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Colonic Diverticula are Not Associated with an Increased Risk of Colorectal Adenomas

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Abstract

Background & Aims—Patients with missed colorectal cancer have been reported to be more likely to have colonic diverticulosis. Such an association could be due to either higher risk of neoplasia or difficulty examining the colon in patients with diverticulosis. The aim of this study was to determine whether colonic diverticula are associated with an increased risk for colonic neoplasia.

Methods—We analyzed data from a prospective study of patients undergoing screening colonoscopy that included detailed assessment of all colonic diverticula and colorectal polyps. We used logistic regression to estimate odds ratios and 95% confidence intervals while adjusting for confounding variables.

Results—Our analyses included 624 participants. Of these, 216 (35%) had one or more colorectal adenomas. Diverticula on colonoscopy were not associated with an increased risk of adenomas (OR 1.0, 95% CI 0.7–1.4) or advanced adenomas (OR 0.8, 95% CI 0.4–1.5). Those with the greatest burden of diverticula (10 or more) did not have an increased risk of adenomas (OR 1.1, 95% CI 0.7–1.8) compared with no diverticula. Colonic diverticula were not associated with an increased risk of proximal (OR 1.0, 95% CI 0.6–1.6) or distal adenomas (OR 1.0, 95% CI 0.6–1.7).

Conclusions—Patients with colonic diverticula do not have an increased risk of colorectal adenomas or advanced adenomas.

Keywords

diverticular disease; colorectal cancer; interval colorectal cancer

Introduction

An estimated 136,000 Americans were diagnosed with colorectal cancer in 2014.(1) Of those, approximately 5,000 cases were missed colorectal cancers.(2) Missed colorectal

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cancer is defined as colorectal cancer diagnosed after a screening or surveillance exam in which no cancer is detected and before the date of the next recommended exam.(3) The majority of missed colorectal cancers are thought to be truly missed lesions, with the rest a result of incomplete resection or newly developed cancer.(4, 5)

Patients with missed colorectal cancer have been reported to be four times more likely to have colonic diverticulosis or a history of diverticular disease compared with patients with detected colorectal cancer.(2) There are two reasons why diverticula could contribute to missed colorectal cancer. First, a higher rate of missed cancer could be due to a higher overall rate of colonic neoplasia, as suggested by several cross-sectional colonoscopy-based studies that reported that patients with diverticulosis have an increased risk of adenomas or advanced adenomas.(6–11) Alternatively, because individuals with diverticulosis have distorted colonic architecture, it might be easier to miss lesions or incompletely resect them. To date, none of the studies assessing the association between colonic diverticula and colorectal adenomas were prospective studies of screening colonoscopy that included a standardized examination for diverticula and adenomas.(6–12)

To assess whether colonic diverticula are associated with an increased presence of adenomas or advanced adenomas, we conducted a prospective study of patients undergoing a complete screening colonoscopy that enumerated and characterized all diverticula and all colorectal polyps.

Methods

We analyzed data from a study designed to assess risk factors and patient attributes associated with colonic diverticula (NIH R01DK094738). In brief, the study recruited outpatients undergoing first-time screening colonoscopy at the University of North Carolina Hospitals in Chapel Hill, North Carolina between 2013–2015. Eligible participants were those 30 years and older with a satisfactory preparation for colonoscopy and a complete exam to the cecum. Exclusion criteria included any prior colonoscopy, a history of previous colon resection, or a prior diagnosis of polyposis, colitis, colon cancer, diverticulosis or diverticular disease. All participants provided written informed consent. The University of North Carolina School of Medicine Institutional Review Board approved the study and this analysis.

Cases were defined as participants with any colorectal adenoma on colonoscopy. Controls were those without an adenoma. Each participant had a detailed screening colonoscopy with all polyps recorded by a research assistant who was in the exam room with the gastroenterologist. The location and size of colorectal lesions were documented. Polyps were removed and reviewed by a gastrointestinal pathologist. One author (RSS) reviewed all pathology reports and classified polyps as adenomatous (tubular, tubulovillous or villous) or nonadenomatous. Advanced adenomas were defined as adenomas >1cm or adenomas with villoglandular histology or severe atypia.

Prior to the colonoscopy, the research assistant reminded the gastroenterologist to examine the colon for diverticula. The gastroenterologist accounted for the number, location, size and

depth of all colonic diverticula during the colonoscopy. The research assistant was present for the entire colonoscopy and recorded these findings.

The research assistant measured the participant's height and weight the day of the colonoscopy. Prior to the colonoscopy, each participant completed a detailed telephone interview on diet, physical activity, race, smoking history, alcohol and NSAID use. Dietary information was collected using the validated National Cancer Institute semi-quantitative food frequency questionnaire.(13)

Analysis

Means and standard deviations were calculated for continuous variables, and categorical data were summarized using proportions. To assess the association between diverticulosis and adenomas, we estimated odds ratios and 95% confidence intervals using logistic regression. The 10% change-in-estimate approach was used to assess the following variables for confounding: age, sex, BMI, NSAID use, smoking history, total energy intake, dietary fiber intake and physical activity. The final effect estimates were adjusted for age, sex and BMI. We performed analyses assessing the association of diverticulosis with adenomas by number of adenomas (exclusive categories of 1, 2, 3, and 4 or more), by advanced versus non-advanced adenomas, and by location (proximal versus distal). We assessed the association with adenomas by any diverticula, and within strata of diverticula count (categories of 1–5, 6–10 and 10 or more). All tests of significance were two-sided and p-values <0.05 were considered significant. All data were entered into and analyzed using SAS 9.3 (SAS, Cary, North Carolina).

Results

Our analyses included 624 participants, each with complete outpatient first-time screening colonoscopy that characterized and enumerated all diverticula and colorectal polyps; 216 (35%) had an adenoma found during the examination. Participants with adenomas were more likely to be male, non-white and to have diverticula though not significantly (Table 1). The mean age of adenoma cases was 56 and 53 for non-adenoma controls. Adenoma cases had a higher mean body-mass index, and used tobacco more frequently than those without adenomas.

Among the 624 participants, 260 (42%) had diverticula on colonoscopy. The mean number of diverticula was 14 (range 1 to more than 100). Participants with diverticula were more likely to be older, female, and had a higher body mass index than those without diverticula. Among those with diverticula, most (62%) had diverticula limited to the descending and sigmoid colon.

Diverticula were not associated with an increased risk of adenomas (OR 1.0, 95% CI 0.7–1.4) or advanced adenomas (OR 0.8, 95% CI 0.4–1.5). In addition, the lack of association between diverticula and adenomas was similar in analyses stratified by sex. Diverticula were not associated with an increased risk of one adenoma (OR 1.0, 95% CI 0.6–1.5), two adenomas (OR 1.1, 95% CI 0.6–2.0), three adenomas (OR 1.1, 95% CI 0.4–2.8) or four or more adenomas (OR 0.7, 95% CI 0.3–1.7) compared to those with no adenomas (Table 2).

Among the 260 participants with diverticulosis, 104 (40%) had 1–5 diverticula, 59 (23%) had 6–10 diverticula and 97 (37%) had 10 or more diverticula on colonoscopy. Those with the greatest burden of diverticula (10 or more) did not have an increased risk of adenomas (OR 1.1, 95% CI 0.7–1.8) compared with no diverticula (Table 3). In analyses stratified by location of the adenomas, colonic diverticula were unassociated with risk of either having only proximal (OR 1.0, 95% CI 0.6–1.6) or only distal adenomas (OR 1.0, 95% CI 0.6–1.7) (Table 4).

Discussion

Colonic diverticula were not associated with colorectal adenomas or advanced adenomas in a large population of patients having complete screening colonoscopy and a standardized assessment for colonic diverticula. Those with the greatest burden of diverticula did not have an increased risk of adenomas. The presence of diverticula was not associated with the number of adenomas found on colonoscopy. There was no association between colonic diverticula and proximal or distal adenomas.

The results of our analysis differ from several colonoscopy-based studies that reported an increased risk of adenomas and advanced adenomas in patients with diverticulosis.(6–11) Most of these studies included patients undergoing a colonoscopy for an indication. None of these studies were restricted to patients having a screening colonoscopy, nor did they include a standardized assessment of colonic diverticula during the procedure.(6–12)

Similar to our findings, one colonoscopy-based study found no association between diverticulosis and colon polyps.(12) This retrospective study of 4,241 patients from the Netherlands abstracted diverticula and polyp status from colonoscopy reports and included patients referred for gastrointestinal symptoms, surveillance or screening.

Patients with missed colorectal cancer are four times more likely to have colonic diverticulosis or a history of diverticular disease compared with patients with detected colorectal cancer.(2) This reported increased risk of missed colorectal cancer in patients with diverticulosis could be a result of detection bias, i.e., those with missed colorectal cancers have had more colonoscopies and thus more opportunities for a diagnosis of diverticulosis than those with sporadic colorectal cancers. Alternatively, individuals with diverticulosis have distorted colonic architecture that could make it easier to miss lesions or for lesions to be incompletely resected.

Contrary to most of the studies to date, our analyses suggest that colonic diverticula are not associated with an increased risk of colonic neoplasia, as evidenced by any colorectal adenomas or advanced adenomas. Our study population was comprised of individuals undergoing first screening colonoscopies, meticulously conducted with specific attention directed at detection of all colonic diverticula. The overall adenoma detection rate of 35% is above the recommended rate of 20% in women and 25% in men.(14)

Gastroenterologists performed all of the colonoscopies in the study. Colonic diverticula were assessed in a standardized manner. A research assistant attended all procedures and documented the location and size of all polyps and diverticula using a standardized form.

Unlike previous studies, we were able to consider and adjust for several confounding variables including lifestyle and health history factors. One possible limitation to our study is that diverticula and adenomas may have been missed, although the adenoma detection rate (38% among those with diverticula, 32% without diverticula) in our study was greater than recommended benchmarks, which argues against significant number of missed lesions.(14) Five patients were excluded from the study for failure to reach the cecum, although there was no indication from the procedure notes that these incomplete procedures were due to diverticula. However, even if all five of these patients had diverticulosis and adenomas, our results would not change, so it is unlikely our results are confounded by incomplete colonoscopies due to diverticula. Furthermore, our study was not designed to assess for an association between diverticula and sessile serrated polyps. Given our finding of no association between diverticula and adenomas, the magnitude of any hypothesized diverticulosis-sessile serrated polyp effect would need to be quite large to account for the entirety of previously reported associations of diverticula and missed cancers and this seems unlikely. Finally, we did not assess whether the physical changes (like muscular hypertrophy or poor distensibility) that sometimes accompany colonic diverticulosis are associated with adenomas. If there were an association between these characteristics and adenomas we would have expected to find that those participants with the greatest burden of diverticula had an increased risk of adenomas. Our analyses found no association between colonic diverticula on colonoscopy and presence of colorectal adenomas or advanced adenomas. Based on these results we conclude that any association between missed cancers and colonic diverticula is not due to greater risk for neoplasia in patients with diverticula.

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STUDY HIGHLIGHTS

1. WHAT IS CURRENT KNOWLEDGE

- Patients with missed colorectal cancer have been reported to be more likely to have colonic diverticulosis.
- Such an association could be due to either higher risk of neoplasia or difficulty examining the colon in patients with diverticulosis.

2. WHAT IS NEW HERE

- Colonic diverticula were not associated with colorectal adenomas or advanced adenomas.
- Moreover, those with a greater burden of diverticulosis did not have an increased risk of adenomas.

Table 1

Baseline Characteristics

Characteristic	Adenoma (n=216)	No Adenoma (n=408)
Age, years, mean ± SD	56 ± 7	53 ± 6
Sex, %		
Male	50	40
Female	50	60
Race, %		
White	71	78
Non-white	26	20
Unknown	3	2
Education, years, mean ± SD		
<12 years	6	4
12 years	10	8
Some college	24	22
College graduate	59	67
BMI, kg/m^2, mean ± SD	30 ± 7	28 ± 7
NSAID, mean use per month ± SD	11 ± 36	15 ± 41
ASA, mean use per month ± SD	4 ± 36	3 ± 14
Smoking status, %		
Never	58	56
Former/Occasional	27	31
Current	15	12
Total energy intake, kcal/day, mean ± SD	2028 ± 860	2085 ± 740
Total fiber, grams/day, mean ± SD	20 ± 11	21 ± 9
Physical activity per week, METS, mean ± SD	2894 ± 3213	2881 ± 2934
Diverticulosis, %	45	39

Abbreviations: SD, standard deviation; BMI, body mass index; NSAID, nonsteroidal anti-inflammatory drug; MET, metabolic equivalent task

Table 2

Diverticulosis and risk of adenoma by number

Adenomas	n cases	Adjusted OR (95% CI)[¶]
0	404	reference
1	120	1.0 (0.6–1.5)
2	51	1.1 (0.6–2.0)
3	21	1.1 (0.4–2.8)
≥4	24	0.7 (0.3–1.7)

[¶]Adjusted for age, sex and body mass index

Table 3

Diverticula count and risk of adenomas

# Diverticula	n cases	Adjusted OR (95% CI)[¶]
0	118	reference
1–5	36	1.0 (0.7–1.7)
6–10	19	0.7 (0.4–1.3)
≥10	43	1.1 (0.7–1.8)

[¶]Adjusted for age, sex and body mass index

Table 4

Diverticulosis and risk of adenoma by location

	Proximal Adenomas Only[§]		Distal Adenomas Only[§]	
	n cases	Adjusted OR (95% CI)[¶]	n cases	Adjusted OR (95% CI)[¶]
No diverticula	37	reference	51	reference
Any diverticula	38	1.0 (0.6–1.6)	34	1.0 (0.6–1.7)

[¶]Adjusted for age, sex and body mass index

[§]Proximal adenomas include adenomas in or proximal to the splenic flexure; distal adenomas are distal to the splenic flexure.