

The Natural History of Colonic Diverticulosis: Much Ado about Nothing?

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Keywords

Diverticulitis · Bleeding · Hemorrhage · Colon · Diverticula · Complication

Abstract

Background: Colonic diverticulosis is the most common incidental lesion found on routine colonoscopy. However, its true natural history is unclear. The aim of this review is to examine the epidemiology of colonic diverticulosis and the incidence of complications, namely acute diverticulitis and diverticular hemorrhage. **Summary:** Many studies have evaluated the epidemiology and risk factors of diverticulosis. Despite the common nature of this entity, little is known about the risk of complications in asymptomatic individuals. It has been suggested that the lifetime risk of acute diverticulitis is 10–25% and that of diverticular hemorrhage is 3–5%. These risk estimates were based on older literature without accurate studies on true prevalence. Three recent retrospective observational cohort studies including subjects identified at colonoscopy have addressed this issue, providing information on the long-term risk of complications of colonic diverticulosis. Cumulative data from these studies support an incidence of acute diverticulitis of 1.5–6.0 per 1,000 patient-years and 0.46 per 1,000 patient-years for diverticular

hemorrhage. **Key Messages:** Diverticulosis is a very common condition in individuals >50 years of age. Based on population-based colonoscopy studies, the natural history of colonic diverticulosis appears favorable with a far lower incidence of complications than previously thought.

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Introduction

Colonic diverticulosis is a condition that develops when pockets or outpouchings (diverticula) form due to structural alterations in the wall of the large intestine [1]. Diverticula usually occur at weakened sites where blood vessels penetrate the walls of the colon and are present in the intestine without signs of inflammation [2]. Colonic diverticulosis is a relatively common condition in the Western world and is the most common incidental lesion on routine colonoscopy [3]. In the West, it is estimated that around 15–30% of the individuals will have diverticulosis by the age of 50 years [3] and as many as 60–70% by the age of 80 years [3, 4], primarily located in the left colon. The prevalence is much lower in less industrialized parts of the world, such as Africa and parts of Asia, where it is found in only 4–5% of the population, with a pre-

dominance of right-sided disease in Asian populations [5, 6]. Recent evidence indicates that this prevalence is expected to further increase worldwide, possibly due to urbanization and the adoption of western lifestyles [7]. Risk factors for colonic diverticulosis include age and possibly a high-fat diet as well as alcohol consumption [8–10].

Most people with colonic diverticulosis remain asymptomatic. However, it is estimated that around 20% will develop symptoms at some point in their lifetime [4]. The clinical spectrum of symptomatic diverticular disease ranges from mild gastrointestinal symptoms similar to those of irritable bowel syndrome to life-threatening complications including perforation and hemorrhage. It has been suggested that 80–85% of the patients with diverticulosis remain asymptomatic, with 10–25% eventually developing diverticulitis and a smaller number developing diverticular hemorrhage [3, 11, 12]. Although supportive evidence is poor, these oft-quoted figures continue to appear in the literature, including medical and surgical guidelines [11, 13]. What is clear, however, is that complicated diverticular disease is a major economic burden in the Western world. It accounts for an estimated 23,600 deaths per year in Europe and for around 312,000 hospital admissions, 1.5 million days of hospital stay, and more than 2.6 billion dollars in 2004 in the USA [14, 15]. The true economic burden is probably larger considering that uncomplicated acute diverticulitis is often diagnosed and managed in an ambulatory setting [16].

The true natural history of colonic diverticulosis, however, is unclear because of the lack of prospective studies involving large cohorts of healthy asymptomatic individuals with incidental colonic diverticulosis. The aim of this review is to examine the literature on the natural history of colonic diverticulosis primarily as it relates to 2 important and potentially life-threatening complications, namely acute diverticulitis and diverticular bleeding. The poorly defined associated syndromes of irritable bowel syndrome-like manifestations and the recently coined segmental colitis-associated diverticulosis identified on colonoscopy and characterized by chronic, sometimes relapsing, mucosal inflammation in an area of the colon (usually the sigmoid) in the presence of diverticula will not be discussed.

Methods

A literature review search was performed using PubMed. Articles were retrieved up until February 2018 and were identified using the following MeSH Terms:

“diverticulosis,” “diverticular disease,” “diverticulitis,” “diverticular bleeding” in association with each of the following terms: “incidence,” “prevalence,” “epidemiology,” “natural history.” Additional articles were identified through review of the reference lists of selected articles. The articles returned by the searches were chosen based on the English language and relevance to this review.

Epidemiology

Colonic diverticulosis is one of the most common conditions affecting the colon. In 1968, a post-mortem study of 300 unselected colons identified diverticula in 37% (111) of the specimens. Prevalence increased with the age at death, reaching nearly 25% of the colons by the age of 50 years and as many as 40–50% by the age of 70–80 years [17]. Barium enema is perhaps the best pre-mortem method to identify the true prevalence of colonic diverticulosis but is understandably not routinely performed in asymptomatic individuals.

Pooled data from the endoscopy database of the Clinical Outcomes Research Initiative (CORI) found a prevalence of diverticulosis of 32.6% in patients aged 50–59 years. This percentage steadily increased to around 71.4% of all examinations in patients aged ≥ 80 years [3]. A recent prospective screening colonoscopy study involving 624 patients reported a higher overall prevalence of diverticulosis of 42% (predominantly in the sigmoid colon). The prevalence increased with age (40% in the 5th decade and 58% in older patients) and identified risk factors such as age, male gender, and a higher BMI. A greater percentage of proximal colon diverticulosis was noted in black compared with white individuals. It is important to note that despite the relatively young mean age of the study population, this study identified a higher incidence of diverticulosis. This could be partially explained by the prospective nature of the study where endoscopists may have been more inclined to thoroughly examine enrolled patients for the presence of diverticula, which may otherwise be missed or go unreported in real life and in retrospective studies.

A prospective study from Lebanon of screening colonoscopy on nearly 700 asymptomatic average-risk individuals found a prevalence of diverticulosis of 27.2%. This prevalence mirrored that of a Dutch Study [18]. However, as mentioned earlier, the prevalence is much lower in Africa and parts of Asia. The explanation for this East-West paradox in disease prevalence and phenotype is unclear

Table 1. Studies investigating the natural history of colonic diverticulosis

Study	Year	Type of study	Patients, <i>n</i>	Duration of follow-up, years	Clinical endpoint and incidence	Mean time to event, years	Limitations and strengths
Shahedi et al. [23]	2013	Retrospective	2,222	15	Acute diverticulitis 1.5–6.0/1,000 patient-years	7.1	No information on diverticular bleeding 97% males Baseline colonoscopy: all indications Large number of patients Rigorously defined endpoint
Niikura et al. [24]	2015	Retrospective	1,514	10	Diverticular bleeding 0.46/1,000 patient-years	4.2 ^a	No information on diverticulitis Baseline colonoscopy: all indications Large number of patients Diverticular bleeding in 35 patients: definitive in 7, presumptive in 28
Shayto et al. [25]	2016	Retrospective	144	10	Acute diverticulitis and diverticular bleeding 5.9/1,000 patient-years	5.1	Small number of patients Average-risk CRC screening population: true asymptomatic population Ascertained both complications Well-defined, prospectively enrolled cohort

^a Median time to event.

but it has been suggested to be due to diet, particularly a high-fat diet, and alcohol consumption may also play a role in disease pathogenesis [8–10].

Natural History

The true natural history of colonic diverticulosis remains largely unclear. It has been suggested that the lifetime risk of acute diverticulitis is 10–25%, with no clear estimate on the less common diverticular bleeding. However, these risk estimates were based on older literature without accurate studies on the prevalence of the condition (uncomplicated diverticula) in asymptomatic populations. Because colonic diverticulosis is a silent condition that cannot be detected without imaging or endoscopy, the study of its true natural history is difficult. The wide adoption of population screening for colorectal cancer (CRC) by colonoscopy has provided the opportunity to study the prevalence, distribution, and risk factors of colonic diverticulosis in healthy subjects albeit restricted

primarily to those aged 50 years or older. Using a large cohort from the Health Professionals Follow-up Study, Strate et al. [19–22] prospectively examined the incidence and risk factors for diverticular disease including diet, obesity, and physical activity. However, all these studies were limited by the fact that there was no pre-assessment of the prevalence of diverticulosis in the study population; instead, the authors were relying primarily on a self-diagnosis or prior knowledge of diverticulosis or its complications for exclusion. Given the largely asymptomatic nature of colonic diverticulosis, these studies fail to provide accurate information on the natural history of this disease.

To date, only 3 studies have examined the true natural history of diverticulosis (Table 1). The first was a large retrospective US study from the Veterans Administration involving 2,222 patients with baseline diverticulosis discovered incidentally on colonoscopy [23]. The actual incidence of acute diverticulitis was as low as 4.3% over a period of 15 years, challenging the previously reported risk rates [3, 11, 12]. The study had some limitations in-

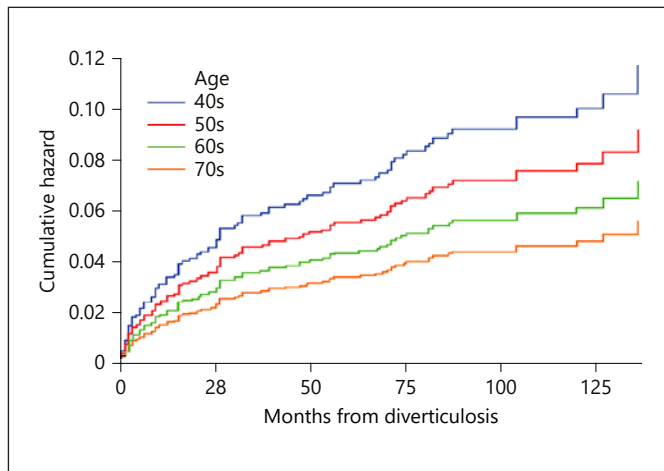


Fig. 1. Kaplan-Meier curves stratified by the decade of life at the time of initial diverticulosis detection and the risk of diverticulitis. Reprinted with permission from Shahedi et al. [23].

cluding patient selection, a restrictive definition of outcome, and the lack of ascertainment of diverticular bleeding, another important complication estimated to occur in 3–5% of the patients with diverticulosis [24]. Over an 11-year period, 23 patients (1%) developed rigorously confirmed diverticulitis for an incidence rate of 1.5 per 1,000 patient-years. The incidence rate increased to 6.0 per 1,000 patient-years when the diagnosis was expanded to cases of diverticulitis without confirmatory imaging or surgery (4.3%). The median time-to-event was 7.1 years. Younger patients had a higher risk of diverticulitis, with the risk increasing per year of life (Fig. 1). The study was retrospective, consisted predominantly of male patients (97%), and evaluated primarily the incidence of “rigorously defined (acute diverticulitis) confirmed by imaging or surgery”. Given that most cases of acute diverticulitis are uncomplicated in nature and are managed in the ambulatory setting [16] often without the need for imaging, it is likely that the authors underestimated the true incidence of acute diverticulitis. Further, the study population was identified retrospectively based on colonoscopy reports and may be an underrepresentation of the population-at-risk as endoscopists may fail to record this common incidental finding at colonoscopy in real life. Importantly, the study population consisted of patients with incidental diverticulosis on all-indication colonoscopies and not a well-defined cohort of patients undergoing screening colonoscopy.

The second study by Niikura et al. [24] from Japan examined the bleeding risk in 1,514 patients with asymp-

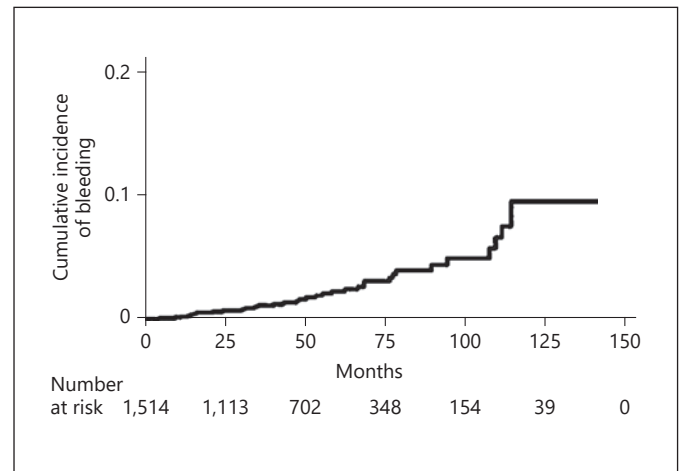


Fig. 2. Incidence of diverticular bleeding in 1,514 patients with asymptomatic diverticulosis identified over a 12-year period in Japan. Reprinted with permission from Niikura et al. [24].

tomatic diverticulosis identified over a 12-year period (2001–2013). The median follow-up period was 3.8 years. Diverticular bleeding occurred in 35 patients (definitive in 7, presumptive in 28). The cumulative incidence of diverticular bleeding was 0.21% at 12 months, 2.2% at 60 months, and 9.5% at 120 months, and the median time-to-event interval was 4.2 years (Fig. 2). The overall incidence rate of bleeding was 0.46 per 1,000 patient-years. On multivariate analysis, age ≥ 70 and bilateral diverticulosis were significant risk factors for bleeding. The limitations of the study were its retrospective nature as well as the all-indication colonoscopy study population. There was no information on the incidence of acute diverticulitis in that study.

The third study by Shayto et al. [25], from Lebanon and published in abstract form, involved a well-defined cohort of patients with incidental diverticulosis identified as part of a prospective cross-sectional study of healthy individuals undergoing colonoscopy for CRC screening, also designed to determine the prevalence and risk factors of diverticulosis. A total of 826 consecutive patients were included in the prospective screening study [26]. Three patients were excluded because of a prior history of diverticulitis. Incidental diverticulosis was noted in 224 out of 823 patients (27.2%) (mean age 62.3 ± 8.2 years; M: F = 1.15) and were isolated to the left colon (67.4%), the right side (5.8%), and both (22.8%). The natural history of incidental diverticulosis in this cohort of 224 patients was studied retrospectively after a median follow-up period of 7 years. Of those, 194 patients had up-to-date medical re-

cords and 144 were reached by telephone and consented to provide additional information. Nine patients were deceased at the time of follow-up due to unrelated causes. Over a mean follow-up of 7.0 years, complicated diverticular disease developed in 6 patients (4.2%): 4 patients developed acute diverticulitis, 1 had probable diverticular bleeding, and 1 developed both acute diverticulitis and diverticular bleeding. The time to event was 5.1 years, and the incidence rate was 5.9 per 1,000 patient-years. None of the variables collected at baseline colonoscopy including age, gender, obesity, exercise, alcohol, constipation, or the use of non-steroidal anti-inflammatory drugs or fiber intake was significantly associated with development of diverticulitis or diverticular bleeding.

In conclusion, colonic diverticulosis is a very common condition and appears to be on the rise due to changes in lifestyle, dietary habits, and an increased life span. Despite the many studies that have been conducted to examine the epidemiology and risk factors of diverticulosis, information on its natural history remain scarce. However, data from 3 recent studies show that the complications of diverticulosis are far less than previously suggested, in the order of 1.5–6 per 1,000 person-years for acute diverticulitis and 0.46 per 1,000 person-years for diverticular hem-

orrhage. It is important to note, however, that this conclusion is largely applicable to the recommended CRC-screening-age population (50–75 years) with incidental diverticulosis. The natural history in younger individuals who have a low prevalence of diverticulosis, in the geriatric population older than 75 years, and in those who fall outside the recommended CRC-screening-age group is unknown. More studies are needed to understand the risk factors of diverticulosis, to confirm these natural history studies, and to further investigate the presence of modifiable risk factors associated with the development of complications.

Statement of Ethics

This review does not involve recruitment of patients, inclusion of patient-specific information or identifiers, or breach of confidentiality. There are no ethical issues or conflicts involved.

Disclosure Statement

The authors declare no conflicts of interest.

References

- 1 Tursi A, Papagrigoriadis S: Review article: the current and evolving treatment of colonic diverticular disease. *Aliment Pharmacol Ther* 2009;30:532–546.
- 2 Tursi A, Papa A, Danese S: Review article: the pathophysiology and medical management of diverticulosis and diverticular disease of the colon. *Aliment Pharmacol Ther* 2015;42:664–684.
- 3 Everhart JE, Ruhl CE: Burden of digestive diseases in the United States part II: lower gastrointestinal diseases. *Gastroenterology* 2009;136:741–754.
- 4 Strate LL, Modi R, Cohen E, Spiegel BM: Diverticular disease as a chronic illness: evolving epidemiologic and clinical insights. *Am J Gastroenterol* 2012;107:1486–1493.
- 5 Coode PE, Chan KW, Chan YT: Polyps and diverticula of the large intestine: a necropsy survey in Hong Kong. *Gut* 1985;26:1045–1048.
- 6 Fatayer WT, MM AK, Shalan KA, Toukan AU, Daker MR, Arnaout MA: Diverticular disease of the colon in Jordan. *Dis Colon Rectum* 1983;26:247–249.
- 7 Templeton AW, Strate LL: Updates in diverticular disease. *Curr Gastroenterol Rep* 2013;15:339.
- 8 Peery AF, Barrett PR, Park D, Rogers AJ, Galanko JA, Martin CF, Sandler RS: A high-fiber diet does not protect against asymptomatic diverticulosis. *Gastroenterology* 2012;142:266–272.e261.
- 9 Song JH, Kim YS, Lee JH, Ok KS, Ryu SH, Lee JH, Moon JS: Clinical characteristics of colonic diverticulosis in Korea: a prospective study. *Korean J Intern Med* 2010;25:140–146.
- 10 Sharara AI, El-Halabi MM, Mansour NM, Malli A, Ghaith OA, Hashash JG, Maasri K, Soweid A, Barada K, Mourad FH, El Zahabi L: Alcohol consumption is a risk factor for colonic diverticulosis. *J Clin Gastroenterol* 2013;47:420–425.
- 11 Stollman NH, Raskin JB: Diagnosis and management of diverticular disease of the colon in adults. *Ad Hoc Practice Parameters Committee of the American College of Gastroenterology. Am J Gastroenterol* 1999;94:3110–3121.
- 12 Touzios JG, Dozois EJ: Diverticulosis and acute diverticulitis. *Gastroenterol Clin North Am* 2009;38:513–525.
- 13 Kohler L, Sauerland S, Neugebauer E: Diagnosis and treatment of diverticular disease: results of a consensus development conference. *The Scientific Committee of the European Association for Endoscopic Surgery. Surg Endosc* 1999;13:430–436.
- 14 Kozak LJ, DeFrances CJ, Hall MJ: National hospital discharge survey: 2004 annual summary with detailed diagnosis and procedure data. *Vital Health Stat* 2006;13:1–209.
- 15 Sandler RS, Everhart JE, Donowitz M, Adams E, Cronin K, Goodman C, Gemmen E, Shah S, Avdic A, Rubin R: The burden of selected digestive diseases in the United States. *Gastroenterology* 2002;122:1500–1511.
- 16 Unlu C, Gunadi PM, Gerhards MF, Boermeester MA, Vrouenraets BC: Outpatient treatment for acute uncomplicated diverticulitis. *Eur J Gastroenterol Hepatol* 2013;25:1038–1043.
- 17 Parks TG: Post-mortem studies on the colon with special reference to diverticular disease. *Proc R Soc Med* 1968;61:932–934.
- 18 Loffeld RJ, Van Der Putten AB: Diverticular disease of the colon and concomitant abnormalities in patients undergoing endoscopic evaluation of the large bowel. *Colorectal Dis* 2002;4:189–192.
- 19 Strate LL, Liu YL, Aldoori WH, Giovannucci EL: Physical activity decreases diverticular complications. *Am J Gastroenterol* 2009;104:1221–1230.

- 20 Strate LL, Liu YL, Aldoori WH, Syngal S, Giovannucci EL: Obesity increases the risks of diverticulitis and diverticular bleeding. *Gastroenterology* 2009;136:115–122.e111.
- 21 Strate LL, Liu YL, Huang ES, Giovannucci EL, Chan AT: Use of aspirin or nonsteroidal anti-inflammatory drugs increases risk for diverticulitis and diverticular bleeding. *Gastroenterology* 2011;140:1427–1433.
- 22 Strate LL, Keeley BR, Cao Y, Wu K, Giovannucci EL, Chan AT: Western dietary pattern increases, and prudent dietary pattern decreases, risk of incident diverticulitis in a prospective cohort study. *Gastroenterology* 2017;152:1023–1030.e1022.
- 23 Shahedi K, Fuller G, Bolus R, Cohen E, Vu M, Shah R, Agarwal N, Kaneshiro M, Atia M, Sheen V, Kurzbard N, van Oijen MG, Yen L, Hodgkins P, Erder MH, Spiegel B: Long-term risk of acute diverticulitis among patients with incidental diverticulosis found during colonoscopy. *Clin Gastroenterol Hepatol* 2013;11:1609–1613.
- 24 Niikura R, Nagata N, Shimbo T, Aoki T, Yamada A, Hirata Y, Sekine K, Okubo H, Watanabe K, Sakurai T, Yokoi C, Mizokami M, Yanase M, Akiyama J, Koike K, Uemura N: Natural history of bleeding risk in colonic diverticulosis patients: a long-term colonoscopy-based cohort study. *Aliment Pharmacol Ther* 2015;41:888–894.
- 25 Shayto R, Hanna K, Ziyade N, Chehab H, Chalhoub JM, Harb AH, Sarkis FS, Soweid A, Barada K, Mourad FH: Sa1411 The natural history of incidental colonic diverticulosis on screening colonoscopy: a prospective cohort study. *Gastroenterology* 2016;150:S308.
- 26 Sharara AI, Khalaf N, Sarkis F, El-Halabi MM, Habib R: Su1072 A novel risk prediction rule for advanced neoplasia at first screening colonoscopy for average risk individuals. *Gastroenterology* 2013;144:S-392.