition, degree of measurement error, and range of physical activity across populations.

Moreover, most studies evaluating association of physical activity and lifestyle factors with the risk of colorectal adenoma were performed in Western populations, and there are relatively fewer data from Asian populations [16, 19–23]. Studies on Asian migrants to Western countries have shown conflicting results, which suggest that although changes in dietary habits and lifestyle are believed to be the reasons underlying the increase in colorectal neoplasms, the interaction between these factors and genetic characteristics or ethnic biological differences might also have an important role [2]. To our knowledge, no large-scale, well-designed study has investigated the association between physical activity and colorectal adenomas in Koreans. The aim of this study was to evaluate the risk factors for colorectal adenomas and the association between physical activity and adenomas.

Methods

Study population

We performed a cross-sectional study on asymptomatic persons who underwent a screening colonoscopy at Seoul National University Hospital Healthcare System Gangnam Center for a routine health check-up from February 2008 to October 2010. A total of 1,526 subjects (aged 21–78 years; mean age 49.2 ± 9.8 years; 873 men and 653 women) were considered eligible. All potential participants were requested to complete a self-administered, structured questionnaire on smoking history, family history of colorectal cancer, and physical activity. Patients with colorectal disease-related symptoms or signs (e.g., recent bowel habit change, unexplained weight loss, anemia, or lower gastrointestinal tract bleeding not attributable to hemorrhoids), personal histories of colorectal cancer or polyps, inflammatory bowel disease, intestinal tuberculosis, incomplete examination of the entire colon because of failure to reach the cecum, or inadequate bowel preparation were excluded. All subjects completed the questionnaire and signed a research consent form. The study protocol and consent form were approved by the ethics committee of Seoul National University Hospital (Institutional Review Board Number: H-1009-015-330).

Colonoscopy

The procedures for performing colonoscopies and histologic evaluations have been described previously [24]. Advanced adenomas were defined as adenomas ≥1 cm, villous adenomas (at least 25 % villous structure), adenomas with high-grade dysplasia, or carcinoma in situ. Subjects with adenomas were classified into two groups by risk stratification for subsequent advanced neoplasia (cancer or advanced adenomas) based on the most advanced lesion in their colonoscopy findings. Low-risk adenomas were defined as one or two small (<1 cm) tubular adenomas without high-grade dysplasia, and high-risk adenomas were defined as advanced adenomas or three or more adenomas.

The colorectal adenoma location was divided into the proximal colon (including the cecum, ascending colon, hepatic flexure, and transverse colon), the distal colon (including the splenetic flexure, descending colon, and sigmoid colon), and the rectum.

Anthropometric data and laboratory tests

All subjects underwent physical examinations by trained staff. The body mass index (BMI) was calculated from measured weight and height as the weight (kg) divided by the height squared (m^2). The waist circumference (WC) was taken at the midpoint between the inferior margin of the last rib and the superior iliac crest. We also measured blood pressure and blood markers such as fasting blood sugar (FBS), triglycerides, and high-density lipoprotein (HDL) cholesterol. Metabolic syndrome was defined clinically based on the presence of three or more of the following Regional Office for the Western Pacific Region of WHO (WPRO) WC criteria of the National Cholesterol Education Program Adult Treatment Panel III: (1) abdominal obesity (WC > 90 cm in men and >80 cm in women), (2) hypertriglyceridemia, ≥150 mg/dl, (3) low HDL cholesterol, <40 mg/dl in men and <50 mg/dl in women, (4) high blood pressure, ≥130 mmHg systolic or ≥85 mmHg diastolic, and (5) FBS ≥ 110 mg/dl.

Physical activity assessment

Physical activity data were obtained using a self-administered questionnaire. The questionnaire focused on the type

of work, activities associated with commuting, and leisure-time activities within the last year. Five options were used to describe the type of work: non-worker, sedentary or standing work (e.g., clerical work, taxi driving), work with walking (e.g., delivery by walking, patrolling on foot), labor work (e.g., construction work, agricultural work, load transport), and hard labor work (e.g., digging or chopping with heavy tools, carrying heavy loads). Housewives were categorized as non-workers. The level of engagement in regular leisure-time activities was ascertained, on average over 1 year, with regularity defined as at least once per week. Information for activities was obtained in terms of the type of activity, the number of days per week that individuals participated in each activity, and the minutes of participation per occasion. Weekly minutes spent walking, bicycling, and jogging while commuting was determined on average over the year. Because the intensity of non-job physical activities including physical activity at leisure time and commuting was not directly recorded, a metabolic equivalent task (MET) was assigned to each reported activity according to the Compendium of Physical Activities [25]. One MET, the energy expended sitting quietly, was equivalent to 3.5 ml of oxygen uptake per kg of body weight per minute for a 70 kg adult [21]. The MET values assigned to the non-job physical activity data were 2.5 for walking at a slow pace, 3.8 for walking at a brisk speed, 7.0 for jogging, 6.0 for hiking, 7.0 for swimming, 8.0 for cycling, 4.5 for golf, 7.0 for tennis, and 5.5 for health club exercise. The MET-hours/week were estimated by multiplying the reported time spent at each activity by the corresponding MET value.

We assessed the validity of the questionnaire for 77 subjects using a seven-day physical activity recall and a seven-day 24-h physical activity diary. The Spearman correlation coefficient was 0.44 ($p < 0.01$) for the MET-hour score between the questionnaire data and seven-day recall data and 0.39 ($p < 0.01$) between the questionnaire data and the seven-day diary data. Sixty-three subjects completed the questionnaire again after an interval of 1 year. The Spearman correlation coefficient for non-job physical activities was 0.62 ($p < 0.01$).

Statistical analysis

Subjects with adenomatous polyps were defined as cases, and without polyps as controls. Subjects with polyps not classified as adenomas were not included in the analysis. Descriptive statistical analyses included calculation of rates and proportions for categorical data and means and standard deviations for continuous data. The associations of anthropometric variables, metabolic syndrome, smoking status, family (first-degree relative) history of colon cancer, and physical activity with colorectal adenomas were evaluated by logistic regression analysis in terms of the odds ratio (OR) and the corresponding 95 % confidence interval (CI). The BMI was categorized into <23.0, 23.0–24.9, and ≥25.0 kg/m^2. Smoking status was categorized into none, <20 pack-years, and ≥20 pack-years. The pack-year unit incorporates the amount and duration of smoking and is defined as the daily consumption of 1 pack (20 cigarettes) over the time period of 1 year. Physical activity was divided into tertiles based on the distribution in the study population. The tertile ranges were ≤12.05 (inactive), 12.06–31.25 (moderately active), and ≥31.26 MET-hours/week (active). ORs and 95 % CIs were calculated, with the lowest tertile of physical activity (inactive) serving as the reference group. All analyses were adjusted for sex and age at baseline. In multivariate regression models, we adjusted for BMI by category, metabolic syndrome (yes/no), smoking (none, <20 pack-years, and ≥20 pack-years), family history of colorectal cancer (yes/no), job-related physical activity [sedentary (non-worker, sedentary, or standing work) and active (work with walking, labor work, or hard labor work)], and non-job physical activity (in tertiles). The p value for the linear trend test across categories was calculated with the median value of each category as a continuous variable.

Multinomial logistic regression analyses were performed by risk stratification (low-risk adenoma group, high-risk adenoma group) and anatomical location (proximal colon, distal colon, rectum, and multiple locations). We tested for interactive effects by including a cross-product term along with the main-effect terms in the regression model. The statistical significance of each variable was tested by the Wald chi-square test.

The results were considered statistically significance if the two-sided p value was less than 0.05 or if the 95 % CI did not include unity. All statistical analyses were performed using SPSS for Windows (SPSS, Chicago, IL., USA).

Results

To evaluate the risk factors for colorectal adenomas, we analyzed 456 subjects with adenomas and 861 subjects without polyps. The 209 subjects with non-neoplastic lesions were not included in the analysis. The demographics and lifestyle characteristics of the study participants are shown in Table 1. Subjects with colorectal adenomas were older (52.4 vs. 47.3 years) and more likely to be male (69.7 %) vs. female (49.6 %) than the control subjects.

The associations between anthropometric and lifestyle factors and adenoma risk are summarized in Table 2. Higher levels of non-job physical activity were associated

Table 1 Baseline characteristics of study participants

	Control ($n = 861$)	Adenoma ($n = 456$)	p value[a]
Number of adenoma			
0	861		
1–2		380	
≥3		76	
Pathologic findings			
Tubular adenoma <1 cm		413	
Tubular adenoma ≥1 cm		30	
Villous adenoma		8	
High-grade dysplasia		3	
Carcinoma in situ		2	
Location of adenomas			
Proximal colon[b], *n* (%)		221 (48.5)	
Distal colon[b], *n* (%)		103 (22.6)	
Rectum, *n* (%)		28 (6.1)	
Multiple locations[c], *n* (%)		104 (22.8)	
Age (years), mean ± SD	47.3 ± 9.7	52.4 ± 9.1	<0.001
Age (years), *n* (%)			<0.001
<40	196 (22.8)	34 (7.5)	
40–49	301 (35.0)	140 (30.7)	
50–59	268 (31.1)	186 (40.8)	
60–69	84 (9.8)	80 (17.5)	
≥70	12 (1.4)	16 (3.5)	
Males, *n* (%)	427 (49.6)	318 (69.7)	<0.001
Non-job physical activity (MET-h/week), mean ± SD	27.5 ± 24.7	25.0 ± 19.4	0.061
Occupation, *n* (%)			0.004
Non-worker	276 (32.2)	107 (23.6)	
Sedentary or standing	544 (63.4)	324 (71.5)	
Walking	27 (3.1)	11 (2.4)	
Labor	9 (1.0)	11 (2.4)	
Hard labor work	2 (0.2)	0 (0.0)	
Smoking habits, *n* (%)			<0.001
Never	501 (59.6)	175 (38.8)	
Former	192 (22.8)	157 (34.8)	
Current	148 (17.6)	119 (26.4)	
Smoking (pack-years), mean ± SD	6.7 ± 11.8	12.9 ± 15.3	<0.001
BMI (kg/m^2), mean ± SD	23.0 ± 3.0	24.0 ± 2.8	<0.001
Waist circumference (cm), mean ± SD	82.7 ± 8.0	86.0 ± 7.6	<0.001
TG (mg/dl), mean ± SD	89.1 ± 58.4	102.6 ± 60.7	<0.001
HDL (mg/dl), mean ± SD	54.5 ± 12.3	52.6 ± 11.4	0.008
Systolic BP (mmHg), mean ± SD	113.6 ± 14.1	118.2 ± 14.1	<0.001
Diastolic BP (mmHg), mean ± SD	73.0 ± 11.6	76.2 ± 11.0	<0.001
FBS (mg/dl), mean ± SD	91.5 ± 14.0	96.8 ± 20.4	<0.001
Family history of colon cancer [yes, *n* (%)]	54 (6.3)	28 (6.1)	0.515

Data are reported for participants with complete information; not all participants had complete data for each variable

SD standard deviation, *BMI* body mass index, *TG* triglyceride, *HDL* high-density lipoprotein, *BP* blood pressure, *FBS* fasting blood sugar

[a] p values (two sided) were based on t test for continuous variables and chi-square test for categorical variables

[b] Proximal colon includes cecum, ascending colon, hepatic flexure, and transverse colon; distal colon includes splenetic flexure, descending colon, and sigmoid colon

[c] Multiple locations were defined as the cases with multiple adenomas in two or more locations of proximal colon, distal colon, or rectum

with a significantly decreased risk of colorectal adenomas (OR = 0.86, 95 % CI 0.62–1.18 for moderately active vs. inactive; OR = 0.56, 95 % CI 0.40–0.79 in active vs. inactive; $p_{\text{trend}} = 0.001$). Smokers had an increased risk of adenoma, and the risk was higher for heavy smokers (OR = 1.59, 95 % CI 1.06–2.36 for <20 pack-years vs.

non-smoker; OR = 1.93, 95 % CI 1.26–2.96 for ≥20 pack-years vs. non-smoker) (p_{trend} = 0.003).

We evaluated the risk factors for low-risk adenomas and high-risk adenomas (Table 3). In the multivariate analysis, the inverse association of physical activity was greater for the risk of high-risk adenomas (OR = 0.39, 95 % CI 0.21–0.73, p = 0.003) than for low-risk adenomas (OR = 0.62, 95 % CI 0.43–0.89, p = 0.009). Smoking was strongly associated with high-risk adenomas (OR = 2.83, 95 % CI 1.31–6.10 for ≥20 pack-years, p = 0.008) than low-risk adenomas (OR = 1.78, 95 % CI 1.13–2.79, p = 0.012). Metabolic syndrome was associated with a significantly increased risk for high-risk adenomas (OR = 2.54, 95 % CI 1.37–4.71, p = 0.003), but no association was observed for low-risk adenomas.

Table 4 shows the risk factors according to the location of the adenomas: proximal colon, distal colon, rectum, and multiple locations. In the multivariate analysis, the negative relation of non-job physical activity was significant for distal colon adenomas (OR = 0.54, 95 % CI 0.30–0.95, p = 0.034) and for the adenomas with multiple locations (OR = 0.39, 95 % CI 0.21–0.72, p = 0.003). Smoking was strongly associated with proximal colon adenomas (OR = 2.14, 95 % CI 1.24–3.69 for ≥20 pack-years, p = 0.006) and adenomas with multiple locations (OR = 2.59, 95 % CI 1.23–5.45 for ≥20 pack-years, p = 0.012). Metabolic syndrome was associated with an increased risk for the adenomas with multiple locations (OR = 2.25, 95 % CI 1.22–4.16, p = 0.009).

With regard to age, non-job physical activity was associated with a significantly decreased risk of adenoma development in older subjects (≥50 years old) (OR = 0.77, 95 % CI 0.50–1.19 for moderately active subjects; OR = 0.56, 95 % CI 0.36–0.85 for active subjects), but not in younger subjects (<50 years old) (OR = 0.93, 95 % CI 0.6–1.38 for moderately active subjects; OR = 0.64, 95 % CI 0.40–1.01) by univariate analyses. However, the interactions between non-job physical activity and age were statistically insignificant (p = 0.600 for moderately active subjects, p = 0.506 for active subjects). In the multivariate analysis, the interactions between non-job physical activity and age were statistically insignificant for low-risk adenomas (p = 0.919 for moderately active subjects, p = 0.853 for active subjects) and for high-risk adenomas (p = 0.427 for moderately active subjects, p = 0.094 for active subjects). According to the location of adenomas, the interactions were insignificant for proximal colon (p = 0.876 for moderately active subjects, p = 0.367 for active subjects), for distal colon (p = 0.248 for moderately active subjects, p = 0.964 for active subjects), for rectum (p = 0.446 for moderately active subjects, p = 0.120 for active subjects), and for multiple locations (p = 0.471 for moderately active subjects, p = 0.398 for active subjects).

Discussion

To the best of our knowledge, this is the first and the largest study of the association between physical activity and colorectal adenoma in asymptomatic Korean individuals. The advantages of this study include the colonoscopy-based outcome assessment, which minimized the possible misclassification of subjects with adenomas or other types of polyps as polyp-free control subjects.

Several mechanisms have been suggested to explain the role of physical activity in preventing colorectal carcinogenesis. Lifestyle factors associated with hyperinsulinemia, such as physical inactivity and being overweight, have been implicated in the adenoma-carcinoma sequence [26–28]. It has also been suggested that physical activity increases gut motility and thus possibly reduces mucosal exposure time to carcinogens [29]. The biological mechanism responsible for the protective effect of physical activity may be partially mediated by decreasing colonic bile acid exposure [30]. Individuals who are more active are also likely to have more opportunity for sun exposure and thereby have higher vitamin D levels, which may also be associated with a reduced risk of colon cancer [31].

In our study, the amount of physical activity in the most active group associated with a significant reduction in adenoma risk is more than 32 MET-hours/week, which is equivalent to 4 h of vigorous activity per week. Several studies that have simultaneously examined the frequency, intensity, and duration of physical activity have shown that roughly 3.5–4 h of vigorous activity per week, which translates to approximately 35 min of vigorous activity every day or 45 min of vigorous activity five days per week, would be needed to achieve a significant reduction in the risk of colon cancer [32]. For those that showed similar levels of risk reduction from moderate-intensity physical activity, 7–35 h per week, which translates to approximately 1–5 h of moderate-intensity activity every day, would be needed [32].

With regard to the concept of "risk stratification" according to the risk for development of a subsequent advanced adenoma or cancer, the present study demonstrated that the inverse association of physical activity was greater for risk of high-risk adenomas (three or more adenomas, or advanced adenomas) than low-risk adenomas [one or two small (<10 mm) tubular adenomas without high-grade dysplasia] (OR = 0.39 vs. OR = 0.62). Several investigations have studied the size or histologic characteristics of adenomas in relation to physical activity, with mixed results [7, 16, 21, 23, 33]. Some studies have reported an inverse relationship between physical activity and advanced adenomas [7, 16, 23]. However, other studies have reported similar reductions in risk for both large (≥1 cm) and small polyps [21, 33]. Considering multiple

Table 2 Associations between anthropometric and lifestyle factors and adenoma risk

	No. of controls ($n = 861$)	No. of cases ($n = 456$)	OR[a]	95 % CI	OR[b]	95 % CI
Non-job physical activity (MET-h/week)						
T1 (≤12.05)	284	155	1.00		1.00	
T2 (12.06–31.25)	286	160	0.78	0.58, 1.05	0.86	0.62, 1.18
T3 (≥31.26)	291	141	0.54	0.39, 0.73	0.56	0.40, 0.79
p-trend[c]			<0.001		0.001	
Job-related physical activity						
Sedentary	820	431	1.00		1.00	
Active	38	22	0.76	0.43, 1.36	0.83	0.44, 1.57
Smoking (pack-years)						
None	501	175	1.00		1.00	
<20	206	125	1.53	1.05, 2.22	1.59	1.06, 2.36
≥20	121	138	2.13	1.43, 3.18	1.93	1.26, 2.96
p-trend[c]			<0.001		0.003	
BMI (kg/m^2)						
<23.0	451	164	1.00		1.00	
23.0–24.9	198	132	1.28	0.94, 1.74	1.21	0.85, 1.72
≥25.0	200	150	1.42	1.05, 1.93	1.25	0.83, 1.88
p-trend[c]			0.026		0.264	
Increased waist circumference						
>90 cm in men, >80 cm in women						
No	533	259	1.00		1.00	
Yes	273	164	1.22	0.93, 1.59	1.07	0.75, 1.52
Triglyceride, ≥150 mg/dl						
No	722	346	1.00		1.00	
Yes	98	80	1.45	1.03, 2.04	1.34	0.86, 2.09
HDL cholesterol						
<40 mg/dl in men, <50 mg/dl in women						
No	662	355	1.00		1.00	
Yes	158	71	0.90	0.65, 1.25	0.80	0.54, 1.19
Blood pressure ≥130 mmHg systolic or ≥85 mmHg diastolic						
No	633	258	1.00		1.00	
Yes	180	146	1.26	0.96, 1.67	1.24	0.90, 1.71
Fasting blood glucose, ≥110 mg/dl.						
No	765	372	1.00		1.00	
Yes	52	53	1.26	0.82, 1.93	1.10	0.67, 1.82
Metabolic syndrome						
No	742	360	1.00		1.00	
Yes	72	65	1.40	0.96, 2.04	0.91	0.49, 1.69
Family history of colorectal cancer						
No	807	428	1.00		1.00	
Yes	54	28	1.04	0.64, 1.71	0.98	0.57, 1.69

Data are reported for participants with complete information; not all participants had complete data for each variable

BMI body mass index, *OR* odds ratio, *CI* confidence interval

[a] Adjusted for age and sex

[b] Adjusted for age, sex, BMI, metabolic syndrome, smoking, family history of colorectal cancer, job-related physical activity, and non-job physical activity

[c] *p* values for the linear trend test across categories was calculated with the median value of each category as a continuous variable

adenomas, a prospective study suggested that higher levels of activity might be associated with a lower risk of multiple adenomas (RR = 0.5) [34]. Why physical activity may be more associated with advanced or multiple adenomas than low-risk adenomas is not clear. Further studies are warranted for this issue.

Table 3 Risk factors for colorectal adenoma according to the risk stratification

	Low-risk adenoma group[a] ($n = 354$)			High-risk adenoma group[b] ($n = 102$)		
	No. of cases	OR[c]	95 % CI	No. of cases	OR[c]	95 % CI
Non-job physical activity (MET-h/week)						
T1 (≤12.05)	117	1.00		38	1.00	
T2 (12.06–31.25)	124	0.84	0.60, 1.19	36	0.86	0.50, 1.50
T3 (≥31.26)	113	0.62	0.43, 0.89	28	0.39	0.21, 0.73
p-trend[d]		0.009			0.003	
Job-related physical activity						
Sedentary	337	1.00		94	1.00	
Active	15	0.76	0.38, 1.51	7	1.27	0.50, 3.22
Smoking (pack-year)						
None	145	1.00		30	1.00	
<20	97	1.54	1.01, 2.34	28	2.21	1.04, 4.69
≥20	100	1.78	1.13, 2.79	38	2.83	1.31, 6.10
p-trend[d]		0.013			0.009	
BMI (kg/m^2)						
<23.0	130	1.00		31	1.00	
23.0–24.9	96	1.23	0.86, 1.77	31	1.12	0.60, 2.06
≥25.0	113	1.40	0.97, 2.02	37	1.07	0.57, 2.01
p-trend[d]		0.072			0.839	
Metabolic syndrome						
No	291	1.00		69	1.00	
Yes	39	0.90	0.57, 1.44	26	2.54	1.37, 4.71
Family history of colorectal cancer						
No	333	1.00		95	1.00	
Yes	21	1.05	0.60, 1.86	7	0.75	0.26, 2.22

BMI body mass index, *OR* odds ratio, *CI* confidence interval

[a] Subjects with one or two adenomas <10 mm

[b] Subjects with an advanced adenoma or ≥3 adenomas

[c] Adjusted for age, sex, BMI, metabolic syndrome, smoking, family history of colorectal cancer, job-related physical activity, and non-job physical activity

[d] *p* values for the linear trend test across categories was calculated with the median value of each category as a continuous variable

In our study, physical activity was associated with a significantly decreased risk for distal colon adenomas (OR = 0.54, 95 % CI 0.30–0.95) and for the adenomas with multiple locations (OR = 0.39, 95 % CI 0.21–0.72). There were no significant associations between physical activity and proximal colon adenomas (OR = 0.67, 95 % CI 0.44–1.03) and rectal adenomas (OR = 0.61, 95 % CI 0.22–1.70). The results of previous studies that evaluated physical activity and the risk of colorectal adenomas by anatomic location are inconsistent [21, 22, 35]. Some studies reported an inverse association between physical activity and distal colorectal adenomas [21, 35] consistent with our study. However, a prospective cohort study reported no difference between physical activity and the risk of colorectal adenoma by anatomic location [22]. The discrepancy might be due to several factors such as differences in classification of anatomical locations, size or number of adenomas, or distribution of advanced histology according to anatomical locations. Further studies are therefore needed to clarify the relationship between physical activity and the risk of colorectal adenomas by anatomic location.

We sought to evaluate the association of physical activity with the risk of developing colorectal adenoma in younger and older populations, and a large number of younger participants were included in this study. Using univariate analyses, non-job physical activity was associated with a significantly decreased risk of adenoma development in older subjects. However, the interactions between non-job physical activity and age were statistically insignificant.

We observed a twofold higher adenoma risk in heavy smokers who had smoked more than 20 pack-years when

Table 4 Risk factors for colorectal adenoma according to the location of the adenoma

	Proximal colon[a] ($n = 221$)			Distal colon[a] ($n = 103$)			Rectum ($n = 28$)			Multiple locations[b] ($n = 104$)		
	No.	OR[c]	95 % CI	No.	OR[c]	95 % CI	No	OR[c]	95 % CI	No.	OR[c]	95 % CI
Non-job physical activity (MET-h/week)												
T1 (≤12.05)	69	1.00		41	1.00		8	1.00		37	1.00	
T2 (12.06–31.25)	84	1.03	0.69, 1.54	33	0.72	0.42, 1.24	10	0.63	0.22, 1.83	33	0.69	0.40, 1.21
T3 (≥31.26)	68	0.67	0.44, 1.03	29	0.54	0.30, 0.95	10	0.61	0.22, 1.70	34	0.39	0.21, 0.72
p-trend[d]		0.056			0.034			0.376			0.002	
Job-related physical activity												
Sedentary	209	1.00		100	1.00		26	1.00		96	1.00	
Active	10	0.83	0.37, 1.84	3	0.56	0.16, 1.92	2	1.33	0.28, 6.30	7	1.16	0.46, 2.93
Smoking (pack-year)												
None	93	1.00		41	1.00		13	1.00		28	1.00	
<20	58	1.76	1.06, 2.93	33	1.52	0.79, 2.92	4	0.59	0.15, 2.29	30	2.02	0.97, 4.24
≥20	61	2.14	1.24, 3.69	27	1.41	0.69, 2.86	9	1.24	0.37, 4.15	41	2.59	1.23, 5.45
p-trend[d]		0.007			0.357			0.636			0.013	
BMI (kg/m^2)												
<23.0	87	1.00		40	1.00		10	1.00		27	1.00	
23.0–24.9	61	1.21	0.79, 1.84	27	0.97	0.55, 1.73	6	1.64	0.51, 5.26	38	1.47	0.80, 2.69
≥25.0	68	1.42	0.92, 2.18	33	1.03	0.57, 1.85	12	2.91	1.00, 8.45	37	1.25	0.66, 2.35
p-trend[d]		0.112			0.938			0.047			0.520	
Metabolic syndrome												
No	183	1.00		81	1.00		23	1.00		73	1.00	
Yes	24	0.94	0.55, 1.62	13	1.04	0.50, 2.17	3	0.63	0.17, 2.34	25	2.25	1.22, 4.16
Family history of colorectal cancer												
No	205	1.00		99	1.00		26	1.00		98	1.00	
Yes	16	1.19	0.63, 2.27	4	0.68	0.24, 1.97	2	1.59	0.35, 7.14	6	0.74	0.25, 2.20

BMI body mass index, *OR* odds ratio, *CI* confidence interval

[a] Proximal colon includes cecum, ascending colon, hepatic flexure, and transverse colon; distal colon includes splenetic flexure, descending colon, and sigmoid colon

[b] Multiple locations were defined as the cases with multiple adenomas in two or more locations of proximal colon, distal colon, or rectum

[c] Adjusted for age, sex, BMI, metabolic syndrome, smoking, family history of colorectal cancer, job-related physical activity, and non-job physical activity

[d] *p* values for the linear trend test across categories was calculated with the median value of each category as a continuous variable

compared with non-smokers. The risk of high-risk adenomas was greater than the risk of low-risk adenomas in heavy smokers (OR = 2.83, 95 % CI 1.31–6.10 for high-risk adenomas; OR = 1.78, 95 % CI 1.13–2.79 for low-risk adenomas). These results are similar to those of previous studies [14, 15, 36]. With regard to anatomic location of adenomas, the present study showed that heavy smokers were at increased risk of adenomas in proximal colon (OR = 2.14, 95 % CI 1.24–3.69) and multiple locations (OR = 2.59, 95 % CI 1.23–5.45), but not in distal colon and rectum. A previous study reported that the effect of smoking was stronger in the proximal colon [37], whereas other studies suggested that smoking was significantly associated with an increased risk of adenomas regardless of the location of the adenomas [14, 38]. Further studies are needed to confirm the relationship between smoking and the location of colorectal adenomas.

In the present study, obese subjects (BMI $\geq$ 25.0 kg/m^2) were at an increased risk of colorectal adenomas by univariate analysis (OR = 1.42, 95 % CI 1.05–1.93), but the association was attenuated and no longer statistically significant after multivariate adjustment. These findings are consistent with previous studies, which reported that no significant associations between BMI and colorectal adenomas were detected in multivariate analysis [7, 16, 39]. Others, however, have shown a positive association between BMI and risk of colorectal adenomas [21, 28, 40]. A recent study from Korea suggested that visceral fat is a more sensitive predictor for the presence of colorectal adenoma, rather than BMI or WC [13]. The association between obesity and the presence of a colorectal neoplasm cannot be easily explored because of many potential confounding factors, and thus, further investigation is required in a large population.

Several studies have reported that metabolic syndrome may be associated with colorectal adenoma [41–44]. Importantly, abdominal obesity, of all the individual metabolic syndrome components, independently increased the risk for colonic precancerous lesions [42, 43]. In our analysis, metabolic syndrome was associated with a significantly increased risk for multiple or advanced adenomas (OR = 2.54), but no association was observed for low-risk adenomas. Metabolic syndrome is one of the targets of tumor prevention trials, and strategies to prevent it might also be useful for the primary prevention of advanced colon tumors [44].

There are some limitations of our study. This is a cross-sectional study. Some of the suspected risk factors may not be associated with prevalent colorectal adenomas but could be risk factors for subsequent incident lesions. A long-term follow-up study is being planned to evaluate the associations of risk factors with the incidence and recurrence of colorectal adenomas.

In conclusion, the present study shows that increased physical activity is associated with a reduced prevalence of adenomas. The inverse association between physical activity and adenoma was stronger for the risk of advanced or multiple ($\geq$3) adenomas.

Conflict of interest The authors declare that they have no conflict of interest.

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