

憩室のある人の4.3%が憩室炎を起こす。

Long-term Risk of Acute Diverticulitis Among Patients With Incidental Diverticulosis Found During Colonoscopy

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BACKGROUND & AIMS: Colonic diverticulosis is the most common finding during routine colonoscopy, and patients often question the significance of these lesions. Guidelines state that these patients have a 10% to 25% lifetime risk of developing acute diverticulitis. However, this value was determined based on limited data, collected before population-based colonoscopy, so the true number of cases of diverticulosis was not known. We measured the long-term risk of acute diverticulitis among patients with confirmed diverticulosis discovered incidentally on colonoscopy.

METHODS: We performed a retrospective study using administrative and clinical data from the Veterans Affairs Greater Los Angeles Healthcare System, collecting data on patients who underwent colonoscopies from January 1996 through January 2011. We identified patients diagnosed with diverticulosis, determined incidence rates per 1000 patient-years, and analyzed a subgroup of patients with rigorously defined events confirmed by imaging or surgery. We used a Cox proportional hazards model to identify factors associated with the development of diverticulitis.

RESULTS: We identified 2222 patients with baseline diverticulosis. Over an 11-year follow-up period, 95 patients developed diverticulitis (4.3%; 6 per 1000 patient-years); of these, 23 met the rigorous definition of diverticulitis (1%; 1.5 per 1000 patient-years). The median time-to-event was 7.1 years. Each additional decade of age at time of diagnosis reduced the risk for diverticulitis by 24% (hazard ratio, 0.76; 95% confidence interval, 0.6–0.9).

CONCLUSIONS: Based on a study of the Veterans Affairs Greater Los Angeles Healthcare System, only about 4% of patients with diverticulosis develop acute diverticulitis, contradicting the common belief that diverticulosis has a high rate of progression. We also found that younger patients have a higher risk of diverticulitis, with risk increasing per year of life. These results can help inform patients with diverticulosis about their risk of developing acute diverticulitis.

Keywords: Colon; Pouch; Prognosis; Diverticular Disease.

See related articles on pages 1532, 1614, 1622, and 1631 in this issue of *Clinical Gastroenterology and Hepatology*.

Diverticulosis imposes a significant burden on Western and industrialized societies.¹⁻⁴ The prevalence of diverticulosis increases with age, affecting approximately 70% of individuals aged 80 years or older in the United States.^{1,2} Patients with diverticulosis may experience acute complications, including diverticulitis, peritonitis, obstruction, fistulization, or abscess formation,⁵⁻⁷ and chronic complications including a picture resembling irritable bowel syndrome.⁸ When a complication of diverticulosis occurs, it is broadly termed *diverticular disease*.⁷ Diverticular disease accounts for more than 300,000 hospital admissions, 1.5 million inpatient care days, and \$2.4 billion in direct costs annually in the United States.^{1,9,10} The

incidence of diverticular complications is increasing, and the number of patients affected by diverticular disease will continue to increase as the population ages.¹¹ These epidemiologic trends are familiar to any endoscopist who performs colon cancer screening because diverticulosis is the most commonly reported lesion found on routine colonoscopy.¹

Despite this growing burden of disease, there are few studies that evaluate the natural history of colonic diverticulosis. The lifetime risk of developing diverticulitis—the most common clinical complication—traditionally is cited as 10% to 25% in those patients

Abbreviations used in this paper: BMI, body mass index; CT, computed tomography; ICD-9, International Classification of Diseases, 9th revision; VA, Veteran's Affairs; VAGLAHS, Veterans Affairs Greater Los Angeles Healthcare System.

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harboring uncomplicated diverticulosis.^{5,6,12} This figure is widely quoted throughout the literature; it appears in original research publications,¹³⁻¹⁵ prominent review articles,^{12,16-19} textbooks,²⁰⁻²² and published guidelines.^{6,23,24} Most publications credit a review article, published by Parks⁵ in 1975, as the first to report the 10% to 25% estimate. However, the article by Parks⁵ itself refers to studies from the mid-20th century and includes references dating as far back as 1937.^{25,26} These studies, which largely serve as the basis for modern estimates, were conducted at a time when population-based colonoscopies were not performed. Without knowing the true denominator of cases in these studies, it is impossible to accurately discern the population prevalence of diverticulosis, much less the true incidence of acute diverticulitis.

There are few modern studies investigating the progression from diverticulosis to acute diverticulitis, and most studies focus on repeated attacks after an index event.^{19,27-29} One small study followed up 119 patients for 5 years and reported a diverticulitis risk of 1.7% among those with baseline gastrointestinal symptoms; the study did not include subjects with asymptomatic diverticular disease.³⁰ These results suggest that the traditionally cited 10% to 25% incidence rate may be an overestimate.

With an aging population and greater use of colonoscopy for colorectal cancer screening, more and more people are discovered to harbor diverticulosis. Patients often question the significance of these lesions; if providers had more accurate information regarding the risk of diverticulosis complications, then they could make better decisions about the timing of interventions such as surgery. In this study, we calculated the risk of developing acute diverticulitis using a large, long-term cohort of patients with confirmed baseline diverticulosis incidentally discovered during colonoscopy.

Methods

Data Source

We performed a retrospective survival analysis using administrative and clinical data from the Veteran's Affairs (VA) Greater Los Angeles Healthcare System (VAGLAHS) collected between January 1996 and August 2011. VAGLAHS maintains electronic medical records from 14 community clinics and 1 inpatient academic medical center: the West Los Angeles VA. The VAGLAHS database includes patient demographics, inpatient and outpatient treatment files, and laboratory, imaging, pathology, and pharmacy data. In addition, VAGLAHS maintains an electronic database (Pentax EndoPro, Montvale, NJ) for all colonoscopies performed since 1996.

Selection of Diverticulosis Cases

We identified patients with prevalent, uncomplicated colonic diverticulosis through a query of the VAGLAHS endoscopy database for cases with the International Classification of Diseases, 9th revision (ICD-9) code for colonic diverticulosis (562.01), regardless of the indication for colonoscopy. We supplemented this approach with an automated natural language processing program that searched endoscopy reports for the truncated term "diverticul*." Physician abstractors reviewed colonoscopy reports identified by the searches and selected patients if their report included written or photodocumented evidence of colonic diverticulosis. We excluded patients who were found to have a pre-existing ICD-9 code for diverticulitis or documentation of diverticulitis in the medical record notes at any point before the index date of diverticulosis.

Outcome Measurement: Identifying Diverticulitis Events

To identify diverticulitis events among those patients with diverticulosis, we queried the VAGLAHS database for either inpatient or outpatient ICD-9 codes for diverticulitis and its complications, including diverticulitis (ICD-9 562.11), diverticular abscesses (569.5), and diverticular perforations (569.83). Because administrative codes can be inaccurate, we performed diagnostic corroboration through medical record review. Physician abstractors used a standardized chart review including automated natural language searching of provider notes for relevant keywords (ie, "diverticulitis," "diverticular") and assessment of laboratory, imaging, and pathology records. For patients to be included, we required a formal chart diagnosis of diverticulitis by a treating physician, based on clinical parameters (eg, leukocytosis, fever), radiographic, and/or surgical specimens. We further stratified diverticulitis events into liberal and strict definitions.

We included cases as liberal cases if they met at least one of the following criteria: (1) a formal chart diagnosis of diverticulitis by the treating physician based on appropriate symptomatology and treatment with antibiotics; (2) diagnosis supported by clinical parameters of abdominal tenderness and at least 1 nonradiographic objective data including fever (temperature, $>38^{\circ}\text{C}$ or 100.4°F), leukocytosis (leukocyte count, $>11 \times 10^9/\text{L}$), or a neutrophil predominance of leukocytes (neutrophils, $>70\%$); (3) objective evidence on computed tomography (CT) scanning of the abdomen and pelvis consistent with diverticular inflammation and its related complications; or (4) the presence of a surgical specimen confirming the diagnosis. However, we assumed there might have been cases falsely diagnosed as diverticulitis without strong supporting evidence for the diagnosis. Thus, we also identified a strict subgroup with rigorously defined diverticulitis events requiring confirmation by CT scanning and/or surgical specimens (criteria 3 and/or 4, as listed previously).

Statistical Analyses

We generated frequency tables for patient characteristics and compared these values between patients who developed diverticulitis vs those who did not, using chi-square testing for categorical variables, and the Student *t* tests for continuous variables. We performed time-to-event survival analyses (Kaplan-Meier curve) and grouped event-time intervals into 60-day segments. We right-censored subjects if they: (1) met our definition of diverticulitis; (2) died; (3) were lost to follow-up evaluation (ie, they had no VA notes, visits, or correspondence for a continuous 2-year period from their last correspondence in the medical record); or (4) were still present by the end the of follow-up period (August 31, 2011). We calculated diverticulitis incidence rates by dividing the number of diverticulitis events by the corresponding person-years of exposure. We repeated this analysis focusing only on rigorously defined cases, and again by age strata by decade of life. We used Cox proportional hazards regression analyses to calculate the hazard ratio and 95% confidence intervals of a diverticulitis event. For purposes of variable selection, we performed univariate analyses on covariates such as age, race, ethnicity, sex, body mass index (BMI), and procedural indication, and included predictors when tests yielded a *P* value of 0.2 or less. We used SAS statistical software (version 9.2; SAS Institute, Cary, NC) for all analyses. The VAGLAHS institutional review board approved this study (VA Project #0016).

Table 1. Patient Characteristics

Variable	No progression to diverticulitis (n = 2127)	Progression to diverticulitis (n = 95)	P value
Mean age, y	67 ± 10.8	63.8 ± 11.2	.004
Sex	97.6% male	96.8% male	.43
Ethnicity			
White	40.8%	43.2%	.670
Black	9.7%	15.8%	
Hispanic	8.2%	11.5%	
Other	41.3%	29.5%	
Mean BMI	28.52	28.46	.61
Colonoscopy indication ^a			
Screening	45%	45%	.25
BRBPR, hematochezia, melena	7%	12%	
Anemia, FOBT+/-FIT+	2%	2%	
Constipation, diarrhea, pain, weight loss	4.8%	6.3%	
Indication not recorded in report	40.9%	34.7%	

BRBPR, bright red blood per rectum; FIT, fecal immunochemical test; FOBT, fecal occult blood test.

^aCases may have had more than one indication.

Results

Patient Characteristics and Descriptive Statistics

Over the 15-year study period, we identified 2222 subjects with chart-confirmed colonic diverticulosis. Table 1 presents the patient characteristics and procedure indications stratified by diverticulitis status. The median follow-up period was 6.75 years (interquartile range, 3.75–9.66 y; maximum, 15 y; minimum, 1 mo; mean ± SD, 6.75 ± 3.6 y).

Incidence Rates of Diverticulitis

We identified 95 patients (4.3%) who developed acute diverticulitis based on any of the defined criteria as discussed earlier, whereas 23 (1%) had rigorously defined diverticulitis events supported by CT scanning and/or a surgical specimen. When including all diagnostic levels of evidence, the overall incidence rate was 6 per 1000 patient-years. When limiting the diagnostic levels to include only the most rigorous diagnostic definition (requiring CT or surgical confirmation), the incidence was 1.5 per 1000 patient-years. Among subjects developing acute diverticulitis, the median time-to-event among all cases was 7.1 years.

Predictors of Diverticulitis

We evaluated a range of baseline clinical and demographic characteristics and their association with subsequent diverticulitis. Table 1 presents univariate analyses comparing the baseline prevalence of age, sex, race, ethnicity, BMI, comorbidity, and procedural indications between the 95 patients developing diverticulitis and the 2127 who did not. Patients progressing to diverticulitis were significantly younger than those not progressing to diverticulitis (63.8 ± 11.2 vs 67 ± 10.8 y; *P* = .004). However, there were no differences in sex, race, ethnicity, or BMI between groups. Similarly, procedural indication did not predict diverticulitis. For example, patients who received a colonoscopy to investigate abdominal pain or defecatory symptoms had the same risk of developing diverticulitis as patients with colonoscopies performed for other indications, including colorectal cancer screening.

Figure 1 shows the Kaplan–Meier curves stratified by decade of life at the time of initial diverticulosis detection by

colonoscopy. According to univariate testing, age at diagnosis was the only predictor of diverticulitis meriting inclusion in the Cox proportional hazards model. For every additional year of age at the time of diverticulosis detection, there was a 2.4% lower hazard of developing diverticulitis (hazard ratio, 0.976; 95% confidence interval, 0.958–0.994). An additional 10 years of age at diagnosis of diverticulosis, for instance, decreased the hazard ratio of diverticulitis by 21.9%. Differences of 20, 30, and 40 years at age of diagnosis decreased hazards by 39.1%, 52.1%, and 62.9%, respectively. Table 2 presents detailed information regarding age-specific incidence rates.

Discussion

The natural history of diverticulosis is poorly understood. Published guidelines and reviews state that 10% to 25% of patients with colonic diverticulosis ultimately will develop diverticulitis over the course of their lifetime.^{5,6,23,31,32} However, this widely cited figure is based on data predating population-based screening colonoscopy.⁵ Therefore, the true

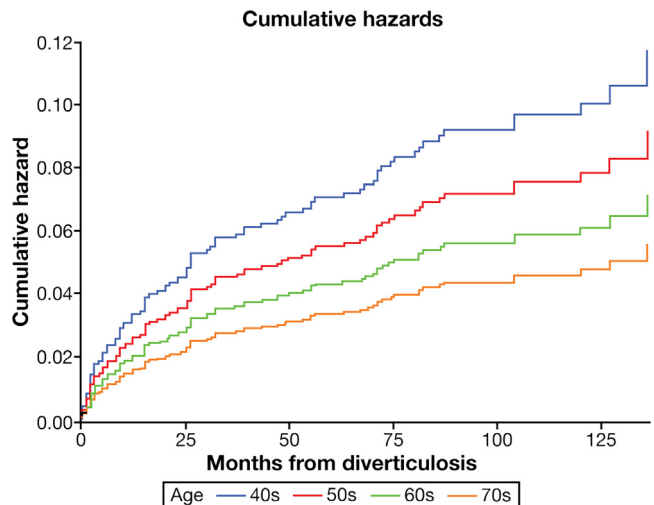


Figure 1. Kaplan–Meier curves stratified by decade of life at the time of initial diverticulosis detection.

Table 2. Incidence Rates Stratified by Decade of Life

Age, y	N	No. of diverticulitis		Proportion with diverticulitis	Incidence per 1000 patient-years	Lower 95% CI	Upper 95% CI
		cases	Person years				
<40	21	2	95	0.095	21.1	0.000	0.221
40–49	68	6	533	0.088	11.3	0.021	0.155
50–59	511	26	3570	0.051	7.3	0.032	0.070
60–69	688	29	4474	0.042	6.5	0.027	0.057
70–79	637	22	4665	0.035	4.7	0.021	0.049
≥80	297	10	1646	0.034	6.1	0.013	0.055
Total	2222	95	14,983	0.043	6.3	0.035	0.051

CI, confidence interval.

denominator of individuals harboring diverticulosis was not accounted for in these calculations.

To calculate the true incidence of acute diverticulitis more accurately, we performed a survival analysis in a large cohort of patients with diverticulosis incidentally discovered during colonoscopy. We found a much lower long-term risk of diverticulitis than stated in published guidelines. The cumulative diverticulitis probability was 4.3% when using a liberal definition not requiring CT scan confirmation. This may represent an upper limit, or even an overestimation of diverticulitis risk, because many of these subjects may not have experienced true diverticulitis at all despite an ICD-9 code, characteristic clinical picture, and an increased white blood cell count. The cumulative rate indeed decreased to only 1% when requiring CT scan or surgery to confirm the diagnosis of acute diverticulitis. These data question the traditional perception about the rate of progression from incidental diverticulosis to acute diverticulitis.

However, we also found that patients who were diagnosed with diverticulosis at a younger age may incur a higher risk of developing diverticulitis than older patients. For every additional decade of life at the time of initial diverticular detection, there was a 24% lower risk of diverticulitis. For patients with diverticulosis aged 40 to 49 years, diverticulitis peaked at 11% over the course of our 11-year follow-up period. Notably, the difference among ages did not occur because younger patients lived longer than older patients. Moreover, survival analysis calculated rates scaled by person-years of follow-up evaluation. Per year of life in follow-up evaluation, younger patients in this cohort assumed a higher risk of diverticulitis than did older patients. This result is consistent with previous data indicating both an increasing incidence of diverticulitis in younger patients and a more virulent course of disease.^{33–35} However, other studies have indicated a similar course of disease among age groups.^{36,37}

Although this study cannot explain why there are differences in diverticulitis risk among ages, it provides insights. For example, some investigators postulate that the higher risk of diverticulitis in younger patients may be linked to the epidemic of childhood obesity because higher BMI predicts higher rates of diverticulitis.^{34,37} However, BMI was not associated with the presence of diverticulitis in our cohort, suggesting that obesity alone may not explain the relationship. Another possibility is that younger patients typically receive colonoscopies for diagnostic as opposed to screening purposes; differences in colonoscopy indication by age might explain variations in diverticulitis risk. For example, younger patients undergoing colonoscopy for irritable bowel syndrome, diarrhea, or abdominal pain might have undiagnosed symptomatic diverticular

disease already, thereby confounding the potentially spurious result that lower age increases risk of diverticulitis. Thus, we recorded the indication for each colonoscopy and subjected the variable to univariate testing. The requirements for inclusion were not met, suggesting that another factor may be driving the differences.

This study had important limitations. This was a retrospective, single-center study in a VA hospital where the patients were Western and predominantly male. Although previous data do not reveal differences in diverticulitis risk by sex,⁶ future research should evaluate the natural history of diverticulosis in other diverse populations. Second, we relied on administrative data to identify cases of diverticulitis. These codes could have been applied inaccurately. True cases of diverticulitis may have been missed altogether. However, we performed extensive reviews of medical records to confirm chart evidence of diverticulitis and also relied on objective markers of disease, including radiographic and surgical evidence. Future series or patient registries may better standardize the definition of diverticulitis in a prospective cohort. Third, baseline diverticulosis cases also may have been underreported. Because diverticulosis is very common, it is possible that some endoscopists simply fail to record the lesion on endoscopy reports. We cannot know whether the natural history of unreported diverticulosis varies from the history of documented diverticulosis. Fourth, although the VA population is highly stable, we cannot know with certainty whether some patients were diagnosed with diverticulitis at non-VA facilities. However, VA providers typically update records with new diagnoses, even if accumulated at outside facilities. Moreover, most VA patients receive all or most of their care in the VA, therefore it seems unlikely that our estimates would change significantly if we had full non-VA data on this cohort. Nonetheless, we cannot know for sure whether we missed important diverticulitis events, and this may lead to modest underreporting of the overall diverticulitis rates. Finally, the indication for the procedure documenting the index diverticulitis was not known for many patients in this series.

Despite these limitations, these results question the traditional teaching about the rate of progression from incidental diverticulosis to acute diverticulitis. Moreover, they also suggest that patients who are diagnosed with diverticulosis at a younger age may incur more risk of developing diverticulitis. These data may help to reframe discussions with patients regarding their probability of developing clinically significant diverticulitis. Future research should identify individual predictors of diverticulitis in a prospective analysis to better stratify patients by risk and further study why younger patients may harbor a higher risk of progression than older patients.

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Conflicts of interest

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