The Burden of Diverticular Disease and Its Complications: West versus East

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Keywords

Diverticular bleeding · Diverticulosis · Diverticulitis · East · West

Abstract

Background: Colonic diverticulosis is prevalent and increasing not only in Western but also in Asian countries. Diverticulosis can be complicated by diverticulitis and diverticular bleeding. Diverticular disease is a burdensome digestive disease, because it is a major cause of hospital admissions and is associated with significant health-care costs. **Summary:** The incidence of diverticulosis increases with age. Most cases of diverticulosis in Western countries involve the left side of the colon, while diverticulosis is predominantly present on the right side of the colon in Asian countries. The incidence of diverticulitis also increases with age. Diverticulitis is predominantly located on the left side of the colon in Western countries, while it is predominantly located on the right side of the colon in Asian countries. The overall complication rate is higher in left-sided than in right-sided diverticulitis. The incidence of diverticular bleeding also increases with age. The right colon is the source of diverticular bleeding in more than 50% of patients in Western countries. In

Asian countries, age greater than 70 years and both-sided diverticulosis increase the bleeding risk. **Key Messages:** In Western countries, diverticulosis and diverticulitis are predominantly located on the left side of the colon, whereas they are predominantly present on the right side of the colon in Asian countries. Diverticular bleeding is predominantly located on the right side in Western countries, and both-sided diverticulosis increases the risk of bleeding in Asian countries. Diverticular disease with complications requires admission and operation; moreover, it recurs frequently. Therefore, diverticular disease is associated with a significant economic burden in terms of health-care costs and resource utilization.

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Introduction

The prevalence of colonic diverticulosis is increasing in Western and Asian countries [1–3]. Diverticular disease is defined as clinically significant and symptomatic diverticulosis complicated by diverticulitis, diverticular bleeding, segmental colitis associated with diverticula, or symptomatic uncomplicated diverticular disease; these

Table 1. Differences in diverticular disease between Western and Asian countries

	Western countries	Asian countries
Prevalence of diverticulosis	5–45%	13–25%
Location of diverticulosis	R < L	R > L, both
Location of diverticulitis	R < L	R > L
Location of complication of diverticulitis	R < L	R < L
Mortality rate of diverticulitis	0.96–2.2%	0.63%
Non-Asian	2.2%	
Asian	4.2%	
Location of diverticular bleeding	R > L	both
Mortality of diverticular bleeding	1.1–4.1%	0.7–4.1%

R, right-sided colon; L, left-sided colon; both, both-sided colon.

are the so-called complications of colonic diverticulosis. The incidence of diverticular disease is increasing over time in both Western and Asian countries [3]. Diverticular disease is responsible for a high number of gastrointestinal admissions and clinical visits. Moreover, it often recurs. Therefore, it is associated with a significant economic burden in terms of health-care costs, hospitalization, and resource utilization not only in Western but also in Asian countries. Furthermore, the incidence of diverticular disease appears to be increasing with aging [4, 5]. However, the prevalence of diverticulosis, diverticulitis, and diverticular bleeding in Western countries is different from that in Asian countries.

The distribution and clinical characteristics of colonic diverticulosis, diverticulitis, and diverticular bleeding, in addition to the differences in presentation between Western and Asian countries, are reviewed in this article.

Diverticulosis

Western countries have prevalence rates of 5–45% for diverticulosis, depending on the method of diagnosis and the age of the population (Table 1) [6, 7]. Prior studies have shown an increase in the prevalence of diverticulosis from the mid-1990s through the early part of the current century. This increase has been most notable among young individuals [1]. Approximately 95% of patients with diverticulosis had diverticula in the sigmoid colon [8]. Diverticula were located only in the sigmoid colon in 65% of patients and in other parts of the colon, along with the sigmoid colon, in 24% of patients; they were equally distributed throughout the colon in 7% of patients and were located in a segment proximal to the sigmoid colon

in 4% of patients. In one prospective study of 624 individuals undergoing screening colonoscopy in the United States, 260 (42%) had colonic diverticulosis [9]. Participants with diverticula were more likely to be older and male; moreover, they had a higher body mass index and waist circumference than those without diverticula. The prevalence of diverticulosis was 35% in those younger than 50 years, 40% in individuals 50–59 years old, and 58% in those older than 60 years [9]. The prevalence of diverticulosis according to the Clinical Outcomes Research Initiative National Endoscopy Database was 33% in individuals 50–59 years old and 71% in those older than 80 years [10].

The distribution of diverticula differs significantly according to race. Among white persons, 75% of diverticula were located in the sigmoid colon, 11% in the descending colon or splenic flexure, 6% in the transverse colon, and 8% in the ascending colon or hepatic flexure [9]. In black persons, 64% of diverticula were located in the sigmoid colon, 8% in the descending colon or splenic flexure, 7% in the transverse colon, and 20% in the ascending colon or hepatic flexure. The distribution of the diverticula in the ascending colon or hepatic flexure was higher in blacks than in whites [9]. This finding supports a possible genetic contribution to the development of diverticulosis, but this distribution may also be caused by differences in health behaviors or environmental factors.

Similarly, a British study of 1,000 barium enemas in patients with gastrointestinal symptoms found that black Africans were more likely to have diverticulosis that involved the proximal colon than white persons [11]. It was found that Asians and blacks, including those from the Caribbean, were protected against left-sided diverticular disease compared to whites, with the odds ratio of left-

sided diverticular disease being 0.23 (95% CI 0.10–0.53, $p < 0.001$) and 0.25 (95% CI 0.14–0.43, $p < 0.001$) of that in whites, respectively. In right-sided diverticular disease, a 1-year increase in age increased the odds by 4% (95% CI 2–6, $p < 0.001$). Women were 0.60 times (95% CI 0.40–0.90, $p = 0.01$) less likely than men, while black Africans were 3.51 times (95% CI 1.70–7.24, $p < 0.001$) more likely than whites, to have right-sided diverticular disease.

The prevalence of diverticulosis has been estimated prospectively in several colonoscopy-based studies in Asia. The prevalence of diverticulosis in Lebanon was similar to that in the United States [12]; that is, the rate was 33% (mean age: 61 years), and most subjects had distal diverticulosis. However, other studies from the Middle East suggest a much lower prevalence. The prevalence of diverticulosis is between 13 and 25% in the Far East, and diverticulosis is predominantly right-sided (Table 1).

Additionally, the prevalence of diverticulosis was 12% in Korea (mean age: 51 years) [13] and 14% in Taiwan (mean age: 53 years) [14]. Barium studies in Japan have shown a significant increase in the prevalence of diverticulosis in the late 1900s, from 2.1% in 1967 and 7.8% in 1983 to 28% in 1997; the increase may be associated with the adoption of a Western lifestyle [15–18]. Yamamichi et al. [2] reported that the incidence of diverticulosis was 13.0% from 1990 to 2000 and 23.9% from 2001 to 2010; the latter value was much higher than the former in all age groups and in both sexes. The incidence of left-sided diverticular disease has markedly increased with age but has not significantly changed over time. In Korea, 15% of patients with colonic diverticulosis had distal diverticula [13], whereas half of the Japanese and Taiwanese populations with colonic diverticulosis had distal diverticula [14, 15].

Increasing age might be a risk factor for colonic diverticula across all of these populations; therefore, diverticula are evidently acquired in these populations and are not congenital [9]. Nagata et al. [3] reported that the proportion of colonic diverticulosis increased significantly from 66.0% in 2003 to 70.1% in 2011 and was affecting an increased number of patients aged 60 years and older. Japan has reported an increase in the prevalence of right-sided diverticulosis similar to the increase in left-sided diverticula seen in Westernized countries [19]. The frequency in patients with the right-sided type was 9.7%, which was 5 times greater than that of patients with the left-sided type; however, the frequency of both types increases with advancing years. The left-sided type increased in frequency with increasing age up to the eighth decade and showed no difference in numbers between

men and women, whereas the right-sided type was more common in younger people and more predominant in men, with a peak in the seventh decade. The changing frequency of the bilateral type, with respect to both year and age, was similar to that of the left-sided type. In Asian countries, right-sided diverticulosis is thought to be of congenital origin, and diverticula developing subsequently on the left may extend into the bilateral colon [12, 17].

Diverticulitis

Diverticulitis (Fig. 1) may be acute or chronic and uncomplicated or complicated by a diverticular abscess, fistula, bowel obstruction, or free perforation. Approximately 4–15% of patients with diverticulosis develop diverticulitis [1, 20, 21]. A nationwide inpatient study of hospitalizations in the United States showed an increase in admissions for acute diverticulitis by 26% from 1998 to 2005 [22]. Moreover, the prevalence of hospitalizations for diverticulitis peaked in 2008 (74.1 of 100,000 patients in 2000, 96.0 of 100,000 patients in 2008, and 91.9 of 100,000 patients in 2010, respectively). Over the past 10 years, the prevalence of hospitalizations for diverticulitis has increased and then plateaued [1].

In Western countries, acute diverticulitis is predominantly left-sided, with right-sided diverticulitis being present in only 1.5% of patients (Table 1) [23]. In a retrospective cohort of patients in the United States with acute diverticulitis, 72% had the disease in the sigmoid colon, 33% in the descending colon, 3% in the transverse colon, and 5% in the ascending colon. The prevalence of diverticulitis was highest in whites (75.5 of 100,000 patients in 2010) [1].

The incidence of diverticulitis increases with age. The mean age at admission for acute diverticulitis is 63 years [24]. While the incidence of acute diverticulitis is lower in younger individuals, approximately 16% of admissions for acute diverticulitis occur among patients aged less than 45 years [4].

The prevalence of diverticulitis is higher in women than in men [1]. Although a male preponderance was noted in early series, subsequent studies have suggested either an equal distribution between the sexes or a female preponderance [25]. Under the age of 50 years, the prevalence of diverticulitis is more common in men; there is a slight female preponderance present between the ages of 50 and 70 years and a marked female preponderance over the age of 70 years [26–28].

Fig. 1. **a** A 41-year-old Japanese man with diverticulitis in the sigmoid colon. A computed tomography (CT) scan shows a diverticulum with a thick wall and mild induration of the perisigmoid fat, as well as thickening of the sigmoid mesocolon. **b** The same man with recurrence of diverticulitis in the sigmoid colon 2 years later. A CT scan shows a diverticulum with a thick wall and mild induration of the perisigmoid fat, as well as thickening of the sigmoid mesocolon. **c** The same man with recurrence of diverticulitis in the ascending colon 4 years later. A CT scan shows a diverticulum with a thick wall and mild induration of the periascending fat, as well as thickening of the ascending mesocolon.

Approximately 25% of patients with acute diverticulitis have associated acute or chronic complications [29]. Diverticular abscesses occur in approximately 17% of patients hospitalized with acute diverticulitis [30, 31]. Intestinal obstruction can occur because of luminal narrowing due to inflammation or compression from a diverticular abscess. Inflammation from acute diverticulitis may result in the formation of a fistula to the adjacent viscera, especially the bladder [32]. Perforation with generalized peritonitis may result from rupture of a diverticular abscess into the peritoneal cavity or from free rupture of an inflamed diverticulum. Although only 1–2% of patients with acute diverticulitis have a perforation with purulent or fecal peritonitis, mortality rates approach 20% [33, 34].

In contrast with Western countries, right-sided diverticulitis has a higher incidence in Asian populations (Table 1) [35–39]. In Singapore, Wong et al. [35] reported that 38% of diverticulitis was on the right side and 49% was on the left side of the colon. In Japan and Korea, diverticulitis was more common on the right side of the colon [36–39]. Kim et al. [36] reported that diverticulitis occurred on the right side of the colon in 53 (76%) out of 70 cases and on the left side of the colon in 17 cases (24%). The mean age of patients with right-sided diverticulitis was significantly lower than that of patients with left-sided diverticulitis. However, the overall complication rate was higher in left-sided than in right-sided diverticulitis. Oh et al. [37] reported that diverticulitis, which was treated surgically, occurred on the right side of the colon in 31 cases (46%) and on the left side of the colon in 37 cases (54%). The proportion of left-sided disease cases was significantly higher than that in previous studies from 1994 and 2001 (27.5 vs. 48.1%). Patients with right-sided disease were significantly younger (50.9 vs. 64.0 years). Furthermore, left-sided disease was significantly associated with a higher incidence of complicated diverticulitis (89.2 vs. 57.5%), combined resection of the small intestine or bladder due to extensive inflammation (21.6 vs. 5.0%), operative complications (51.4 vs. 27.5%), and in-hospital mortality (10.8 vs. 0%), along with a longer postoperative hospitalization duration (21.3 ± 10.2 vs. 10.6 ± 8.1 days). Manabe et al. [38] reported the results of a Japanese multicenter study, which showed that although diverticulitis more frequently affected the right colon (70.1%) among 1,112 patients, diverticulitis of the left colon was significantly more frequent (61.0%) in elderly patients.

Schneider et al. [39] reported that the mortality rate in 310,983 emergency department visits for primary diverticulitis was 0.96%, based on the 2010 Nationwide Emergency Department Sample in the United States. Choi et

Fig. 2. A 72-year-old Japanese man with diverticular bleeding in the ascending colon. Colonoscopy shows bleeding from the base of a diverticulum.

al. [40] reported, based on the National Inpatient Sample with diverticulitis and colectomy in the United States, that Asian inpatients with diverticulitis were more likely to undergo a right hemicolectomy than were non-Asian inpatients (22.7 vs. 4.1%) and that there were statistically significant differences in mortality (non-Asian 2.2 vs. Asian 4.2%) (Table 1). In contrast, Manabe et al. [38] reported that the mortality rate of colonic diverticulitis in 21 Japanese hospitals was significantly higher in patients with complications than in those without complications (2.8 vs. 0.2%) (Table 1). In Korea, the mortality rate was significantly higher in patients with left-sided colonic diverticular disease than in patients with right-sided colonic diverticular disease (10.8 vs. 0%) [37].

Diverticular Bleeding

Among patients with diverticulosis, diverticular bleeding occurs in approximately 5–15% and is massive in one-third of patients (Fig. 2) [41]. The prevalence of hospitalizations per 100,000 persons for diverticular bleeding decreased over a 10-year period from 32.5 to 27.1 in the United States [1]. Approximately 15–25% of adults with uncomplicated diverticula will progress to bleeding [42]. One study found a rate of 3% in patients with asymptomatic diverticulosis [43], but this was not a cohort study.

Another study reported that the incidence of bleeding was 0.30 per 1,000 patient-years [44], but the diagnosis of asymptomatic and complicated diverticulosis in this study was based on questionnaires, not colonoscopy. Because this bleeding can be massive and recurs frequently in 14–38% of patients [43, 45], it involves repeated examination, hospitalization, and blood transfusion, with a substantial adverse impact on quality of life.

The incidence of diverticular bleeding increases with age, and 46% of patients were older than 80 years [1]. Both women and men had similar rates of diverticular bleeding; however, diverticular bleeding was decreasing in men compared to women.

Colonic diverticular bleeding occurs on the right side of the colon in 50–90% of patients with diverticula (Table 1) [42, 46, 47]. This reveals a marked increase in the risk of bleeding for the right-sided diverticula, as in Western countries only 25% of diverticula are located on the right side of the colon [48]. The prevalence of diverticular bleeding was higher in black persons (34.4 of 100,000 in 2010) than in white persons [1]; therefore, hospitalization for diverticular bleeding was significantly more common in black persons than in white persons. The distribution of the diverticula in the ascending colon or hepatic flexure was higher in blacks than in whites [9].

In Asia, Niikura et al. [5] reported that the cumulative incidence of bleeding from diverticulosis was approximately 2% in 5 years and 10% in 10 years and that the overall incidence was 0.46 per 1,000 patient-years. An age of more than 70 years and both-sided diverticulosis increased the risk of bleeding. Nagata et al. [3] reported that diverticular bleeding was found in 427 of 28,192 patients (1.5%; mean age: 69.7 years) with a higher incidence in men (66.3%); the bleeding was predominantly of the both-sided type (47.0%) (Table 1). The proportion of diverticular bleeding was increasing significantly from 1.02% (22 of 2,157 subjects) in 2003 to 1.67% (69 of 4,159 subjects) in 2011, and it was associated with an increased number of patients aged 40–59 years. Kinjo et al. [49] also reported that patients with colonic diverticular bleeding were older male patients (≥ 70 years old) and that colonic diverticular bleeding was more frequent in the late-period group (2007–2013) than in the early-period group (1995–2006).

Dao et al. [50] reported that the overall mortality rate among a total of 99,415 discharges for diverticular hemorrhage in the National Inpatients Sample in the United States was 1.8% and that transferred patients had higher in-hospital mortality rates than admitted patients (3.5 vs. 1.8%, $p < 0.001$). Another study in Western countries re-

ported that the mortality rate was 1.1–4.1% (Table 1) [51, 52]. Chen et al. [53] reported that the overall mortality rate in 73 patients with colonic diverticular bleeding in Taiwan was 4.11%. In contrast, Niikura et al. [54] reported, using a national database in Japan, that the in-hospital mortality rate in patients with diverticular bleeding was 0.7% (62/8,422) (Table 1).

Segmental Colitis

Segmental colitis associated with diverticulosis (SCAD) or diverticular colitis is defined as a type of active chronic inflammation that resembles inflammatory bowel disease. It mostly appears in the sigmoid colon affected by diverticular disease with sparing of the rectum and proximal colon [55–58]. The prevalence of SCAD in patients with diverticulosis ranges from 0.26 to 1.5% [56–58]. The prevalence of SCAD is higher in men, with a mean age of 64 years [58]. However, SCAD has also been reported in younger patients. Only a few cases of SCAD have been reported in Asian countries.

Burden of Diverticular Disease

Approximately 25% of patients with acute diverticulitis develop associated acute or chronic complications requiring admissions and operations. Moreover, diverticular disease recurs frequently. Diverticular disease is associated with a significant economic burden in terms of health-care costs and resource utilization [59]. There are more than 2.5 million clinic visits, 330,000 emergency department visits, and 200,000 hospital admissions for diverticular disease without hemorrhage each year in the United States [60]. Delvaux [61] reported that there were almost 800,000 hospital admissions for diverticular disease in European countries. As a countermeasure for the burden of diverticular disease, a systematic review reported that there was no difference in failure rates of medical treatment (6.5 vs. 4.6%) and recurrence rates (13.0 vs. 12.1%) between patients who received ambulatory care and those who received inpatient care for uncomplicated diverticulitis [62]. Ambulatory treatment was associated with daily cost savings of between 600 and 1,900 EUR per patient treated. One study showed that provision of care by an integrated multidisciplinary digestive health service can significantly reduce overall costs ($p = 0.0497$) and the length of hospital stay ($p = 0.017$) in patients admitted for diverticulitis compared to costs for care provided by non-

integrated inpatients services [63]. Moreover, a recent systematic review showed that care by gastroenterologists was associated with a significantly shorter length of stay than care provided by general physicians [64].

Recent evidence suggests that delaying elective surgery for patients with recurrent, uncomplicated diverticular disease is the optimal treatment strategy from both an economic perspective and a clinical perspective, as this approach results in a reduced symptom burden, fewer admissions, less additional treatment, lower rates of mortality and colostomy, an increase in quality-adjusted life years, and significant cost savings [65]. In patients for whom surgery is indicated, a recent meta-analysis showed that, compared to open surgery, laparoscopic surgery for diverticular disease was associated with a significantly reduced length of stay and fewer complications [66]. Recently, Bollom et al. [62] reported that the number of emergency department visits due to diverticulitis and associated costs continued to rise between 2006 and 2013, whereas the rate of bowel surgeries and inpatient admissions through the emergency department for diverticulitis has decreased [67].

Diverticular bleeding can be massive and recurs frequently; therefore, it involves repeated examination, hospitalization, and blood transfusion. In Asia, based on the diagnosis procedure combination data, Ito et al. [68] reported that rebleeding and blood transfusion were related to high cost of hospitalization for colonic diverticular bleeding. Assertive endoscopic hemostasis might decrease the cost of hospitalization in patients with colonic diverticular rebleeding.

Conclusion

Diverticulosis is complicated by diverticulitis, diverticular bleeding, and segmental colitis associated with diverticula, all of which occur frequently. The prevalence of diverticulosis, diverticulitis, and diverticular bleeding in Western countries is different from that in Asian countries. In Western countries, diverticulosis and diverticulitis are predominantly located on the left side of the colon; in contrast, they are predominantly present on the right side in Asian countries. Diverticular bleeding is predominantly located on the right side in Western countries. Both-sided diverticulosis increases the risk of bleeding in Asian countries. The differences in prevalence between Western and Asian countries may be associated with congenital factors, environment, food style, or intestinal microbiota. In the near future, the reasons for the

mechanism of differences in the prevalence of diverticulosis, diverticulitis, and diverticular bleeding between Western and Asian countries are expected to be clarified, and prevention strategies for diverticular disease are expected to be established.

Disclosure Statement

The authors declare no conflicts of interest.

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