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Adiposity in relation to colorectal adenomas and hyperplastic polyps in women

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Abstract

Objective—To examine whether BMI is independently related to colorectal adenomas and hyperplastic polyps.

Methods—We conducted a cross-sectional study among 1,420 asymptomatic women aged 40–79 years who had undergone complete colonoscopy. Logistic regression was used to estimate the odds ratios (OR) and the corresponding 95% confidence intervals (CI) of adenomas and hyperplastic polyps.

Results—We identified 953 women (67.1%) with no polyps, 292 (20.6%) with adenomas, and 175 (12.3%) with hyperplastic polyps. Among those with polyps, 75 women (5.3% of total women) were classified as having both adenomas and hyperplastic polyps. After adjusting for potential risk factors for colorectal cancer, BMI was related to increased risk of adenomas (OR comparing obese to normal weight women=1.57; 95% CI=1.07–2.29). Further, BMI was associated with enhanced risk of hyperplastic polyps (OR=3.76; 95% CI=2.35–6.01) and the combination of adenomas and hyperplastic polyps (OR=2.84; 95% CI=1.41–5.72).

Conclusions—Excess body mass is positively related to colorectal adenomas and hyperplastic polyps, particularly when both kinds of polyps are present in combination. Future studies should continue to delineate possible differences in potential risk factors between colorectal adenomas and hyperplastic polyps. Such work should help further elucidate the possible causes of colorectal cancer.

Keywords

Adiposity; obesity; colorectal adenoma; hyperplastic polyps; women

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Conflict of interest statement
All authors declare that they have no conflict of interest.

Introduction

Convincing epidemiologic evidence shows that greater body mass index (BMI) is related to increased risk of colon cancer [1]. Given an apparent adverse effect of adiposity on colon cancer, this factor may plausibly enhance the risk of developing adenomatous polyps, a known precursor lesion of colorectal cancer [2] and an established surrogate endpoint for colorectal cancer in mechanistic studies [3] and clinical trials [4].

Because adenomas represent the initial manifestation of the adenoma-dysplasia-carcinoma sequence [2], understanding the association between potential risk factors for this first stage of carcinogenesis is crucial for the primary prevention of colorectal cancer. To help clarify this issue, we conducted a cross-sectional of study of BMI in relation to adenomas overall and adenomas defined by stage, multiplicity, and anatomic location. In addition, we considered a separate evaluation of BMI in relation to hyperplastic polyps as a distinct endpoint because certain forms of hyperplastic polyps, such as serrated or mixed type are thought to represent precursor lesions for colorectal malignancy [5]. Hyperplastic polyps may play a role in colorectal carcinogenesis through biologic mechanisms that involve increased levels of insulin-like growth factors and insulin [5].

Our study differs from most previous investigations in presenting relations stratified by four groups of endpoints: cases with any adenomatous polyps; cases with adenomatous polyps after excluding those with hyperplastic polyps; cases with hyperplastic polyps after excluding those with adenomatous polyps; and cases with the combination of both types of polyps. We gave particular attention to the avoidance of bias and confounding by studying a population of asymptomatic women enrolled for complete screening colonoscopy, using information on body mass collected prior to the diagnosis of colorectal polyps, and controlling for a broad range of potential confounding variables.

Subjects and Methods

Study participants

The current study was conducted between July 1, 1999 and December 31, 2002 among women referred for colorectal cancer screening at four regional military centers (Bethesda, MD; Washington, DC; San Diego, CA; and Portsmouth, VA). The study enrolled asymptomatic women aged 50–79 years who were at average risk of developing colorectal cancer and asymptomatic women aged 40–79 years who had a family history of colorectal cancer. To make certain that women were asymptomatic and at average risk for colorectal neoplasia, women were excluded if they had any of the following conditions: personal history of adenomas, colorectal cancer, inflammatory bowel disease, or hereditary polyposis syndromes; rectal bleeding or hematochezia within 12 months before referral; iron-deficient anemia in the preceding 6 months; unintentional weight loss of greater than 10 pounds in the previous 6 months; or normal findings on colonoscopy or barium enema in the past 10 years or normal findings on flexible sigmoidoscopy in the past 5 years. The latter cutoffs were chosen because they correspond to the recommended time intervals for colorectal cancer screening among individuals aged 50 years or older who are at average risk for developing colorectal cancer. In addition, all participants had a blood-cell count, ferritin measurement, or fecal occult blood test completed within 6 months before referral. Among the 1483 women who met the eligibility criteria and participated in the study, we analyzed the 1420 subjects (95.8%) who had undergone complete colonoscopy to the cecum and had complete information on weight and height. Written informed consent was obtained from all study subjects. This study was approved by the institutional review board at each participating institution. Further details of the study have been reported previously [6, 7].

Identification of cases of colorectal adenoma and hyperplastic polyps

Over 99% of colonoscopic examinations were performed by gastroenterologists or colorectal surgeons. The anatomic location of all polyps was determined based on the depth of the colonoscope and anatomical landmarks. We defined proximal colorectal polyps as those located in the cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure; we defined distal colorectal polyps as those located in the descending colon and sigmoid colon. We classified rectal polyps separately.

The diameter of the polyps was estimated using a guidewire before polypectomy was performed. We classified small adenomas as those with a diameter <10mm and large adenomas as those with a diameter ≥10 mm. To classify hyperplastic polyps by size we used a cutoff of 5 mm. If multiple polyps were present, data were based on the largest. Histologic specimens from each polyp were reviewed by an expert gastrointestinal pathologist who was blinded to the initial pathological diagnosis made at colonoscopy. Adenomas were classified as tubular, villous, or mixed tubular-villous following standard criteria [8]. Grade of colorectal polyp was defined according to the most advanced histopathologic lesion. We defined advanced adenomas as those with a diameter of at least 10 mm, adenomas with villous component, or adenomas with high-grade dysplasia. Non-advanced adenomas were adenomas that did not meet those criteria. Women were considered as cases with multiple (≥ 2) polyps even if their polyps were detected in separate colorectal sites.

We assessed the relation of BMI to colorectal polyps according to four groups: cases with any adenomas; cases with adenomas after excluding those with hyperplastic polyps; cases with hyperplastic polyps only (which involved excluding those with adenomas); and cases with the combination of both types of polyps. Controls were defined as women with no adenomas or hyperplastic polyps.

Assessment of BMI

Before colonoscopy, women completed a detailed questionnaire regarding demographic, dietary, and lifestyle information, including current weight and height. Weight and height were used to calculate the BMI, which we divided into three categories that incorporated the definitions of normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2) and obesity (30 kg/m^2 or greater) proposed by the World Health Organization (WHO) [9].

Statistical analysis

We calculated means and standard errors for continuous data and proportions for categorical data. Logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI) for polyps, by tumor size, grade, multiplicity, and site. Analyses were adjusted for factors previously identified to be associated with colorectal adenomas in our dataset or associated with colorectal adenomas or colorectal cancer in the literature. Covariates were classified according to the following groups: age (5-year categories), study center (4 categories), race or ethnic group (White; Black; and Asian, Hispanic, and other combined), family history of colorectal cancer or colorectal polyps (yes or no), history of colonoscopy or barium enema in the previous 10 years (yes or no), history of flexible sigmoidoscopy in the previous 5 years (yes or no), smoking (never; former; current smoker of <20 cigarettes per day; and current smoker of ≥20 cigarettes per day), aspirin use (yes or no), menopausal status (yes or no), current menopausal hormone therapy (yes or no), physical activity (low; intermediate; high), and intakes of alcohol (grams/day; continuous), red meat grams/day; (continuous), and vitamin D (I.U./day; continuous). We conducted an alternative analysis using polytomous logistic regression. To evaluate whether any of the variables modified the BMI and adenoma association, we entered into the appropriate multivariate model the main effects terms for BMI and the covariate along with a term for their product, the coefficient

for which was evaluated using a Wald test. All reported p-values are two-tailed. The analyses were performed using SAS software release 8.2 (SAS Institute, Cary, NC).

Results

Of the 1,420 women in the current study, 953 (67.1%) had no polyps, and 292 (20.6%) were classified as having adenomas (regardless of hyperplastic polyp status), of which 217 (15.3%) had adenomas but no hyperplastic polyps. Further, 175 (12.3%) had hyperplastic polyps but no colorectal adenomas, and 75 (5.3%) were characterized as having the combination of colorectal adenomas and hyperplastic polyps.

We first evaluated selected characteristics of the women according to polyp status to assess the potential for confounding (Table 1). As compared with women with no polyps, women with polyps were older, they had a higher BMI, and they were more likely to previously or currently smoke. In contrast, women with polyps reported less frequent use of menopausal hormones than women with no polyps. Women with adenomas only reported less frequent aspirin use than women with hyperplastic polyps only or those with no polyps. In contrast, women with hyperplastic polyps only were more likely to previously or currently smoke and to consume alcohol than women with adenomas only or women with no polyps. Women with the combination of adenomas and hyperplastic polyps were more likely to have a family history of colorectal cancer and to have formerly smoked than women with no polyps.

We next examined the association between BMI and colorectal adenomas (Table 2). In age-adjusted and multivariate analyses, greater body mass was related to a statistically significant increase in adenoma risk. As compared with normal weight women, the multivariate ORs of adenomas for overweight and obese women were 1.36 (95% CI=0.99–1.88) and 1.57 (95% CI=1.07–2.29), respectively (P value, test for trend=0.02). Risk differed little according to whether adenomas were advanced or non-advanced. The positive association with body mass was strengthened when we used multiple adenomas as our endpoint (multivariate OR=2.27; 95% CI=1.17–4.41). Proximal adenomas also exhibited a strong positive relation with BMI (multivariate OR=1.85; 95% CI=1.15–2.97), whereas the association with distal adenomas was null (multivariate OR=1.09; 95% CI=0.54–2.23). There were an insufficient number of rectal adenomas to evaluate their relation with BMI.

We repeated our analysis of BMI in relation to colorectal adenomas after excluding cases of hyperplastic polyps (i.e. excluding cases with the combination of adenomas and hyperplastic polyps) (Table 3). As compared with normal weight women, the multivariate ORs for total adenomas in overweight and obese women were 1.17 (95% CI=0.82–1.68) and 1.25 (95% CI=0.81–1.93), respectively (P value, test for trend=0.24). The weak positive and statistically non-significant association with BMI was consistent for advanced and non-advanced adenomas, and the relation was slightly stronger for multiple adenomas and proximal adenomas. Overweight versus normal weight was related to an increased risk for distal adenomas and no further increase in risk for distal adenomas was observed for obesity. Numbers of cases with rectal adenomas were insufficient for examining their association with BMI.

We investigated the association between BMI and hyperplastic polyps only (Table 4). Risk of hyperplastic polyps rose sharply with increasing levels of BMI. As compared with normal weight women, the multivariate ORs of total hyperplastic polyps for overweight and obese women were 2.36 (95% CI=1.55–3.58) and 3.76 (95% CI=2.35–6.01), respectively (p value, test for trend<0.0001). A slightly stronger positive association with body mass was observed for small hyperplastic polyps (multivariate OR comparing obese with normal weight

women=4.07; 95% CI=2.37–6.99) than large hyperplastic polyps (multivariate OR=3.11; 95% CI=1.34–7.21), although confidence limits overlapped considerably. Proximal hyperplastic polyps (multivariate OR=3.59; 95% CI=1.42–9.12) appeared to show a similar association with BMI as distal hyperplastic polyps (multivariate OR=3.87; 95% CI=1.87–7.97).

We examined BMI in relation to the combination of adenomas and hyperplastic polyps (Table 5). Using normal weight women as the reference group, the multivariate ORs of the combination of colorectal adenomas and hyperplastic polyps for overweight and obese women were 2.19 (95% CI=1.18–4.07) and 2.84 (95% CI=1.41–5.72), respectively (P value, test for trend=0.02). Elevated risks were observed for numerous combinations of adenomas and hyperplastic polyps, but risk estimates lacked stability, as suggested by the wide confidence intervals.

We performed case-case comparisons using multinomial logistic regression to assess differences in the relation with adiposity between the case groups. As compared with adenoma-only cases, the multivariate ORs comparing overweight and obesity to normal weight women for cases with hyperplastic polyps were 2.11 (95% CI=1.26–3.55) and 2.94 (95% CI=1.61–5.36), respectively. The multivariate ORs comparing overweight and obesity to normal weight women for cases with both types of polyps as compared with adenoma-only cases were 2.31 (95% CI=1.14–4.68) and 2.09 (95% CI=0.92–4.77), respectively. When compared with hyperplastic polyp-only cases, cases with both types of polyps showed no association with adiposity, although statistical power was low and risk estimates were imprecise; the multivariate ORs comparing overweight and obesity to normal weight women were 0.76 (95% CI=0.35–1.64) and 0.71 (95% CI=0.29–1.73), respectively.

The relations of BMI to colorectal adenomas and hyperplastic polyps were not modified by age, race, family history of colorectal cancer, history of sigmoidoscopy, smoking, aspirin use, physical activity, or menopausal hormone therapy (data not shown).

Discussion

In this cross-sectional study of asymptomatic women enrolled for complete screening colonoscopy, we found a statistically significant positive relation between BMI and the prevalence of colorectal adenomas. The positive association between BMI and adenomas was consistent for advanced and non-advanced lesions and it was more pronounced for multiple than individual adenomas and was more apparent for proximal than distal adenomas. The positive relation between BMI and colorectal adenomas was attenuated and became statistically non-significant after we repeated our analysis after excluding the subset of adenoma cases that also had hyperplastic polyps (i.e. those with a combination of adenomas and hyperplastic polyps). We also noted a strong positive association between BMI and the prevalence of hyperplastic polyps. In addition, BMI was positively linked to the combination of colorectal adenomas and hyperplastic polyps. Taken together, our results suggest that adiposity plays an important role in the development of both colorectal adenomas and hyperplastic polyps.

Our findings regarding BMI and colorectal adenomas are in agreement with those from abundant studies [10–36] that found a positive relation of BMI to colorectal adenomas. However, evidence has not been entirely consistent, with many previous studies [37–50] reporting no statistically significant association between the two. Our observation of a markedly stronger relation of BMI to the combination of colorectal adenomas and hyperplastic polyps than to colorectal adenomas alone suggests that some of the

heterogeneity in previous studies of BMI and colorectal adenomas may be due to a potentially unaccounted for positive association between BMI and hyperplastic polyps.

Variation in results from previous studies of BMI and colorectal adenomas may also be explained by differences with respect to the endpoints considered. Evidence regarding adiposity in relation to adenoma size or degree of dyplasia shows that about half [10, 12, 15, 18, 22, 23, 27, 31, 34, 35, 39] of available investigations found a stronger positive association between BMI and large or advanced adenomas (typically defined as those with ≥10 mm diameter, villous elements, or high-grade dysplasia) than non-advanced or total adenomas. However, the findings from our and numerous other studies [14, 16, 17, 25, 28, 32, 33, 37, 42, 48] suggest no major difference between the relation of BMI to advanced adenomas to that with non-advanced or total adenomas.

We found a positive relation of BMI to proximal adenomas but no association with distal adenomas, confirming results from one study [31] that reported a stronger relation of BMI to adenomas of the proximal than distal colon. In addition, several sigmoidoscopy studies [10, 23, 34] found a positive association between BMI and adenomas of the distal colon and a weaker [23] or no association [10, 34] between BMI and adenomas of the rectum. In contrast, three previous investigations [25, 28, 42] reported similar relations of BMI to adenomas of the proximal and those of the distal colon. Additional studies with complete colonoscopy and large sample sizes are required to further clarify whether adiposity differentially affects the development of proximal versus distal colorectal adenomas.

We observed a strong positive relation of BMI to hyperplastic polyps. The positive association between BMI and hyperplastic polyps did not vary appreciably according to polyp size or anatomic location, but the relation with BMI was stronger when we considered multiple hyperplastic polyps as an endpoint. Very few studies have evaluated the relation of BMI to hyperplastic polyps, and results tend to be mixed. One study [51] reported an OR of 4.50 (95% CI=1.84–10.97) for hyperplastic polyps comparing extreme BMI quartiles. Another study [30] found no association of BMI to hyperplastic polyps among women but noted a borderline positive relation among men (OR=1.7; 95% CI=0.9–3.4; p for trend=0.04) comparing extreme BMI categories. That study [30], similar to our study of women, reported a marked positive relation of BMI to the combination of adenomas and hyperplastic polyps among men (OR=2.9; 95% CI=1.2–5.6; p for trend=0.02). Three studies [20, 30, 42] compared the relation of BMI to hyperplastic polyps to that with adenomas, one [42] of which noted a similarly null relation of BMI to hyperplastic and adenomatous polyps, the second [30] of which reported a similarly positive association of BMI to hyperplastic and adenomatous polyps, and the third [20] of which found a weaker relation of BMI to hyperplastic polyps than to adenomas.

If BMI is indeed positively related to hyperplastic polyps, the question arises as to the potential metabolic pathways through which increased body mass may favor the development of hyperplastic polyps. Data regarding this issue are very limited. One study found that circulating levels of insulin-like growth factor (IGF)-1 and insulin were positively correlated with the number of hyperplastic polyps in patients with acromegaly [52]. Hyperplastic polyps have generally been considered to be innocuous lesions. However, evidence [53] suggests that hyperplastic polyps, particularly large hyperplastic polyps, bear the potential for dysplasia and malignant potential. Perceivably, BMI may enhance colorectal cancer risk via the development of multiple hyperplastic polyps through biologic mechanisms that involve increased levels of insulin-like growth factors and insulin. In addition, hyperplastic polyps may give rise to serrated polyps and colorectal cancer by causing BRAF mutations associated with microsatellite instability [54].

Our study has numerous important strengths. The study population comprised asymptomatic women enrolled for complete screening colonoscopy, which helped avoid misclassification of non-cases who may have had a greater prevalence of asymptomatic polyps. A particular strength was the specific focus on both adenomatous and hyperplastic polyps, enabling us to compare distinct polyp types drawn from the same underlying population and examined using the same methodology. A standardized pathology review ensured comprehensive ascertainment of polyp type, which allowed us to isolate those presenting with both kinds of polyps as a distinct group. The validity of self-reported height and weight in our study should not represent a major concern because self-reported height and weight are known to be highly accurate, with correlation coefficients between self-reported and measured height and weight typically greater than 0.9 [55]. In addition, we used information on height and weight collected prior to colonoscopy to circumvent recall bias. The availability of information on a broad range of potential confounding variables minimized potential confounding.

Our study also had some limitations. The sample size was modest, which did not allow us to examine relations with great statistical power, especially in our analyses stratified by adenoma stage, multiplicity, and location. Thus, findings from our subgroup analyses should be interpreted with caution. We lacked data on serrated adenomas and we were not able to identify a sufficient number of subjects who fit the criteria for hyperplastic polyposis. Our study lacked data on central or visceral adiposity, such as waist circumference or waist-hip ratio. Observational studies that have examined BMI in relation to colorectal cancer have tended to find stronger positive associations among men than women [56]. One reason for such differences is that using BMI as a measure of adiposity may not reflect central or visceral adiposity in women.

Because participants in our study represented women who consented to participate in a colonoscopy study, our findings may not apply to the general population. Our results also may not extend to premenopausal women because the majority of participants in our study were postmenopausal. We cannot exclude the possibility that our results were affected by residual confounding by smoking or diet since those variables are measured with imprecision. A potential limitation of cross-sectional studies is determining the temporal sequence of events, but this is a minor issue in our study because it is unlikely that adenomas or hyperplastic polyps preceded or caused adiposity among women in our sample. We assessed BMI only once at the time of diagnosis, which may not have reflected BMI during the etiologically relevant time period of exposure with respect to the development of adenomas.

In summary, in this study of complete colonoscopy among asymptomatic U.S. women, BMI was positively related both to colorectal adenomas and hyperplastic polyps. A notably strong apparent adverse effect of adiposity was evident among women with both kinds of polyps. Future epidemiologic investigations should continue to identify risk factors that distinguish colorectal adenomas from hyperplastic polyps. Such work may help further elucidate the possible causes of colorectal cancer.

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Table 1

Selected characteristics of women overall and women according to the presence or absence of colorectal adenomas and hyperplastic polyps

Variable	All women (n=1,420)	Women without polyps (n=953)	Women with any colorectal adenomas (n=292)	Women with colorectal adenomas only (n=217)	Women with hyperplastic polyps only (n=175)	Women with the combination of colorectal adenomas and hyperplastic polyps (n=75)
Age (years)	58.3	57.5	60.7	61.1	58.5	59.6
Race or ethnic group (%)						
White	77.2	76.4	73.9	73.7	86.9	74.7
Black	11.7	11.2	13.7	13.4	10.9	14.7
Asian	8.3	9.0	10.3	11.1	1.1	8.0
Hispanic	1.9	2.1	1.7	1.4	1.1	2.6
Other	0.9	1.3	0.3	0.5	0	0
Family history of colorectal cancer (%)	16.6	15.7	20.2	16.1	14.9	32.0
Body mass index (kg/m^2)	26.5	26.1	26.9	26.6	28.2	28.0
Physical activity (MET-hours/week)	45.4	45.4	45.5	46.1	44.8	43.6
Regular aspirin use (%)	31.6	34.5	30.5	30.4	38.3	30.7
Postmenopausal (%)	87.3	86.6	90.4	90.3	86.3	90.7
Menopausal hormone therapy (%)	63.2	66.2	58.2	58.9	55.4	56.0
Current smoker (%)	34.8	32.4	37.3	37.3	43.4	37.3
Past smoker (%)	4.4	3.3	6.5	4.6	7.4	12.0
Dietary intakes						
Total energy (kcal/day)	1546	1549	1482	1482	1632	1483
Alcohol (grams/day)	6.6	6.2	5.7	6.3	10.3	4.1
Red meat (grams/day)	26.5	26.5	28.2	27.3	23.5	30.6
Vitamin D (I.U./day)	223.5	222.1	220.2	240.5	237.5	163.7

Table 2

Relation of body mass index to any colorectal adenomas (regardless of hyperplastic polyp status)

Variable	Body mass index (kg/m^2)			P for trend
	≤24.9	25.0–29.9	≥30.0	
Total adenomas				
No. of cases/controls	120/477	103/295	69/181	
Age-adjusted OR (95% CI)	1.0	1.37 (1.01–1.87)	1.49 (1.05–2.12)	0.03
Multivariate-adjusted OR (95% CI)	1.0	1.36 (0.99–1.88)	1.57 (1.07–2.29)	0.02
Nonadvanced adenomas				
No. of cases/controls	94/477	74/295	52/181	
Age-adjusted OR (95% CI)	1.0	1.27 (0.89–1.79)	1.45 (0.99–2.14)	0.12
Multivariate-adjusted OR (95% CI)	1.0	1.29 (0.90–1.84)	1.57 (1.03–2.34)	0.09
Advanced adenomas				
No. of cases/controls	26/477	29/295	17/181	
Age-adjusted OR (95% CI)	1.0	1.74 (0.99–3.06)	1.68 (0.87–3.24)	0.03
Multivariate-adjusted OR (95% CI)	1.0	1.49 (0.82–2.76)	1.52 (0.73–3.16)	0.06
Multiple adenomas				
No. of cases/controls	25/477	37/295	23/181	
Age-adjusted OR (95% CI)	1.0	2.33 (1.36–3.99)	2.37 (1.29–4.35)	0.002
Multivariate-adjusted OR (95% CI)	1.0	2.18 (1.23–3.87)	2.27 (1.17–4.41)	0.007
Proximal adenomas only				
No. of cases/controls	60/477	53/295	45/181	
Age-adjusted OR (95% CI)	1.0	1.41 (0.94–2.11)	1.93 (1.25–2.99)	0.007
Multivariate-adjusted OR (95% CI)	1.0	1.34 (0.87–2.04)	1.85 (1.15–2.97)	0.02
Distal adenomas only				
No. of cases/controls	39/477	36/295	13/181	
Age-adjusted OR (95% CI)	1.0	1.47 (0.91–2.37)	0.86 (0.45–1.66)	0.74
Multivariate-adjusted OR (95% CI)	1.0	1.70 (1.03–2.83)	1.09 (0.54–2.23)	0.71
Rectal adenomas only				
No. of cases/controls	11/477	2/295	1/181	
Age-adjusted OR (95% CI)	1.0	0.28 (0.06–1.26)	0.23 (0.03–1.84)	0.24
Multivariate-adjusted OR (95% CI)	1.0	0.19 (0.03–1.06)	0.14 (0.01–1.41)	0.19

Multivariate-adjusted models included age (5-year categories), study center (4 categories), race or ethnic group (White; Black; and Asian, Hispanic, and other combined), family history of colorectal cancer or colorectal polyp (yes or no), history of colonoscopy or barium enema in the previous 10 years (yes or no), history of flexible sigmoidoscopy in the previous 5 years (yes or no), smoking (never; former; current smoker of <20 cigarettes per day; and current smoker of ≥20 cigarettes per day), aspirin use (yes or no), menopausal status (yes or no), current menopausal hormone therapy (yes or no), physical activity (low; intermediate; high), and intakes of alcohol (grams/day; continuous), red meat (grams/day; continuous), and vitamin D (I.U./day; continuous).

Table 3

Relation of body mass index to colorectal adenomas only (excluding cases of hyperplastic polyps)

Variable	Body mass index (kg/m^2)			P for Trend
	≤24.9	25.0–29.9	≥30.0	
Total adenomas				
No. of cases/controls	99/477	72/295	46/181	
Age-adjusted OR (95% CI)	1.0	1.17 (0.83–1.65)	1.19 (0.79–1.78)	0.32
Multivariate-adjusted OR (95% CI)	1.0	1.17 (0.82–1.68)	1.25 (0.81–1.93)	0.24
Nonadvanced adenomas				
No. of cases/controls	77/477	57/295	34/181	
Age-adjusted OR (95% CI)	1.0	1.18 (0.81–1.73)	1.14 (0.73–1.78)	0.61
Multivariate-adjusted OR (95% CI)	1.0	1.25 (0.84–1.85)	1.24 (0.77–2.02)	0.44
Advanced adenomas				
No. of cases/controls	22/477	15/295	12/181	
Age-adjusted OR (95% CI)	1.0	1.08 (0.54–2.15)	1.45 (0.69–3.05)	0.16
Multivariate-adjusted OR (95% CI)	1.0	0.92 (0.44–1.90)	1.25 (0.54–2.89)	0.25
Multiple adenomas				
No. of cases/controls	23/477	23/295	14/181	
Age-adjusted OR (95% CI)	1.0	1.56 (0.85–2.85)	1.55 (0.77–3.12)	0.08
Multivariate-adjusted OR (95% CI)	1.0	1.43 (0.75–2.71)	1.39 (0.65–2.99)	0.16
Proximal adenomas only				
No. of cases/controls	52/477	38/295	28/181	
Age-adjusted OR (95% CI)	1.0	1.17 (0.74–1.83)	1.38 (0.83–2.27)	0.37
Multivariate-adjusted OR (95% CI)	1.0	1.13 (0.69–1.82)	1.36 (0.78–2.36)	0.43
Distal adenomas only				
No. of cases/controls	28/477	29/295	11/181	
Age-adjusted OR (95% CI)	1.0	1.62 (0.94–2.79)	0.99 (0.48–2.05)	0.92
Multivariate-adjusted OR (95% CI)	1.0	2.03 (1.14–3.62)	1.30 (0.59–2.87)	0.45
Rectal adenomas only				
No. of cases/controls	10/477	1/295	1/181	
Age-adjusted OR (95% CI)	1.0	0.15 (0.02–1.20)	0.26 (0.03–2.08)	0.33
Multivariate-adjusted OR (95% CI)	1.0	0.08 (0.01–0.80)	0.10 (0.01–1.26)	0.19

Multivariate-adjusted models included age (5-year categories), study center (4 categories), race or ethnic group (White; Black; and Asian, Hispanic, and other combined), family history of colorectal cancer or colorectal polyp (yes or no), history of colonoscopy or barium enema in the previous 10 years (yes or no), history of flexible sigmoidoscopy in the previous 5 years (yes or no), smoking (never; former; current smoker of <20 cigarettes per day; and current smoker of ≥20 cigarettes per day), aspirin use (yes or no), menopausal status (yes or no), current menopausal hormone therapy (yes or no), physical activity (low; intermediate; high), and intakes of alcohol (grams/day; continuous), red meat (grams/day; continuous), and vitamin D (I.U./day; continuous).

Table 4

Relation of body mass index to hyperplastic polyps only (excluding cases of colorectal adenomas)

Variable	Body mass index (kg/m^2)			P for trend
	≤24.9	25.0–29.9	≥30.0	
Total hyperplastic polyps				
No. of cases/controls	52/477	68/295	55/181	
Age-adjusted OR (95% CI)	1.0	2.13 (1.44–3.16)	2.82 (1.85–4.30)	<0.0001
Multivariate-adjusted OR (95% CI)	1.0	2.36 (1.55–3.58)	3.76 (2.35–6.01)	<0.0001
Small hyperplastic polyps				
No. of cases/controls	36/477	50/295	40/181	
Age-adjusted OR (95% CI)	1.0	2.26 (1.43–3.56)	2.94 (1.81–4.79)	<0.0001
Multivariate-adjusted OR (95% CI)	1.0	2.56 (1.58–4.14)	4.07 (2.37–6.99)	<0.0001
Large hyperplastic polyps				
No. of cases/controls	16/477	18/295	15/181	
Age-adjusted OR (95% CI)	1.0	1.79 (0.89–3.60)	2.48 (1.19–5.18)	0.04
Multivariate-adjusted OR (95% CI)	1.0	1.73 (0.80–3.73)	3.11 (1.34–7.21)	0.03
Multiple hyperplastic polyps				
No. of cases/controls	11/477	31/295	24/181	
Age-adjusted OR (95% CI)	1.0	4.62 (2.27–9.38)	5.74 (2.73–12.1)	<0.0001
Multivariate-adjusted OR (95% CI)	1.0	5.06 (2.34–10.94)	8.88 (3.87–20.39)	<0.0001
Proximal hyperplastic polyps only				
No. of cases/controls	15/477	15/295	11/181	
Age-adjusted OR (95% CI)	1.0	1.57 (0.75–3.28)	1.84 (0.82–4.13)	0.46
Multivariate-adjusted OR (95% CI)	1.0	2.19 (0.98–4.90)	3.59 (1.42–9.12)	0.05
Distal hyperplastic polyps only				
No. of cases/controls	18/477	31/295	20/181	
Age-adjusted OR (95% CI)	1.0	2.83 (1.55–5.16)	2.95 (1.52–5.73)	0.0005
Multivariate-adjusted OR (95% CI)	1.0	2.98 (1.57–5.64)	3.87 (1.87–7.97)	0.0001
Rectal hyperplastic polyps only				
No. of cases/controls	15/477	11/295	16/181	
Age-adjusted OR (95% CI)	1.0	1.19 (0.54–2.65)	2.95 (1.42–6.16)	0.01
Multivariate-adjusted OR (95% CI)	1.0	1.04 (0.44–2.44)	2.83 (1.22–6.56)	0.03

Multivariate-adjusted models included age (5-year categories), study center (4 categories), race or ethnic group (White; Black; and Asian, Hispanic, and other combined), family history of colorectal cancer or colorectal polyp (yes or no), history of colonoscopy or barium enema in the previous 10 years (yes or no), history of flexible sigmoidoscopy in the previous 5 years (yes or no), smoking (never; former; current smoker of <20 cigarettes per day; and current smoker of ≥20 cigarettes per day), aspirin use (yes or no), menopausal status (yes or no), current menopausal hormone therapy (yes or no), physical activity (low; intermediate; high), and intakes of alcohol (grams/day; continuous), red meat (grams/day; continuous), and vitamin D (I.U./day; continuous).

Table 5

Relation of body mass index to the presence of both colorectal adenomas and hyperplastic polyps

Variable	Body mass index (kg/m^2)			P for trend
	≤24.9	25.0–29.9	≥30.0	
Total adenomas and hyperplastic polyps				
No. of cases/controls	21/477	31/295	23/181	
Age-adjusted OR (95% CI)	1.0	2.35 (1.31–4.19)	2.88 (1.54–5.39)	0.004
Multivariate-adjusted OR (95% CI)	1.0	2.19 (1.18–4.07)	2.84 (1.41–5.72)	0.02
Nonadvanced adenomas and any hyperplastic polyp				
No. of cases/controls	17/477	17/295	18/181	
Age-adjusted OR (95% CI)	1.0	1.64 (0.82–3.27)	2.85 (1.42–5.69)	0.02
Multivariate-adjusted OR (95% CI)	1.0	1.52 (0.73–3.16)	2.73 (1.25–5.94)	0.08
Advanced adenomas and any hyperplastic polyp				
No. of cases/controls	4/477	14/295	5/181	
Age-adjusted OR (95% CI)	1.0	5.38 (1.73–16.71)	3.09 (0.81–11.90)	0.08
Multivariate-adjusted OR (95% CI)	1.0	5.58 (1.56–19.95)	3.34 (0.74–15.04)	0.14
Proximal adenomas only and any hyperplastic polyp				
No. of cases/controls	8/477	15/295	17/181	
Age-adjusted OR (95% CI)	1.0	3.00 (1.25–7.21)	5.45 (2.29–12.98)	<0.0001
Multivariate-adjusted OR (95% CI)	1.0	2.80 (1.13–6.96)	4.63 (1.81–11.83)	0.003
Distal/rectal adenomas only and any hyperplastic polyp				
No. of cases/controls	12/477	8/295	2/181	
Age-adjusted OR (95% CI)	1.0	1.09 (0.44–2.71)	0.45 (0.10–2.06)	0.28
Multivariate-adjusted OR (95% CI)	1.0	1.14 (0.39–3.33)	0.37 (0.06–2.45)	0.27
Small hyperplastic polyps and any adenoma				
No. of cases/controls	16/477	17/295	15/181	
Age-adjusted OR (95% CI)	1.0	1.73 (0.86–3.49)	2.47 (1.19–5.16)	0.01
Multivariate-adjusted OR (95% CI)	1.0	1.72 (0.81–3.67)	2.92 (1.27–6.69)	0.01
Large hyperplastic polyps and any adenoma				
No. of cases/controls	5/477	14/295	8/181	
Age-adjusted OR (95% CI)	1.0	4.38 (1.55–12.41)	4.16 (1.32–13.09)	0.12
Multivariate-adjusted OR (95% CI)	1.0	4.68 (1.49–14.74)	4.52 (1.27–16.10)	0.32
Proximal hyperplastic polyps only and any adenoma				
No. of cases/controls	7/477	7/295	6/181	
Age-adjusted OR (95% CI)	1.0	1.53 (0.53–4.45)	2.08 (0.68–6.37)	0.51
Multivariate-adjusted OR (95% CI)	1.0	1.17 (0.37–3.72)	1.59 (0.45–5.64)	0.89
Distal/rectal hyperplastic polyps only and any adenoma				
No. of cases/controls	10/477	20/295	12/181	
Age-adjusted OR (95% CI)	1.0	3.31 (1.52–7.23)	3.31 (1.39–7.89)	0.005
Multivariate-adjusted OR (95% CI)	1.0	3.36 (1.46–7.71)	3.66 (1.40–9.58)	0.005

Multivariate-adjusted models included age (5-year categories), study center (4 categories), race or ethnic group (White; Black; and Asian, Hispanic, and other combined), family history of colorectal cancer or colorectal polyp (yes or no), history of colonoscopy or barium enema in the previous 10

years (yes or no), history of flexible sigmoidoscopy in the previous 5 years (yes or no), smoking (never; former; current smoker of <20 cigarettes per day; and current smoker of ≥20 cigarettes per day), aspirin use (yes or no), menopausal status (yes or no), current menopausal hormone therapy (yes or no), physical activity (low; intermediate; high), and intakes of alcohol (grams/day; continuous), red meat (grams/day; continuous), and vitamin D (I.U./day; continuous).