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Obesity Increases the Risks of Diverticulitis and Diverticular Bleeding

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Abstract

Background and Aims—Studies of obesity and diverticular complications are limited. We assessed the relationship between Body Mass Index (BMI), waist circumference and waist-to-hip ratios and diverticulitis and diverticular bleeding.

Methods—A prospective cohort study was performed of 47,228 male health professionals (40–75 years old) that were free of diverticular disease in 1986 (baseline). Men reporting newly diagnosed diverticular disease on biennial follow-up questionnaires were sent supplemental questionnaires. Weight was recorded every 2 years and waist and hip circumferences were collected in 1987.

Results—We documented 801 incident cases of diverticulitis and 383 incident cases of diverticular bleeding during 18 years of follow-up. After adjustment for other risk factors, men with a BMI ≥30 kg/m^2 had a relative risk (RR) of 1.78 (95% confidence interval [CI], 1.08–2.94) for diverticulitis and 3.19 (95% CI, 1.45–7.00) for diverticular bleeding, compared to men with a BMI of <21 kg/m^2. Men in the highest quintile of waist circumference, compared with those in the lowest, had a multivariable RR of 1.56 (95% CI, 1.18–2.07) for diverticulitis and 1.96 (95% CI, 1.30–2.97) for diverticular bleeding. Waist-to-hip ratio was also associated with the risk of diverticular complications, when the highest and lowest quintiles were compared: multivariable RR 1.62 (95% CI; 1.23–2.14) for diverticulitis and multivariable RR 1.91 (95% CI; 1.26–2.90) for diverticular bleeding. Adjustment for BMI did not change the associations seen for waist-to-hip ratio.

Conclusions—In this large prospective cohort, BMI, waist circumference and waist-to-hip ratio significantly increased the risks of diverticulitis and diverticular bleeding.

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INTRODUCTION

Diverticular disease is a common gastrointestinal indication for hospital admission and outpatient clinic visits.[1, 2] It is estimated that 65% of adults will develop diverticulosis by 80 years of age, and10–30% of individuals with diverticulosis will suffer from complications including diverticulitis and diverticular bleeding. [3, 4]

Dietary fiber deficiency is regarded as a major risk factor for the development of diverticular disease. Indeed, the prevalence of diverticulosis rose dramatically following the introduction of refined cereal grains.[5] However, other dietary and lifestyle changes potentially related to diverticular disease parallel the adoption of a low-fiber diet including obesity.

Obesity is increasingly recognized as a risk factor for disease.[6] A number of digestive diseases have been associated with obesity including cirrhosis, gallstone disease, gastroesophageal reflux disease, cancers of the colon, esophagus and pancreas.[7–9] Some of the obesity-related mechanisms thought to play a role in these disorders may also influence diverticular complications, most notably the link between obesity and chronic inflammation.[10] In addition, recently discovered differences in the intestinal flora of obese individuals may be relevant to diverticular disease.[11, 12]

Several retrospective case series and a small case-control study have noted a preponderance of obesity in patients with diverticulitis, particularly patients younger than 40 years of age,[14–19] but could not directly examined the association with obesity. Two prospective cohort studies, a prior analysis of the first 6 years of the Health Professionals Follow-up Study and a Swedish male cohort, found positive associations between body mass index (BMI) and symptomatic diverticular disease (diverticulitis, diverticular bleeding or nonspecific pain or bowel symptoms in the setting of diverticulosis).[20, 21] However, these studies were underpowered to examine diverticulitis, diverticular bleeding and nonspecific symptoms as distinct clinical outcomes, although the pathophysiology of these complications and thus the effects of obesity are presumably quite different.[22] In addition, in the Swedish study, important potential confounders including diet were not evaluated.[21] Previous studies have not considered other measures of central obesity which are particularly important in other gastrointestinal diseases.[7, 23, 24] We prospectively examined the associations between BMI, waist circumference and waist-to-hip ratio and the risk of diverticulitis and diverticular bleeding using 18 years of follow-up data from a prospective cohort of male health professionals.

MATERIALS and METHODS

Study Population

The study cohort consisted of 51,529 male dentists, veterinarians, pharmacists, optometrists, osteopathic physicians and podiatrists who have been prospectively followed as part of the Health Professionals Follow-up Study. At baseline in 1986, participants were between the ages of 40–75 years, and returned detailed questionnaires concerning diet, lifestyle and medical history. Medical information has been updated biennially and dietary information every 4 years via self-administered questionnaires. The study was approved by the institutional review boards of the Harvard School of Public Health and Brigham and Women's Hospital.

We excluded from the analysis men who reported at baseline a diagnosis of diverticulosis, diverticulitis or diverticular bleeding, cancer (except non-melanoma skin cancer), or inflammatory bowel disease. In addition, men with average daily intakes outside the range of 800 – 4,300 kcal, and men who failed to return the food frequency questionnaire were excluded.

The remaining baseline population included 47,228 men who were followed from 1986 to 2004.

Assessment of Diverticulitis and Diverticular Bleeding

The primary study endpoints were incident diverticulitis and diverticular bleeding. Biennial follow-up questionnaires inquired about newly diagnosed diverticulosis or diverticulitis beginning in 1990. Participants reporting diverticular disease were sent a 5-question supplemental questionnaire addressing: 1) Date of diagnosis; 2) Procedures done to confirm the diagnosis; 3) Symptoms or tests leading to the detection of diverticular disease; 4) Diet modification prior to the diagnosis; and 5) Treatment received. Trained abstractors entered data including information contained in free text.

Individuals who reported a new diagnosis of diverticular disease were classified as having diverticulitis if they reported abdominal pain attributed to diverticular disease and one of the following: 1) Complications of fistula, abscess, perforation or obstruction; 2) Treated with antibiotics, hospitalization, or surgery; 3) Categorized as severe or acute; presenting with fever, requiring medication, or evaluated with computed tomography. Diverticular bleeding was defined as rectal bleeding attributed to diverticular disease and one of the following: 1) Requiring hospitalization, intravenous fluids, blood transfusions, angiography, nuclear medicine scanning or surgery; 2) Described as profuse bleeding; or 3) Without other potential gastrointestinal, rectal or anal sources in men whose bleeding was not evaluated as part of a routine endoscopy or barium enema. The first 2 criteria for each endpoint definition were used in sensitivity analyses for the endpoint definitions.

To address the accuracy of self-report, 179 available medical records from men reporting diverticular disease on the 1990 and 1992 main study questionnaires were reviewed. Diverticular disease was confirmed in 97%. The overall concordance between the diagnosis in the medical record and the self-reported diagnosis based on our outcome definitions was 85%. In the remaining cases, 50% had a diagnosis of diverticulitis or diverticular bleeding on chart review, but were classified as uncomplicated disease based on self-report. The breakdown of self-reported diagnoses and the concordance with chart review was: 91 cases of uncomplicated diverticulosis (51%) with 86% concordance; 77 cases of diverticulitis (43%) with 84% concordance, and 11 cases of diverticular bleeding (6%) with 73% concordance.

Assessment of Anthropometric Measures

Body mass index was calculated as weight (kg)/height squared (m). Body weight was updated biennially, and height was reported at baseline. In addition, participants reported their weight at age 21 years on the baseline questionnaire. Waist and hip measurements were self-ascertained in 1987 and 1996. Illustrated instructions guided measurements of the waist at the level of the umbilicus, and of the hips at the largest circumference while standing in close-fitting clothing. In a prior validation study, the correlation coefficients between the average of 2 technician measurements and self-reported measurements were 0.97 for weight, 0.95 for waist circumference, 0.88 for hip circumference.[25]

Assessment of Other Potential Risk Factors

Dietary fiber, fat and red meat, physical activity and usage of non-steroidal anti-inflammatory drugs and acetaminophen were also entertained as potential confounders. These have been shown to be risk factors for diverticular complications in this cohort and/or in other studies.[20, 26–31] Nutritional information was assessed every 4 years from a food frequency questionnaire. Physical activity was assessed on biennial questionnaires, and expressed in metabolic equivalents (MET) hours per week. Current, regular use of non-steroidal anti-inflammatory analgesics including aspirin, and acetaminophen was assessed every 2 years.

The validity and reproducibility of the dietary questionnaires and physical activity assessment have been demonstrated previously.[32, 33]

Statistical Analysis

We calculated person-years of follow-up from the date of return of the baseline questionnaire in 1986 to the date of the first diagnosis of diverticulosis or diverticular complications, the date of death, or December 31, 2004, whichever came first. Men who reported a new diagnosis of gastrointestinal cancer, diverticulosis, diverticulitis, diverticular bleeding, or inflammatory bowel disease were censored at the date of diagnosis. Information about potential risk factors including body weight and size was obtained prior to the diagnosis of diverticular disease.

We divided BMI into 6 categories that encompass commonly used criteria for overweight and obesity.[34] Body mass index at age 21 was grouped in quintiles ranging from BMI < 21 kg/m^2 to BMI ≥25 kg/m^2 due to the smaller number of men with large values of BMI at this age. Six categories of weight change since age 21 years were created (< 5 pounds, 5–14.9 pounds, 15–24.9 pounds, 25–34.9 pounds, 35–44.9 pounds, >45 pounds). Quintiles were used to categorize waist circumference, and waist-to-hip ratio. Variables were created for missing values of waist circumference and waist-to-hip ratio.

Relative risks (RR) and corresponding 95% confidence intervals (CI) were calculated for each endpoint using Cox proportional hazards models stratified by age in 1-year intervals and study period in 2-year intervals.[35] Men in the highest categories of each anthropometric measurement were compared to men in the lowest category. Multivariable RRs were calculated by simultaneously adjusting for other known or potential risk factors for diverticular disease including total dietary fat (quintiles) and total dietary fiber (quintiles), red meat (quintiles), total caloric intake (quintiles), physical activity (quintiles) and current usage of non-steroidal anti-inflammatory medications (yes/no) and acetaminophen (yes/no).[20, 26–31] In addition, in the multivariable analyses of waist circumference we adjusted for height in inches (<66, 66–67.9, 68–69.9, 70–71.9, ≥72 inches) to control for variation in waist due to body size.

In the analyses, the most recent information available for each variable was utilized. We updated BMI, physical activity and medication usage biennially. Dietary covariates were updated every 4 years. Waist and hip measurements from 1987 were used in the analysis. For example, if a patient reported a study endpoint in 1989, data from the 1988 questionnaire would be used for BMI, physical activity and medications and from the 1986 questionnaire for diet.

We performed several secondary analyses. We restricted the main analyses to participants who had undergone a flexible sigmoidoscopy or colonoscopy in order to assess the possibility of detection bias. We also performed a sensitivity analysis for each endpoint by restricting the analysis to men meeting either of the first 2 endpoint criteria. For diverticulitis these included abscess, fistula, perforation, obstruction, hospitalization, surgery or antibiotics, and for diverticular bleeding men reporting profuse bleeding or bleeding requiring hospitalization, intravenous fluids, blood transfusions, angiography, nuclear medicine scanning or surgery. Lastly, we investigated the relationship between body weight and asymptomatic diverticulosis. These analyses were limited to men who had undergone lower endoscopy due to the potential for detection bias with asymptomatic disease.

Tests for linear trend were performed by treating the median value of each of the measurement categories as a continuous variable. We tested the proportional hazards assumption for each anthropometric variable by creating interaction terms between the participant age and study period and the measurements. There were no significant violations (all p values >0.05). All analyses were two-sided, and a p value of less than 0.05 was considered statistically significant. We used SAS software, version 9.1 (SAS Institute Inc., Cary, North Carolina) for the analyses.

RESULTS

During 730,446 person years of follow-up, we identified 801 incident cases of diverticulitis, and 383 incident cases of diverticular bleeding. At baseline, 3.7% of men had a BMI less than 21 kg/m2, 29.8% a BMI between 23 and 25 kg/m^2, and 8.1% a BMI of at least 30 kg/m^2. The associations between baseline characteristics and BMI, waist circumference and waist-to-hip ratio were similar (Table 1). Men with elevated BMI, waist circumferences and/or waist-to-hip ratio were on average more likely to be sedentary, to use analgesics, and to consume fat and red meat. Age did not differ across BMI categories; but men with a small waist circumference and/or low waist-to-hip ratio were generally younger than those with larger measurements.

We observed a positive association between BMI and the risk of both incident diverticulitis and diverticular bleeding (Table 2). In the adjusted analysis, men with a BMI ≥30 kg/m^2 had a 78 % increased risk of diverticulitis when compared to men with a BMI of < 21 kg/m^2. The effect of BMI was even stronger for diverticular bleeding. Men with a BMI ≥30 kg/m^2 were more than three times as likely to develop bleeding relative to those with a BMI of < 21 kg/m^2. In a 10 year period, 14.7 cases of diverticulitis and 8.2 cases of diverticular bleeding would be expected to occur per 1,000 obese men (BMI ≥30 kg/m^2) compared to 6.6 cases of diverticulitis and 2.6 cases of diverticular bleeding in 1,000 lean men (BMI of < 21 kg/m^2). The multivariable relative risks were similar after limiting the analysis of BMI to men who had undergone lower endoscopies (RR, 1.70; 95% Confidence Interval (CI), 0.89–3.25; P for trend 0.02 for diverticulitis, and RR, 2.7; 95% CI, 1.09–7.16; P for trend 0.0008 for bleeding). The magnitude of the associations between BMI and diverticular outcomes was strengthened when the analyses were limited to men meeting the strictest outcome criteria (multivariable RR, 2.08; 95% CI, 0.81–5.34; P for trend 0.07 for diverticulitis (n=235), and multivariable RR, 4.87; 95% CI, 0.62–38.4; P for trend 0.17 for bleeding (n=70)). We did not find a significant association between BMI and asymptomatic diverticulosis (n-1,721) in a highest vs. lowest category comparison (multivariable RR, 1.16; 95% CI, 0.79–1.69; P for trend 0.80, respectively).

To assess the relationship between body weight in early adulthood and diverticular complications, we analyzed BMI at age 21 years. Body mass index at age 21 years was not significantly associated with diverticulitis or diverticular bleeding in the multivariable analyses. The effect of current BMI on the risk of both diverticular outcomes remained unchanged after adjustment for BMI at age 21 years.

We also explored the relationship between weight gain and incident diverticular complications, and again found positive associations. After controlling for weight at age 21 years in addition to other known or potential risk factors, men who gained more than 45 pounds since age 21 years had a relative risk of 1.66 (95% CI, 1.28–2.16; P for trend 0.003) for diverticulitis, and 2.44 (95% CI, 1.62–3.66; P for trend <0.0001) for diverticular bleeding when compared to men who gained less than 5 pounds.

Waist Circumference

Waist circumference was positively associated with diverticulitis and diverticular bleeding (Table 3). The multivariable relative risks for men in the highest quintile of waist circumference compared with the lowest were 1.56 (95% CI, 1.18–2.07; P for trend 0.002) for diverticulitis, and 1.96 (95% CI, 1.30–2.97; P for trend <0.001) for diverticular bleeding. These relationships were essentially unchanged when restricting the analyses to men who had undergone a lower endoscopy (multivariable RR, 1.58; 95% CI, 1.10–2.27; P for trend 0.004 for diverticulitis, and multivariable RR, 2.04; 95% CI, 1.14–3.64; P for trend 0.003 for bleeding), and were attenuated in men who met the strictest outcome definitions (multivariable RR 1.40, 0.85–2.31;

P for trend 0.20 for diverticulitis, and 1.28, 0.51–3.19; P for trend 0.40 for bleeding). Waist circumference was not significantly associated with asymptomatic diverticulosis (multivariable RR, 1.17; 95% CI, 0.96–1.44; P for trend 0.42, respectively, in a highest vs. lowest quintile comparison).

Waist-to-hip Ratio

Waist-to-hip ratio was similarly associated with an increased risk of incident diverticular complications (Table 4). The multivariable relative risks for men in the highest quintile of waist-to-hip ratio compared with those in the lowest were 1.62 (95% CI, 1.23–2.14; P for trend 0.0004) for diverticulitis, and 1.91 (1.26–2.90; P for trend 0.0003) for diverticular bleeding. The associations between waist-to-hip ratio and diverticular outcomes remained largely unchanged after adjusting for BMI (multivariable RR; 95% CI, 1.50, 1.13–2.00; P for trend 0.003 for diverticulitis, and multivariable RR, 1.66; 95% CI, 1.08–2.54; P for trend 0.004 for diverticular bleeding). However, the relationship with BMI was attenuated when adjusted for waist-to-hip ratio (multivariable RR, 1.61; 95% CI, 0.97–2.67; P for trend 0.22 for diverticulitis and multivariable RR, 2.73 (95% CI, 1.24–6.05; P for trend 0.09 for bleeding). Restricting the analysis to men who had undergone lower endoscopy, or who met the strictest definitions of outcome had little impact on the associations between waist-to-hip ratio and diverticular outcomes: Multivariable relative risks for diverticulitis 1.48 (95% CI, 1.04–2.12; P for trend 0.02), and 1.87 (95% CI, 1.12–3.09; P for trend 0.01), respectively, and for diverticular bleeding 1.90 (95% CI, 1.09–3.33; P for trend 0.01), and 2.53 (95% CI, 0.83–7.78; P for trend 0.05), respectively. In a highest to lowest quintile comparison, waist-to-hip ratio was not associated with asymptomatic diverticulosis (multivariable RR, 1.05; 95%CI, 0.84–1.31; P for trend 0.66).

DISCUSSION

In this large, prospective cohort of men, we found that BMI was independently associated with the risk of diverticulitis and diverticular bleeding. Positive associations were also found between weight gain, waist circumference and waist-to-hip ratio, further implicating body fat as a risk factor for diverticular complications. The strength of the relationships between obesity and each anthropometric measurement was similar after adjustment for other potential confounders, and when restricting the analysis to men who had undergone lower endoscopy, or who met the strictest definitions of outcome.

Few studies have evaluated the relationship between obesity and the risk of diverticulitis. Several retrospective case series noted the prevalence of obesity in patients presenting with diverticulitis.[15–19] In these studies, 75% or more of patients were overweight or obese using a variety of criteria. Three of these studies were limited to patients younger than 40 years of age.[15, 17, 19] In a case-control study, comparisons were made between 18 unmatched controls with uncomplicated diverticulosis, and 43 patients with diverticulitis.[14] Body mass index was significantly higher in patients with recurrent diverticulitis or perforated diverticulitis compared to patients with uncomplicated disease or a single episode. None of these studies directly assessed the risk of diverticulitis associated with increasing BMI, or made adjustments for potential confounders. In a prior analysis of physical activity and diverticular disease using the Health Professionals Follow-up Study, we found a weak association between increasing BMI and symptomatic diverticular disease (diverticulitis, diverticular bleeding or nonspecific pain or bowel symptoms in the setting of diverticulosis).[20] In a study of 112 cases from a prospective cardiovascular prevention trial in Sweden, BMI was significantly associated with symptomatic diverticular disease in men.[21]

Our study extends the findings of these previous studies in several important ways. First, detailed, prospective follow-up allowed us to control for important confounders that were not assessed in other cohorts or case series. These include dietary fiber, fat and red meat, and the use of non-steroidal anti-inflammatory drugs which are putative risk factors for diverticular complications,[20, 26–31] and are also associated with obesity.[36–38] Second, prior studies had limited sample sizes. In comparison to the prior Health Professionals Follow-up Study, the current study utilizes 12 additional years of follow-up. The large number of cases in the current study enabled us to evaluate diverticular bleeding, diverticulitis and diverticulosis without these complications as separate endpoints. This is important because diverticular bleeding and diverticulitis are distinct entities that likely evolve through different biologic pathways.[22] Non-specific bowel symptoms are difficult to ascribe to diverticulosis, and may be more common in obese individuals in general.[39, 40] Third, we were able to examine the influence of weight gain and fat distribution in addition to BMI. Visceral fat has proven to be particularly important in colon cancer and other gastrointestinal disorders.[7, 23, 24, 41] Finally, previous studies (except the HPFS) have included only hospitalized patients, and may not be generalizable to the larger group of patients managed in the outpatient setting.[42]

The biological mechanisms by which obesity increases the risk of diverticular complications are unknown, and indeed factors underlying the progression from diverticulosis to diverticular complications remain poorly understood. However, obesity is plausibly linked to several factors thought to contribute to diverticular complications.[43] Adipose tissue secretes a number of cytokines known to participate in local and generalized inflammation.[10] Therefore, obesity may enhance or precipitate the inflammatory process in diverticulitis. In addition, recent reports indicate that intestinal microbes differ between obese and lean individuals.[12] Alterations in the intestinal microflora are also postulated to play a role in the development of diverticulitis, although the exact nature of these alterations is unknown.[11, 44] Obesity may influence diverticular bleeding through pathways that affect vascular integrity.[22] Lastly, obesity may contribute to the development of diverticulosis. Obesity was not associated with asymptomatic diverticulosis in our study or in previous reports.[4, 45] However, the confidence intervals in our analysis were relatively wide and random misclassification due to imperfect recall of endoscopy results could have biased the results towards the null.

We found that waist-to-hip ratio was significantly associated with diverticular complications after adjustment for BMI. In addition, the relationship with BMI was attenuated when adjusted for waist-to-hip ratio. Waist-to-hip ratio may be a better indicator of visceral fat than BMI, and visceral fat is more metabolically active than subcutaneous fat.[46] Thus, fat distribution and its metabolic consequences may be important in the development of diverticular complications. Alternatively, this finding may reflect the imperfect nature of BMI as a measure of adiposity, as BMI does not differentiate fat from lean body mass. Therefore, waist-to-hip ratio may detect residual variation in overall obesity that is not accounted for by BMI.

Certain limitations of our study are worth noting. Self-reported diverticular disease and body measurements introduce the possibility of misclassification bias. However, study participants were health care professionals, review of 179 medical records endorsed the validity of self-reported diverticular disease, self-reported body measurements were verified in previous studies, and sensitivity analyses for the endpoint definitions revealed similar results. Residual confounding is another possible explanation for our findings, but we controlled for diet and physical activity (which had modest associations with the study endpoints, see Table 1 in the on line appendix) and our results did not change appreciably. In addition, obese men may be more likely to be diagnosed with diverticular disease because of more frequent medical contact. However, the lack of an association between obesity and asymptomatic diverticulosis, and the similarity in the results when the analyses were restricted to men who had undergone a lower endoscopy diminish the likelihood of detection bias. Lastly, our study was limited to men over the age of 40 years. Nonetheless, diverticulosis is rare in young individuals, and males and females appear to be affected equally.[45, 47]

In summary, our results suggest that obesity, and perhaps central obesity in particular, is associated with an increased risk of diverticulitis and diverticular bleeding. The magnitude of the increased risk and the dose-response gradient was greater for diverticular bleeding than for diverticulitis. An association between body fat and diverticular complications has important clinical implications given the increasing prevalence of these disorders,[48, 49] and the considerable risk of recurrent complications.[50, 51] Indeed, with few known modifiable risk factors, current preventative measures rely heavily on prophylactic colectomy.[47] The link between obesity and diverticular disease may also direct future studies aimed at uncovering mechanisms of disease.

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Abbreviations

BMI
: Body Mass Index

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Table 1

Baseline Characteristics According to Body Mass Index, Waist Circumference, and Waist-to-Hip Ratio

	Body Mass Index			Waist Circumference[a]			Waist-to-hip Ratio[a]		
	<21	23–25	≥30	Q1	Q3	Q5	Q1	Q3	Q5
No. of individuals	1728	14083	3814	6185	5183	5902	6266	5849	5993
Age, mean (SD), y	54 (10.7)	54 (9.9)	54 (8.9)	51 (9.6)	54 (9.7)	56 (9.5)	51 (9.1)	54 (9.6)	57 (9.6)
Smoking, current (%)	14	9.5	9.4	8.8	8.5	10.1	7.9	8.7	10.6
NSAID use (%)	27	32	37	28	33	36	30	34	35
Physical activity, mean, (MET, h/wk)	29	28	16	31	23	17	31	24	19
Daily intake, mean Calories (kcal/day)	2036	1978	2014	2001	2009	2026	1998	2004	2021
Alcohol (g/day)	10	12	10	11	12	12	10	12	13
Fat, total (g/day) [b]	68	70	76	68	71	75	70	71	73
Fiber, total (g/day) [b]	22	22	20	23	21	20	22	21	20
Red meat (servings/day)	3.8	4.0	5.0	3.8	4.4	4.9	4.0	4.3	4.7

NOTE: All variables except age are age-standardized. MET denotes metabolic equivalent; NSAID denotes non-steroidal anti-inflammatory

[a]Quintiles of waist circumference (Q1: < 34.25 inches, Q3: 36.25 to 37.75 inches, Q5: ≥40.25 inches) Quintiles of waist-to-hip ratio (Q1:< 0.89, Q3: 0.93 to 0.95, Q5: 0.96 to 0.98,≥0.98)

[b]Total fat and fiber are adjusted for total energy intake (kcal)

Table 2

Body Mass Index and the Relative Risk of Diverticulitis and Diverticular Bleeding

	Body Mass Index, kg/m^2						P value for Trend
	<21	**21–22.9**	**23–24.9**	**25–27.4**	**27.5–29.9**	**≥30**	
Diverticulitis							
Incident cases (n)	18	83	189	256	138	117	
Person-years	27077	94855	190528	229361	109135	79491	
Age-adjusted RR[a]	1.00	1.30	1.46	1.60	1.76	2.02	<.001
(95% CI)	--	(0.78–2.17)	(0.90–2.37)	(0.99–2.59)	(1.08–2.89)	(1.23–3.33)	
Multivariable RR[b]	1.00	1.29	1.40	1.48	1.58	1.78	.004
(95% CI)	--	(0.77–2.14)	(0.86–2.28)	(0.92–2.39)	(0.97–2.59)	(1.08–2.94)	
Diverticular bleeding							
Incident cases (n)	7	39	84	135	53	65	
Person-years	27077	94855	190528	229361	109135	79491	
Age-adjusted RR[a]	1.00	1.68	1.83	2.45	2.04	3.46	<.001
(95% CI)	--	(0.75–3.77)	(0.84–3.96)	(1.15–5.26)	(0.92–4.49)	(1.58–7.57)	
Multivariable RR[b]	1.00	1.68	1.83	2.38	1.91	3.19	<.001
(95% CI)	--	(0.75–3.76)	(0.85–3.97)	(1.11–5.09)	(0.87–4.23)	(1.45–7.00)	

[a] Age-adjusted RRs adjusted for age in 1-year intervals and study period in 2-year intervals

[b] Multivariable RRs adjusted for age in 1-year intervals, study period in 2-year intervals, dietary intake of calories, fat, fiber, red meat, physical activity, current use of non-steroidal anti-inflammatories and acetaminophen

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Table 3

Waist Circumference and the Relative Risk of Diverticulitis and Diverticular Bleeding

	Waist Circumference, quintiles[a]					P Value for Trend
	1	2	3	4	5	
Diverticulitis						
Incident cases (n)	86	115	93	125	137	
Person-years	99564	102191	81158	107476	87986	
Age-adjusted RR[b]	1.00	1.27	1.29	1.29	1.72	<.001
(95% CI)	--	(0.96–1.68)	(0.96–1.73)	(0.98–1.69)	(1.31–2.26)	
Multivariable RR[c]	1.00	1.22	1.22	1.20	1.56	.002
(95% CI)	--	(0.92–1.62)	(0.91–1.64)	(0.91–1.59)	(1.18–2.07)	
Diverticular bleeding						
Incident cases (n)	36	36	48	62	75	
Person-years	99564	102191	81158	107476	87986	
Age-adjusted RR[b]	1.00	0.90	1.45	1.37	2.01	<.001
(95% CI)	--	(0.57–1.43)	(0.94–2.24)	(0.91–2.07)	(1.35–3.00)	
Multivariable RR[c]	1.00	0.91	1.44	1.36	1.96	<.001
(95% CI)	--	(0.57–1.44)	(0.93–2.23)	(0.90–2.08)	(1.30–2.97)	

[a] Quintiles of waist circumference (Q1: ≤34.25 inches, Q2: 34.5 to 36 inches, Q3: 36.25 to 37.75 inches, Q4:38 to 40 inches, Q5: ≥40.25 inches)

[b] Age-adjusted RR adjusted for age in 1-year intervals and study period in 2-year intervals

[c] Multivariable RR adjusted for age in 1-year intervals, study period in 2-year intervals, dietary intake of calories, fat, fiber, red meat, physical activity, current use of non-steroidal anti-inflammatories and acetaminophen, as well as height

Table 4

Waist-to-Hip Ratio and the Relative Risk of Diverticulitis and Diverticular Bleeding

	Waist-to-Hip Ratio, quintiles[a]					P Value for Trend
	1	**2**	**3**	**4**	**5**	
Diverticulitis						
Incident cases (n)	84	109	107	121	135	
Person-years	101529	103135	91468	92241	88660	
Age-adjusted RR[b]	1.00	1.26	1.39	1.54	1.81	<.001
(95% CI)	--	(0.95–1.68)	(1.04–1.85)	(1.16–2.04)	(1.37–2.38)	
Multivariable RR[c]	1.00	1.22	1.30	1.41	1.62	<.001
(95% CI)	--	(0.92–1.63)	(0.97–1.73)	(1.06–1.87)	(1.23–2.14)	
Diverticular Bleeding						
Incident cases (n)	33	40	50	56	77	
Person-years	101529	103135	91468	92241	88660	
Age-adjusted RR[b]	1.00	1.08	1.47	1.57	2.20	<.001
(95% CI)	--	(0.68–1.71)	(0.94–2.28)	(1.01–2.41)	(1.45–3.32)	
Multivariable RR[c]	1.00	1.05	1.37	1.43	1.91	<.001
(95% CI)	--	(0.66–1.67)	(0.88–2.13)	(0.92–2.20)	(1.26–2.90)	

[a] Quintiles of waist-to-hip ratio (Q1:< 0.89, Q2: 0.89–0.92, Q3: 0.93 to 0.95, Q4: 0.96–0.98, Q5: 0.96 to 0.98, >0.98).

[b] Age-adjusted RR adjusted for age in 1-year intervals and study period in 2-year intervals

[c] Multivariable RR adjusted for age in 1-year intervals, study period in 2-year intervals, dietary intake of calories, fat, fiber, red meat, physical activity, current use of non-steroidal anti-inflammatories and acetaminophen

Appendix Table 1

Relative Risks of Variables Potentially Associated with Diverticulitis and Diverticular Bleeding

Variable	Diverticulitis HR (95% CI)	Diverticular Bleeding HR (95% CI)
BMI		
<21	1 [Reference]	1 [Reference]
21–22.9	1.29 (077–2.14)	1.68 (0.75–3.76)
23–24.9	1.40 (0.86–2.28)	1.83 (0.85–3.97)
25–27.4	1.48 (0.92–2.39)	2.38 (1.11–5.09)
27.5–29.9	1.58 (0.97–2.59)	1.91 (0.87–4.23)
≥30	1.78 (1.08–2.94)	3.19 (1.45–7.00)
Total Fat Intake		
Q1	1 [Reference]	1 [Reference]
Q2	1.00 (0.78–1.29)	0.88 (0.64–1.21)
Q3	1.25 (0.98–1.60)	1.00 (0.73–1.38)
Q4	1.20 (0.93–1.55)	0.68 (0.48–0.98)
Q5	1.14 (0.88–1.48)	0.67 (0.47 –0.97)
Total Fiber Intake		
Q1	1 [Reference]	1 [Reference]
Q2	0.91 (0.74–1.11)	1.04 (0.78–1.40)
Q3	0.83 (0.67–1.03)	0.64 (0.46–0.90)
Q4	0.83 (0.66–1.03)	0.73 (0.52–1.01)
Q5	0.64 (0.49–0.83)	0.61 (0.42–0.87)
Red Meat Intake		
Q1	1 [Reference]	1 [Reference]
Q2	1.37 (1.02–1.84)	1.18 (0.81–1.71)
Q3	1.48 (1.17–1.89)	0.95 (0.68–1.32)
Q4	1.40 (1.08–1.81)	0.88 (0.62–1.27)
Q5	1.40 (1.08–1.81)	0.99 (0.70–1.42)
Total Energy Intake (kcal)		
Q1	1 [Reference]	1 [Reference]
Q2	1.09 (0.88–1.35)	1.45 (1.07–1.97)
Q3	0.96 (0.77–1.21)	1.03 (0.73–1.45)
Q4	0.93 (0.74–1.17)	0.84 (0.58–1.21)
Q5	0.90 (0.70–1.14)	1.42 (1.01–1.98)
Physical Activity (MET,h/wk)		
≤8.2	1 [Reference]	1 [Reference]
8.3–19.0	0.89 (0.73–1.08)	0.85 (0.65–1.12)
19.1–33.5	0.79 (0.65 –0.97)	0.70 (0.52–0.94)
33.6–57.3	0.80 (0.63–1.00)	0.61 (0.43–0.87)
≥57.4	0.85 (0.65–1.12)	0.71 (0.48–1.06)
NSAID use		
No	1 [Reference]	1 [Reference]
Yes	1.31 (1.13–1.53)	1.69 (1.35–2.12)

Variable	Diverticulitis HR (95% CI)	Diverticular Bleeding HR (95% CI)
Acetaminophen		
No	1 [Reference]	1 [Reference]
Yes	1.20 (0.92–1.55)	1.35 (0.95–1.92)