Diverticular disease: Epidemiology and management

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Diverticular disease of the colon is among the most prevalent conditions in western society and is among the leading reasons for outpatient visits and causes of hospitalization. While previously considered to be a disease primarily affecting the elderly, there is increasing incidence among individuals younger than 40 years of age. Diverticular disease most frequently presents as uncomplicated diverticulitis, and the cornerstone of management is antibiotic therapy and bowel rest. Segmental colitis associated with diverticula shares common histopathological features with inflammatory bowel disease and may benefit from treatment with 5-aminosalicylates. Surgical management may be required for patients with recurrent diverticulitis or one of its complications including peridiverticular abscess, perforation, fistulizing disease, and strictures and/or obstruction.

Key Words: Acute diverticulitis; Diverticulitis; Epidemiology; Recurrent diverticulitis; Segmental colitis associated with diverticula (SCAD)

Diverticular disease is one of the most common problems encountered by general surgeons and gastroenterologists. The term refers to complications that arise from colonic diverticulosis including lower gastrointestinal hemorrhage, inflammation, pain, abscess formation, fistula, strictures, perforation and death (1). It is an important cause of morbidity and a significant economic burden (1,2). In 2004, 312,000 admissions and 1.5 million days of inpatient care per year in the United States were due to diverticular disease, at a cost of more than $US2.6 billion (3,4). A Canadian study (5) estimated that 133,875 admissions for diverticular disease occurred in the province of Ontario between 1998 and 2001. In this present review, we evaluate the epidemiology of diverticular disease and highlight changing trends in its demographics in North America and worldwide. We also outline the current recommendations for the medical and surgical management of diverticular disease.

EPIDEMIOLOGY

The incidence of diverticular disease has increased over the past century (2,5,6). Autopsy studies from the early part of the 20th century reported colonic diverticula rates of 2% to 10% (6). This has increased dramatically over the years. More recent data (5) suggest that up to 50% of individuals older than 60 years of age have colonic diverticula, with 10% to 25% developing complications such as diverticulitis. Hospitalizations for diverticular disease have also been on the rise. According to an American study evaluating hospitalization rates between 1998 and 2005 (2), rates of admission for diverticular disease increased by 26% during the eight-year study period. Similar trends have been observed in Canadian and European data over the same time period (5,7).

Diverticular disease has traditionally been believed to be a disease affecting the elderly (8). The prevalence of diverticular disease is as high as 65% by 85 years of age and estimated to be as low as 5% in those 40 years of age or younger (8). However, more recent literature has reported an increase in the incidence of diverticular disease among younger patients. For example, a large review of the Nationwide Inpatient Sample (NIS) of 267,000 admissions for acute diverticulitis between 1998 and 2005 (2) showed that the average age of patients decreased over the study period from 64.6 to 61.8 years. Incidence rates increased most dramatically among groups 18 to 44, and 45 to 64 years of age (incidence per 1000 population: 0.151 to 0.251, and 0.659 to 0.777, respectively). In contrast, incidence remained stable over the study period in persons between 65 and 74 years of age, and actually decreased in persons 75 years of age or older. Moreover, a very high incidence of diverticular disease in young patients was reported in a review of 238 patients admitted with diverticulitis to the surgical service at the Medical Center Hospital in San Antonio, Texas (USA) between 1981 and 1990 (9). In this review, 26% of patients were 40 years of age or younger. These patients had a more aggressive form of disease, requiring more surgical intervention than older patients, and they exhibited a five-fold increase in the risk of complications, such as fistula, compared with their older counterparts. Given the presumption of the low incidence of diverticular disease in young patients, nearly one-half of these patients were often misdiagnosed at presentation – most commonly with appendicitis.

Sex differences among patients with diverticular disease have also been noted throughout the literature, with more recent data showing a change in sex demographics. For example, early reports (10) suggested a higher incidence of diverticular disease among men. A review of all patients admitted to Massachusetts General Hospital (Massachusetts, USA) between 1964 and 1973 (1) showed no difference between sexes (1). However, more recent data have shown that although diverticular disease is still more common among men 50 years or younger, the incidence among women predominates in older age groups (5,7,9). The ratio of men to women with diverticulitis among 61 patients admitted to the Medical Center Hospital in San Antonio who were younger than 40 years of age was 2:1, while women were
more frequently admitted in the older age group with a ratio of 1.5:1 (9). The rates of hospitalization were higher among men younger than 50 years of age, but higher for women older than 50 years of age in a review of hospital discharges from 1989 to 2000 in England (United Kingdom) (7). This was consistent with the findings of a Canadian study (5) reporting that men had a hospitalization rate for diverticular disease of 45 per 100,000 in the 40- to 49-year age group compared with 38 per 100,000 in the same age group of women. The incidence was 299 per 100,000 in the 80 years and older age group among men, and 436 per 100,000 in the same age group among women. Women had a higher overall admission rate compared with men between 1998 and 2005 in the review of the NIS database (2) mentioned above. Men accounted for 39% of admissions compared with 60.7% for women. This pattern was still evident at the end of the study period (female rate of admission 58.9%; male rate of admission 41.1%). Possible hypotheses for these sex differences have included the protective effect of testosterone on preventing weakening of the colonic wall, and the effect of pregnancy and labour and delivery on contributing to weakening of the wall of the colon.

Diverticular disease has long been regarded as a disease of western countries. The highest prevalence of this condition is in the United States, Europe and Australia, where approximately 50% of the population 60 years of age and older have diverticulosis (5,6). This common occurrence is in contrast to that in the developing world, where countries in Africa and Asia have prevalence rates of less than 0.5% (6,11,12). The western diet, particularly its deficiency in dietary fibre, has long been implicated as a causative factor for these geographical variations (6,13-16). This hypothesis was supported by a study that compared stool weight and transit time in 1200 individuals in the United Kingdom and rural Uganda (13). The United Kingdom subjects, who were shown to have lower fibre intake, had a transit time of 80 h and a mean stool weight of 110 g/day. This was significantly lower than in the Ugandan subjects, who had much shorter transit times (34 h) and greater mean stool weights (450 g/day). The prolonged transit time and small stool volumes were believed to predispose to diverticular disease by increasing intraluminal pressure. Moreover, there is growing evidence that the rates of symptomatic diverticular disease are on the rise because areas in the developing world are becoming increasingly westernized (14,15). For example, the rates of diverticular disease have increased among urban black populations of South Africa compared with rural black populations in the same country (14). The role of dietary fibre deficiency as a contributor to diverticular disease was further supported by a large prospective cohort study of more than 47,000 men who were followed over a four-year period (16). Dietary fibre intake was found to be inversely associated with the risk of developing diverticular disease, with an RR of 0.58 (95% CI 0.41 to 0.83; P=0.01).

In addition to the geographical variability in the prevalence of diverticular disease, there is significant variability in the location of diverticula within the colon in different regions of the world. In western countries, it has been well described that diverticulosis is primarily left sided, particularly involving the sigmoid colon (2,6-8). This is in contrast to findings in Asia, where right-sided diverticulosis dominates (17-19). In a review of 615 cases of diverticulosis detected on double-contrast barium enema examinations between 1975 and 1982 in Tokyo, Japan (17), 70% were right sided. Similar diverticular distribution has been shown in Hong Kong and Singapore (18,19). The reason for these differences remains unclear. Early hypotheses suggested that left-sided diverticula were acquired, whereas right-sided diverticula were more likely to be true diverticula and, thus, congenital (20,21). However, subsequent studies have shown that, similar to left-sided diverticula, the majority of right-sided diverticula are 'false' and are likely acquired (18,22). In fact, as Asian populations have begun to adopt a more westernized diet, the rates of diverticular disease have been shown to increase to the same extent noted in the west (17). This increase in diverticular disease, however, remains predominantly right sided. Factors other than deficiencies in dietary fibre are likely to play a role in the development of right-sided diverticulosis as demonstrated by studies that show that even with a high-fibre diet, the rates of right-sided disease are high. For example, a study from China (23) reported a diverticulosis rate of 62% in patients with high-fibre intake (greater than 14 g/day). More research is needed in this area to better identify potential causative factors.

**MANAGEMENT OF DIVERTICULAR DISEASE**

**Diverticula-associated pain**

The clinical spectrum of diverticular disease is variable, ranging from uncomplicated presentations, such as episodic pain or mild diverticulitis, to potentially life-threatening complicated disease such as abscess, perforation or hemorrhage. Episodes of mild nonspecific abdominal pain, often left sided, can sometimes be attributed to diverticulitis (24). This pain usually occurs in the absence of fever or abnormal laboratory investigations, and is accompanied by an unremarkable physical examination. It may be difficult to clearly associate these episodes with the presence of diverticulosis. These patients can often be observed without any intervention. Alternatively, there is some evidence that increasing dietary fibre may improve symptoms. This was reported in a small randomized trial of 18 patients (25) that showed significant improvement in pain and a decreased number of painful episodes in the high-fibre group at three months.

**Segmental colitis associated with diverticula**

The clinical entity of segmental colitis associated with diverticula (SCAD) has become increasingly recognized and is characterized by friable mucosa in the region of diverticula, but typically not involving the diverticula itself and never involving the rectum (26). Patients may present with chronic abdominal pain, particularly left sided, with occasional hematochezia. Pathologically, the mucosa can be indistinguishable from inflammatory bowel disease (27). Case reports have suggested that patients with SCAD may progress to develop Crohn's disease or ulcerative colitis, hypothesizing that there is a pathophysiological link (28). Given this finding, some investigators have evaluated the use of 5-aminosalicylates as a therapy (29). In an uncontrolled Italian study (30), 70 of 86 patients treated with mesalamine 2.4 g/day for 10 days followed by eight weeks of treatment with 1.6 g/day showed complete resolution of symptoms with no recurrence.

**Uncomplicated diverticulitis**

Diverticulitis without any significant complications accounts for more than 75% of cases (31,32). These patients typically present with left lower quadrant pain, fever and leukocytosis, and the diagnosis is confirmed on computed tomography scan. The mainstay of treatment in these patients with uncomplicated diverticulitis is antibiotics, bowel rest or a clear fluid diet, with pain control as needed (24). Antibiotic therapy should be aimed at the usual enteric bacteria with Gram-negative and anaerobe coverage. Common outpatient regimens include oral ciprofloxacin and metronidazole, or amoxicillin/clavulanate. For hospitalized patients, an intravenous regimen with broad-spectrum coverage should be selected and may include the following: ceftriaxone and metronidazole; monotherapy with beta-lactam/beta-lactamase coverage should be selected and may include the following: ceftriaxone. The duration of treatment is typically seven to 10 days.

The decision to admit a patient is based on their clinical status at presentation, the absence of high fever, or significant laboratory or radiographic abnormalities (Figure 1) (24). These patients should be reliable and well supported at home, with the ability to return to hospital if their clinical condition worsens. The immunosuppressed patient should be admitted even if the presentation is mild because they may have more subtle signs, and some data suggest that they are less likely to respond to conventional medical therapy (35). Patients with uncomplicated diverticulitis should be followed and be expected to improve two to three days after presentation, at which time, diet can slowly be advanced (24). Failure to improve should prompt repeat imaging to search for complications and undergo surgical consultation.
Approximately 25% of patients will require surgery for nonresolving diverticulitis (37). Four to six weeks following resolution of the first attack of diverticulitis, patients should undergo endoscopic evaluation to characterize the distribution of diverticula and to exclude any other diagnosis such as colorectal cancer (36).

There are limited data regarding strategies to reduce the risk of diverticulitis recurrence. Given the epidemiological associations between deficiencies in fibre and the incidence of diverticulitis described above, some studies have suggested that a high-fibre diet may be an effective prevention strategy (5,6,12-16); however, supportive evidence is limited. One of the few randomized studies to evaluate this strategy involved 58 patients randomly assigned to a diet high in bran crispbread, ispaghula drink or placebo (38). There was no difference in the subsequent development of symptomatic diverticular disease among the three groups, although the high-fibre group experienced lower rates of constipation. This is in contrast to a small study of 18 patients (25) that showed decreased episodes of diverticulitis at three months in a high-fibre group. Given its potential benefit, the most recent guidelines from the American Society of Colon and Rectal Surgeons (39) advocate the use of a high-fibre diet after resolution of diverticulitis in an attempt to reduce recurrence. A large number of physicians recommend a diet low in nuts and seeds in an effort to reduce the risk of recurrent diverticulitis. In fact, a survey of 373 colorectal surgeons (34) suggested that approximately one-half recommend the avoidance of seeds and nuts. However, a large cohort study of 47,000 male health professionals followed over an 18-year period (40) found no association between a diet high in corn, seeds or nuts, and subsequent risk of developing diverticulitis. Thus, avoidance of seeds and nuts is not supported by the literature and likely has no role in the management of these patients.

Recurrent diverticulitis

Approximately one-third of patients will experience recurrence of diverticulitis following an initial episode of uncomplicated diverticulitis (11,12). Some of the earlier literature suggested that recurrent diverticulitis typically had a more severe course. Consequently, guidelines in the 1990s and earlier recommended elective sigmoid resection following the second episode of diverticulitis (11,36). However, more recent evidence (41,42) has shown that recurrent diverticulitis does not necessarily follow a more aggressive course. The most recent guidelines released by the American Society of Colon and Rectal Surgeons (39) recommend that the decision to perform a sigmoid resection following an episode, and recovery following a second episode of acute diverticulitis, should be made on a case-by-case basis, taking into consideration the patient’s age and comorbidities, as well as the frequency and severity of the attacks. These recommendations are consistent with those from the Society for Surgery of the Alimentary Tract (43). Although there is no consensus on the threshold number of attacks of diverticulitis before surgery is recommended, a decision analysis (44) showed that deferring surgery until the fourth attack decreased mortality by 0.5% and need for colostomy by 0.7% compared with operating after the second attack.

Diverticulitis in younger patients

The optimal management of young patients presenting with uncomplicated diverticulitis is unclear. As mentioned above, some evidence suggests that young patients are more likely to experience a virulent course and are at a higher cumulative risk of recurrence because of their young age (9,29). This has led some experts to recommend surgery for young patients (younger than 50 years of age) after the initial episode of diverticulitis (9,29). For example, in a study of 52 patients younger than 50 years of age admitted with diverticulitis (45), those younger than 40 years of age had a higher rate of complicated disease compared with those older than 40 years of age (72% versus 35%); and they were significantly more likely to require immediate surgery (40% versus 13%, respectively; P=0.04). However, the most recent guidelines from the American Society of Colon and Rectal Surgeons (36,39) advocated that the timing for surgery in younger patients with acute diverticulitis be determined on a case-by-case basis.

The optimal management of young patients presenting with uncomplicated diverticulitis appears to be increasing (2). A 38% increase in elective operations was noted in a review of the NIS between 1998 and 2005 (2), with the most significant increase reported in patients 44 years of age or younger (73% increase). These trends have been accompanied by declines in the rates of surgical mortality (1.6% to 1.0%) and length of hospital stay (5.9 days to 5.3 days). More than 90% of elective surgeries for diverticulitis resulted in primary anastomoses. The American Society of Colon and Rectal Surgeons has recommended laparoscopic resection whenever possible (39). A Dutch randomized controlled trial (46) that randomly assigned 104 patients to either open or laparoscopic sigmoid resection found that a laparoscopic approach was associated with fewer major complications, less pain and shorter length of hospital stay.

Complicated diverticulitis

Up to 25% of patients with acute diverticulitis develop complicated disease (7). This includes abscess formation, fistulas, strictures/obstruction and perforation. Abscess occurs with the perforation of a diverticulum that is usually contained (24). Small abscesses (smaller than 3 cm) can be treated with antibiotics alone (47). Larger abscesses (larger than 4 cm) may require computed tomography-guided percutaneous drainage followed by eventual surgery after resolution of the abscess (48). Perforating diverticular disease may also lead to fistula, with the most common locations being colovesical and colovaginal (49). Fistula complications require surgical management.

Recurrent episodes of diverticulitis can lead to fibrosis and strictureing of the colon, resulting in obstruction most often in the sigmoid colon (24). In managing these strictures, malignancy must first be excluded with surgery indicated if this cannot be definitively achieved (39). Endoscopic dilation can often provide temporary relief of symptoms and allow more access to a stricture to obtain biopsy (50). Moreover, the role of endoscopic stenting in diverticular disease...
is evolving. In a review of 16 patients who underwent stenting for diverticular strictures (51), the procedure was successful in all individuals, allowing subsequent elective resection to be single stage. Similar results have been reported in smaller series (52), all of which support the role of stenting as a temporary measure to enable more elective surgery when the patient’s status is more optimized. Although frank perforation and peritonitis are uncommon complications of diverticulitis, subsequent mortality may be as high as 30% (53). Thus, prompt recognition of this complication along with early resuscitation, antibiotics and exploratory surgery are cornerstones of management. These patients usually require a Hartmann’s procedure, with subsequent closure of colostomy after several months (54). Emergent surgeries for complicated diverticular diseases are commonly performed in multiple stages, usually involving temporary stomas (54). However, even in emergency settings, primary anastomosis may be considered under certain conditions. The Hinchee’s classification system is a decision-making tool designed to aid in determining the suitability of primary anastomosis in complicated diverticular disease (55). The classification is characterized by the following four stages: pericolic or mesenteric abscess; walled-off pelvic abscess; generalized purulent peritonitis; and generalized fecal peritonitis. Although somewhat controversial, some studies, including a recent meta-analysis (56), suggest that patients with stage I or II disease can be safely treated with a primary anastomosis, even in the emergent setting. However, the review of the NIS database from 1998 to 2005 (2) reported low rates of primary anastomosis in the acute setting.

SUMMARY
Diverticular disease is an increasingly common problem that has widely varying presentation ranging from mild outpatient-treated problems to life-threatening perforations requiring emergency surgery. A higher index of suspicion in younger patients is needed because diverticular disease appears to be increasing in incidence among this age group. While it remains primarily a surgically treated disease, medical treatments, such as mesalamine and evolving endoscopic techniques, allow the gastroenterologist to play an important role in managing these patients. It remains a clinical challenge for physicians at all levels including general practitioners, emergency room physicians, gastroenterologists and general surgeons.

KEY POINTS
• A diagnosis of diverticular disease should not be overlooked in younger patients because hospitalization rates in those younger than 40 years of age has significantly increased over the past decade.
• In most cases, uncomplicated acute diverticulitis may be medically managed with antibiotics and bowel rest or clear liquid diet.
• Uncomplicated acute diverticulitis can be managed on an outpatient basis in selected patients who do not have comorbidities (including immunocompromised state) and can tolerate a liquid diet in the absence of fever, significant leukocytosis or evidence of complicated disease on imaging.
• Recurrent diverticulitis or complications of diverticulitis including abscess, perforation, fistulizing disease and strictures/obstruction usually require surgery.
• SCAD has histopathological features similar to inflammatory bowel disease and often responds to 5-aminosalicylic therapy.

REFERENCES
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