Diversion colitis and pouchitis: A mini-review

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Abstract

Diversion colitis is characterized by inflammation of the mucosa in the defunctioned segment of the colon after colostomy or ileostomy. Similar to diversion colitis, diversion pouchitis is an inflammatory disorder occurring in the ileal pouch, resulting from the exclusion of the fecal stream and a subsequent lack of nutrients from luminal bacteria. Although the vast majority of patients with surgically-diverted gastrointestinal tracts remain asymptomatic, it has been reported that diversion colitis and pouchitis might occur in almost all patients with diversion. Surgical closure of the stoma, with reestablishment of gut continuity, is the only curative intervention available for patients with diversion disease. Pharmacologic treatments using short-chain fatty acids, mesalamine, or corticosteroids are reportedly effective for those who are not candidates for surgical reestablishment; however, there are no established assessment criteria for determining the severity of diversion colitis, and no management strategies to date. Therefore, in this mini-review, we summarize and review various recently-reported treatments for diversion disease. We are hopeful that the information summarized here will assist physicians who treat patients with diversion colitis and pouchitis, leading to better case management.

Key words: Diversion colitis; Diversion pouchitis; Ileitis; Inflammatory bowel disease

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however diversion colitis occurs in almost all diverted patients. Pharmacologic treatment using short-chain fatty acids, mesalamine, or corticosteroids are reportedly effective for those who are not candidates for surgical reestablishment; however, there are no established assessment criteria for determining the severity of diversion colitis, and no management strategies to date. In this mini-review, we summarize and review various recently-reported diversion disease treatments. We hope this review will be useful for future treatment.

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INTRODUCTION

Diverision colitis was first described by Morson et al\textsuperscript{[1]} in 1974 as a non-specific inflammation in the diverted colon. Glotzer et al\textsuperscript{[2]} labeled this inflammation “diversion colitis” in 1981. Since then, the disease has been reported in both retrospective\textsuperscript{[3-20]} and prospective studies\textsuperscript{[21-27]} which have described the characteristic clinical, endoscopic, and pathological findings. Surprisingly, the prospective study reported that almost all cases exhibit colitis, evidenced by endoscopic analyses, 3 to 36 mo after the colostomy\textsuperscript{[21]}. Symptomatic cases make up only around 30% of all cases diagnosed via endoscopic studies, and the precise pathogenesis of this condition remains unclarified.

Although a wide range of symptoms are reportedly associated with the disease, including abdominal discomfort, tenesmus, anorectal pain, mucous discharge, and rectal bleeding\textsuperscript{[3,4]}, there are no established diagnostic criteria for assessing disease severity. Diverision pouchitis is similar to diversion colitis, featuring inflammation of the ileal pouch that results from fecal stream exclusion and the subsequent lack of nutrients from luminal bacteria. Therefore, the difference between the pouchitis and diversion pouchitis is whether the lesion is exposed to the fecal stream or not. Patients generally present with varying symptoms such as tenesmus, bloody or mucous-like discharge, and abdominal pain\textsuperscript{[28]}. The incidence of diversion pouchitis is unknown; however, it appears more commonly in patients with underlying inflammatory bowel disease (IBD). Nonsurgical approaches for the treatment of diversion pouchitis include the use of short chain fatty acids (SCFA), topical 5-aminosalicylic acids, and topical glucocorticoids. Unfortunately, efficacy study outcomes are conflicting, and the only curative approach is surgical re-anastomosis with the reestablishment of gut continuity\textsuperscript{[29-30]}.

In their 1989 examination of non-surgical treatment options procedure, Harig et al\textsuperscript{[3]} reported the efficacy of short-chain fatty acids. The usefulness of the 5-ASA enema in patients with diversion colitis was reported for the first time by Triantafillidis et al\textsuperscript{[21]} in 1991; Glotzer et al\textsuperscript{[2]} reported the efficacy of steroid enemas in patients with diversion colitis in 1984, and similar results were subsequently reported by Lim et al\textsuperscript{[22]} and Jowett et al\textsuperscript{[23]}.

LITERATURE ANALYSIS

A literature search was conducted using PubMed and Ovid, with the terms “diversion colitis” or “diversion proctitis” and “diversion pouchitis” used to extract studies published over the preceding 45 years. All appropriate English-language publications from relevant journals were selected. We summarized the available information on demographics, clinical symptoms, endoscopic and histological findings, treatment, and the clinical course.

CLINICAL CHARACTERS

Epidemiology

A total of 69 articles, including 25 case reports, were matched to our definition of diversion colitis and pouchitis assessment; this information is summarized in Tables 1 and 2. Based on our review, the prevalence estimates of these conditions appear extremely high, reaching almost the entire population of interest if the phenomenon is followed prospectively, beginning at 3 to 36 mo after colostomy\textsuperscript{[21]}. In a recent study, Szczepkowski et al\textsuperscript{[3]} described more than 90% incidence of diversion colitis on endoscopy in a series of 145 patients. The study further reported that there were no significant associations between diversion colitis and age, sex, type of stoma, or mode of surgery performed. The frequency of disease occurrence ranged from 70%-74% in patients without pre-existing IBD\textsuperscript{[22]} and 91% in patients with pre-existing IBD\textsuperscript{[6,21]}. In patients with histories of Crohn’s disease chronic severe inflammation, often with transmural disease, has been described after defunctioning colostomies\textsuperscript{[34]}. It has also been hypothesized that diversion colitis may be a risk factor for ulcerative colitis in predisposed individuals, and that ulcerative colitis can be triggered by anatomically discontinuous inflammation in the large bowel\textsuperscript{[35]}. Among the 46 reported cases of diversion colitis and
| Case (No) | Reference | Reporting yr | Country | Age (yr) | Gender (male/female) | Primary Illness (reason for diversion) | Type of diversion (surgical procedure) | Period of up to diagnosis from operation | Symptoms | Endoscopy findings | Pathological findings | Diagnosis |
|-----------|-----------|--------------|---------|----------|----------------------|----------------------------------------|----------------------------------------|------------------------------------------|-----------|-------------------|----------------------|-----------|
| 1         | Glotzer et al[2] | 1981 | United States | 49       | M                     | Free perforation sigmoid diverticulum  | Loop sigmoid colostomy                | 2.5 mo                                   | No symptoms | Erythema, friability, petechiae, atrophy | Crypt abscess, surface epithelial cell degeneration, acute inflammation, chronic inflammation, regeneration | Diversion colitis |
| 56        | F         | 1984 | United States | 28       | M                     | Perforated sigmoid colon for gunshot | Loop sigmoid colostomy                | 6 wk                                    | No symptoms | Multiple aphthae | Not obtained | Diversion colitis |
| 78        | M         | 1984 | United States | 21       | M                     | Gunshot                               | Loop sigmoid colostomy                | 2 mo                                    | No symptoms | Multiple, small, polypoid lesions in the rectum and sigmoid colon up to the cutaneous part of the mucous fistula. | Not obtained | Diversion colitis |
| 3         | Scott et al[4] | 1984 | United States | 22       | F                     | Crohn’s Disease                       | Ileostomy and subtotal colectomy      | 2 yr                                    | No symptoms | Not obtained | Moderate loss of goblet cells with focal edema and lymphocytosis of the lamina propria. | Diversion colitis |
| No. | Sex | Diagnosis               | Procedure                  | Duration | Symptom(s)       | Findings                                                                 | Complication                                                                 |
|-----|-----|-------------------------|----------------------------|----------|------------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| 34  | F   | Crohn's ileitis         | Ileocaecostomy and Loop Ileostomy | 2 yr     | No symptoms      | Exudate, Focal chronic inflammation, edema, erosions, and an increased number of lymphoid follicles. |
| 31  | M   | Crohn's ileitis         | Ileocaecostomy and Loop Ileostomy | 1 yr     | No symptoms      | Aphthous lesions, Chronic inflammation                                   |
| 32  | M   | Crohn's ileitis         | Ileocaecostomy and Loop Ileostomy | 1 yr     | No symptoms      | Friable, exudate, Not obtained                                           |
| 5   | F   | Perforated sigmoid diverticulum | Loop sigmoid colostomy      | 22 yr    | Rectal bleeding  | Diffuse multiple superficial ulcerations and intense inflammatory infiltrate composed mainly of plasma cells, lymphocytes, and some eosinophils. |
| 6   | M   | Perineal laceration as result of a motor vehicle accident | End sigmoid colostomy       | 1 yr     | Rectal bleeding  | Moderate to severe nonspecific inflammation.                             |
| 7   | M   | Neurogenic focal incontinence | Mucus fistula               | 13 mo    | Bloody discharge | Endoscopic index of 10                                                   |
|     |     |                         |                            |          |                  | Inflammatory infiltrate of both acute and chronic cells in the lamina propria and the crypt abscess. Lining epithelial cells show decreased mucin secretion. |
| 63  | F   | Irradiation of rectum   | Mucus fistula               | 2 wk     | Bloody discharge | Endoscopic index of 10                                                   |
| 54  | M   | Perianal fistulas        | Rectosigmoid pouch          | 35 mo    | Bloody discharge | Endoscopic index of 9                                                    |
| 56  | M   | Diverticulitis           | Mucus fistula               | N/A      | N/A              | Endoscopic index of 8                                                   |
| 8   | F   | Diverticula with perforation | Hartman's type of operation laparotomy | 16 mo    | Bloody rectal discharge | Severe inflammatory infiltration, formation of lymph follicles, surface erosions, edema, and crypt abnormalities. |
| 9   | F   | Small bowel perforation with a ruptured chronic pelvic abscess secondary to diverticular disease | End transverse colostomy | 10 wk    | Bloody rectal discharge | Acute and chronic inflammation with cryptitis.                           |
| 10  | F   | Chronic constipation     | Loop transverse colostomy   | 25 yr    | Sepsis (no symptoms such as rectal bleeding) | Large ulcers with overlying pseudomembrane | Inflammation primarily with plasma cells and lymphocytes was noted, as well as a moderate numbers of polymorphonuclear cells, large lymphoid aggregates were seen in the lamina propria. |
| Case | Authors | Year | Age | Gender | Location | Procedure | Time | Symptoms | Pathology | Diagnosis |
|------|---------|------|-----|--------|----------|------------|------|----------|-----------|-----------|
| 11   | Lai et al. | 1997 | 49 M | United States | Colostomy | 10 yr | Rectal pain and bleeding | Partial stricture 70 cm proximally to the rectum. The colonic mucosa appeared granular and friable with evidence of linear ulceration. | Extravasation of erythrocytes, lymphocytic and neutrophilic cells infiltrates, and edema were present within the lamina propria. No evidence of malignancy and glandular dysplasia was found. Pathologic report was consistent with chronic colitis. | Diversion colitis |
| 12   | Lim et al. | 1999 | 60 F | United States | End sigmoid colostomy | 6 mo | Blood and mucus per rectum | Edematous mucosa with blood-stained mucopurulent exudate | Active chronic colitis with focal cryptitis and crypt abscesses. | Diversion colitis → UC |
| 16   | M | 6 M | Imperforate anus | Ileostomy and colostomy | 6 mo | Blood and mucus per rectum | Granular, erythematous mucosa with contact bleeding | Active inflammation with polymorphs infiltrating crypts and a diffuse increase in lymphocytes and plasma cells in the lamina propria. | Diversion colitis → UC |
| 13   | Jowett et al. | 2000 | 75 F | United Kingdom | End colostomy | 8 mo | Blood and mucus per rectum | Granular, congested, and oedematous mucosa with contact bleeding | Mixed inflammatory cell infiltrate with distortion of the crypt architecture and cryptitis. | Diversion colitis (→ UC) |
| 14   | Lim et al. | 2000 | 66 M | United Kingdom | Hartmann's procedure with colostomy. | 18 mo | No symptoms | Mildly inflamed | Active colitis | Diversion colitis (→ UC) |
| 15   | Kiely et al. | 2001 | 6 M | United Kingdom | Total colectomy and ileostomy | 9 mo | Rectal bleeding | Endoscopic index of 8 | Lymphoid hyperplasia, lymphoplasmacytosis, crypt abscesses and moderate mucosal architectural disruption. | Diversion proctocolitis |
| 3    | M | 5 M | Perforated typhoid disease | Subtotal colectomy and ileostomy | 5 mo | Rectal bleeding and abdominal pains | Endoscopic index of 8 | Lymphoplasmacytic infiltration of lamina propria, and architectural disruption. | Diversion proctocolitis |
| 8    | F | 4 M | Aplastic anemia, a large solitary rectal ulcer | Loop sigmoid colostomy | 4 mo | Rectal discharge | Endoscopic index of 9 | Lymphoplasmacytic and neutrophilic infiltrate in the lamina propria, mucin depletion, and Paneth cell metaplasia. | Diversion proctocolitis |
| 3    | M | 6 M | Hirschsprung's disease | Ileostomy | N/A | Rectal bleeding | Florid colitis | Lymphoid hyperplasia, lymphoplasmacytosis and mucin depletion, and Paneth cell metaplasia. | Diversion proctocolitis |
| 10   | M | 10 M | Rectovesical fistula | Loop sigmoid colostomy | N/A | Rectal discharge | Florid colitis | Lymphoid hyperplasia, lymphoplasmacytosis. | Diversion proctocolitis |
| 16   | Komuro et al. | 2003 | 46 M | Japan | Loop transverse colostomy | N/A (On surveillance colonoscopy) | No symptoms | Mild colitis with a decreased vascular pattern, oedema and mucosal tear | Diversion colitis |
pouchitis, there was a slight male predominance (28 males, 18 females), and the age of the patients ranged from 3 to 85 years old\cite{2,5,13,29,31-33,35-52}. The period from diagnosis to surgical treatment was a median of 8 mo, ranging from 2 wk to 25 years (Table 1). The types of diversions included: 9 cases of loop sigmoid colostomy; 3 cases of end sigmoid colostomy; 9 cases of loop transverse colostomy; 4 cases of loop ileostomy; 7 cases of ileostomy and colostomy; 3 cases of proctocolectomy; 2 cases of Hartmann’s type with colostomy; and only one case of other operations (Table 1).

**Pathogenesis**

The basic mechanisms underlying diversion colitis are still unclear. Glotzer hypothesized that it might be the result of bacterial overgrowth, the presence of harmful bacteria,
Table 2  Clinical course of case reports

| Case (No) | Ref.       | Age (yr) | Gender (male/female) | Ineffective treatment | Effective treatment | Prognosis                                                                 |
|----------|------------|----------|----------------------|-----------------------|---------------------|--------------------------------------------------------------------------|
| 1        | Glotzer et al[31] | 49       | M N/A                | Closure 4 mo post-diversion | Asymptomatic. Proctoscopy and biopsy normal. 2.5 and 30 mo post closure. |                                                                 |
| 56       | F N/A                  | Closure 3 mo post-diversion | Recurrent Ca. Mucosa not inflamed grossly or microscopically 18 mo post closure. |                                                                 |
| 78       | M N/A                  | Closure 6 mo post-diversion | Asymptomatic. 1 yr post closure. |                                                                 |
| 70       | F N/A                  | Closure 5 mo post-diversion | Asymptomatic. Normal sigmoidoscopy 2 mo post closure. |                                                                 |
| 43       | F N/A                  | Closure 2 yr post-diversion | Asymptomatic. Normal sigmoidoscopy 3 yr post closure. |                                                                 |
| 41       | F N/A                  | None | Asymptomatic 2 yr after ileostomy. |                                                                 |
| 65       | M N/A                  | None | Abdominal cramps purulent rectal discharge. Continued inflammation 8 yr after colostomy. |                                                                 |
| 83       | M N/A                  | None | Asymptomatic. Continued mild inflammation 4.5 yr after colostomy. |                                                                 |
| 26       | M N/A                  | Steroid enemas | Improved. Continued 8 yr after colostomy. |                                                                 |
| 70       | M N/A                  | Steroid enemas | Tenesmus, discharge and fever 4 yr after colostomy. Resolved with steroid enemas. |                                                                 |
| 2        | Lusk et al[40]         | 28       | M -                  | Colostomy closure | Normal at 16 mo follow-up. | One month later, the patient was examined by flexible sigmoidoscopy, which demonstrated normal mucosa throughout with no sign of pseudopolyps. |                                                                 |
| 68       | M -                    | Colostomy closure | Continued inflammation at 8 yr. |                                                                 |
| 3        | Scott et al[46]         | 21       | M -                  | Colostomy closure |                                                                 |                                                                 |
| 4        | Korelitz et al[42]     | 22       | F Steroid enemas     | Ileocolic reanastomosis (ileostomy closure) | 3 mo (interval from reanastomosis to normal sigmoidoscopy), 7 yr (duration normal). |                                                                 |
| 34       | F -                    | Ileostomy closure | 1 mo (interval from reanastomosis to normal sigmoidoscopy), 2 yr (duration normal). |                                                                 |
| 31       | M -                    | Ileostomy closure | 3 mo (interval from reanastomosis to normal sigmoidoscopy), 18 mo (duration normal). |                                                                 |
| 32       | M -                    | Ileostomy closure | 2 mo (interval from reanastomosis to normal sigmoidoscopy), 14 mo (duration normal). |                                                                 |
| 5        | Fernand et al[39]      | 67       | F -                  | Left hemicolectomy and left salpingo- oophorectomy | She recovered well and discharged 9 d later. |                                                                 |
| 6        | Frank et al[13]        | 38       | M Oral and topical steroids | Abdominoperineal resection of the diverted loop and permanent colostomy | No evidence of inflammatory bowel disease has developed. Barium study of the small bowel was normal 1 yr after surgery. |                                                                 |
| 7        | Harig et al[32]        | 63       | M N/A                | Short-chain-fatty acid irrigation | N/A |                                                                 |
| 63       | F N/A                  | Short-chain-fatty acid irrigation | N/A |                                                                 |
| 54       | M N/A                  | Short-chain-fatty acid irrigation | N/A |                                                                 |
| 56       | M N/A                  | Short-chain-fatty acid irrigation | N/A |                                                                 |
| 8        | Triantafillidis et al[34] | 64       | F -                  | 5 aminosalicylic acid enemas comparison with Betamethasone enemas | There were no differences in the degree of clinical improvement, or in the endoscopic and histologic scores seen at the end of the trials, between betamethasone and 5-ASA. Clinically asymptomatic at a 6-mo follow-up. |                                                                 |
| 9        | Tripodi et al[33]      | 85       | F -                  | 5-aminosalicylic acid enemas | Without complications and has been doing well postoperatively. |                                                                 |
| 10       | Lu et al[35]           | 45       | F Intravenous metronidazole | Colectomy of the diverted segment | 6 wk of treatment with 5-ASA, the patient had decreased rectal pain and bleeding. PSL was tapered off over four months and she remained well. |                                                                 |
| 11       | Lai et al[36]          | 49       | M -                  | Oral prednisolone, oral mesalazine, and mesalazine enemas |                                                                 |                                                                 |
| 12       | Lim et al[37]          | 60       | F -                  | Oral prednisolone, oral mesalazine, and mesalazine enemas | He subsequently made a good recovery and steroid therapy was discontinued. |                                                                 |
| 0        | M -                    | Closure of the loop ileostomy—oral prednisolone, oral olsalazine and oral metronidazole—sigmoid loop colostomy | The defunctioned rectosigmoid was partially removed, leaving the lower rectum and anal canal; the loop colostomy was refashioned into an end colostomy—colectomy and removal of residual rectal stump and anal canal was performed and an end ileostomy fashioned |                                                                 |
| 13       | Jowett et al[38]       | 75       | F -                  | Topical steroid enemas. | UC |                                                                 |
| 14       | Lim et al[39]          | 66       | M -                  | Steroid enemas | 6 mo later he developed ulcerative colitis. |                                                                 |
nutritional deficiencies, toxins, or disturbance in the symbiotic relationship between luminal bacteria and the mucosal layer. Reportedly, concentrations of carbohydrate-fermenting anaerobic bacteria and pathogenic bacteria are reduced in de-functioned colons and these reports indicate that the overgrowth of anaerobic bacteria or a pathogenic bacterium is unlikely to be an important etiological factor. On the other hand, there is an increase of nitrate-reducing bacteria in patients with diversion colitis and nitrate-reducing bacteria produce nitric oxide (NO) which plays a protective role in low concentrations, but at higher levels it becomes toxic to the colonic tissue. Thus, it has been suggested that increases in nitrate-reducing bacteria may result in toxic levels of NO, leading to the diversion colitis.

| Reference | Author et al. | Age | Gender | Treatment | Management | Notes |
|-----------|--------------|-----|--------|-----------|------------|-------|
| Kiely et al. | 2018 | 6 | M | PSL and AZA | SCFA | Oral PSL was continued at the reduced rate of 5mg on alternate days until he underwent an uneventful rectal excision and J-pouch anal anastomosis 1 mo later. Two months after this, his ileostomy was closed. His ileostomy was closed 3 mo later, and he was remained symptom free. Her ulceration was virtually healed and showed a reduction in endoscopic index from 9 to 3. Treatment was maintained until her colostomy was reversed a month later. After stoma closure, SCFAs were discontinued with no further recurrence of symptoms. |
| Komuro et al. | 2018 | 46 | M | N/A | SCFA | For redo pull-through rectal excision. |
| Tsononi et al. | 2018 | 40 | M | Mesalazine suppository and steroid enemas | Metronidazole suppository | Improved quickly and remains well and asymptomatic 12 wk after treatment. |
| Boyce et al. | 2018 | 29 | M | - | Completion proctectomy | Completion proctectomy was uneventful and from which the patient made an unremarkable recovery. |
| Haugen et al. | 2018 | 36 | F | Antegrade irrigations of her distal bowel with tap water | SCFA enemas was not option due to insurance and spina bifida | Weekly to twice weekly irrigations completely stopped the malodorous and troublesome discharge. |
| Talisetti et al. | 2018 | 19 | F | SCFA enema, steroids, metronidazole | Colectomy (entire colon was ultimately resected. Since only 15 cm of jejunum appeared healthy, her mid and distal small bowel was also resected up to 15 cm from the ligament of Treitz) | N/A |
| Kominami et al. | 2018 | 84 | M | 5-aminosalicylic acid enemas maintenance therapy. | Short-chain fatty acid enema | Undergoing 5-aminosalicylic acid enemas maintenance therapy. |
| Watanabe et al. | 2018 | 76 | F | Leukocytapheresis, following low dose of metronidazole and ciprofloxacin | Enemas containing 5-aminosalicylic acid and steroids and antibiotic therapy | After 18 mo, her condition remains stable without the need for medication. |
| Gundling et al. | 2018 | 75 | F | Autologous fecal transplantation | Enemas containing 5-aminosalicylic acid and steroids and antibiotic therapy | All symptoms improved dramatically within 5 d after the first treatment. Colonoscopy 28 d after the first treatment showed no major signs of inflammation in the colonic stump. |
| Matsumoto et al. | 2018 | 65 | M | A combined mesalazine plus corticosteroid enema. | Corticosteroid and mesalazine enemas, prednisolone injections. | Finally proctectomy and ileal pouch-anal anastomosis were successfully performed. |
| Custon et al. | 2018 | 44 | M | Dextrose (hypertonic glucose) spray endoscopically | - | The patient did not experience further episodes of recurrent bleeding during the 6-mo follow-up. No prescribed medicines were given after the endoscopic therapy. |

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Recently, ischemia has been proposed as a cause of diversion colitis\(^8\). The explanation surely lies in changes to the luminal flora consequent to fecal stream interruption. Normal luminal bacteria produce SCFA, such as butyric acid. Butyrate is the principal oxidative substrate for colonocytes\(^5\) and patients with diversion colitis may improve following topical treatment with SCFA, especially with butyrate enemas\(^5,36\). This hypothesis is based on evidence that suggests SCFA relax vascular smooth muscle and that butyrate deficiencies may induce increased tone in the pelvic arteries, therefore leading to relative ischemia of the colorectal mucosa and intestinal wall\(^5\). It is obvious that additional, basic research is necessary in order to discern disease mechanisms. We have summarized the pathogenesis of this disease entity in Figure 1.

**Symptoms**

Most patients are asymptomatic\(^22\), however about one third of patients may exhibit symptoms of diversion colitis\(^2,3,6,9\). Patients generally present with varying symptoms such as abdominal discomfort, tenesmus, anorectal pain, mucous discharge, and rectal bleeding. The most common symptoms include bloody, serous, or mucous discharge in 40% of the population, and abdominal pain and tenesmus in 15% of the population\(^9\). There have been several reports of severe rectal bleeding\(^24,29,56\). There is a report of massive rectal distension causing bilateral ureteric obstruction\(^37\) and a case report of diversion colitis causing severe sepsis requiring a colectomy\(^38\). These symptoms can start within 1 mo to 3 years after surgery\(^22,24\). Our review also showed that clinical symptoms of rectal bleeding were seen in 25 cases, abdominal pain in 3 cases, anal pain in 3 cases, and sepsis in 1 case\(^38\). On the other hand, 21 of 46 cases had no symptoms (Table 1), as previously reported\(^24\). Additionally, in the presence of Crohn’s disease and ulcerative colitis, the number of symptomatic patients rises to 33% and 87% respectively\(^33\). Our review showed cases with primary illness of diverticula with perforation \((n = 11)\), fecal incontinence \((n = 6)\), chronic constipation or ileus \((n = 5)\), ulcerative colitis \((n = 5)\), Crohn’s disease \((n = 4)\), carcinoma \((n = 3)\), and various other diseases (Table 1).

**Macroscopic findings**

Macroscopically, diversion colitis may involve the whole de-functioned colon or isolated segments. These findings include erythema, diffuse granularity, and blurring of vascular pattern in about 90% of the population. It is also associated with mucosal friability (80%) edema (60%), aphthous ulceration, and bleeding, to varying degrees\(^2,3,8-12,39,40\). There is a case report of diversion colitis causing mucosal tears within the defunctioned colon\(^41\). Recently, Hundorfean et al\(^37\) reported a first description and in vivo diagnosis of diversion colitis after surgery, by virtual chromoendoscopy and fluorescein-guided confocal laser endomicroscopy. Our literature review showed that endoscopic findings were evidenced in 44 out of 46 cases, and severe inflammation with ulceration (endoscopic index \(\geq 8\)) in 17 cases.

**Microscopic findings**

The pathological finding of diversion colitis and pouchitis...
usually vary with degree of severity, therefore, no specific microscopic findings have been noted. The histological features of diversion colitis can mimic those of IBD, even when a pre-existing IBD has not been documented. The most notable feature often seen in diversion colitis is lymphoid follicular hyperplasia. Atrophy, crypt branching, mucin depletion, crypt distortion, regenerative hyperplasia, paneth cell metaplasia, thickening of muscularis mucosa, diffuse active mucosal inflammation with crypt abscesses, ulceration, and vacuolar and epithelial degeneration along with features of chronic inflammation (usually confined to the mucosa) are seen with varying degrees of severity. More recently, features of ischemia, such as superficial coagulative necrosis and fibrosis, have been described. Our review showed that 37 out of 46 cases exhibited pathological findings including 15 cases of crypt abscess or cryptitis, and 14 cases of lymphoid follicular hyperplasia (which was not previously identified as a feature of diversion colitis). These features are non-specific and, to date, no characteristic feature or features of diversion colitis have been identified.

**Treatment**

Because of the small number of patients and the unknown etiology, there is no established standard therapy for diversion colitis and pouchitis. Szczepkowski et al proposed a management strategy for patients with de-functioned distal stomas. He divided patients with diversion colitis into three groups based on a study of 145 patients. These groups consisted of Group 1 (no clinical, morphological or endoscopic evidence of diversion colitis), Group 2, (mild or moderate signs of diversion colitis), and Group 3 (severe diversion colitis). Group 1 can be treated conservatively. Group 2 can be treated using conservative management prior to restoration of colonic continuity and Group 3 should ideally undergo restoration of colonic continuity. If a surgical option is not feasible, pharmacologic treatment options should be tried to resolve the inflammation. A summary of the clinical courses of case reports is shown in Table 2.

**Surgery**

Treatment of diversion colitis should be primarily directed at restoring bowel continuity to restore the luminal flow. This will resolve the symptoms and assist the bowel to return to normal. Re-anastomosis has proven to be consistently effective in halting the symptoms of diversion colitis in a number of studies. Re-anastomosis of diverted segments in patients with preexisting inflammatory bowel disease is a more difficult decision because inflammation in the diverted segment could represent inflammatory bowel disease or diversion colitis, each of which dictate different courses of action. Resection is not typically required. Indications for resection include uncontrolled perianal sepsis, perianal fistulous disease, anal incontinence, and uncontrolled symptoms related to diversion colitis.

**Diet and lifestyle**

Nutritional imbalance in the excluded colon is likely responsible for the pathologic changes and symptoms of diversion colitis. However, current evidence does not support the effectiveness of lifestyle modifications or nutritional imbalance. Pharmacologic treatment is generally indicated for the temporary control of symptoms in preparation for surgery. It is used occasionally for patients who are not considered surgical candidates because of severe medical comorbidities, poor sphincter function, or reasons of technical difficulty.

**Short-chain-fatty acid**

Short-chain fatty acids, mainly butyrate, are the major fuel source for the epithelium. Their absence in the diverted tract may produce mucosal atrophy and inflammation. Bacteria produce SCFAs as byproducts of carbohydrate fermentation in the colonic lumen, and SCFAs provide the primary energy source for colonic mucosal cells. In human neutrophils, SCFAs reduce the production of reactive oxygen species, which are the agents of oxidative tissue damage. Treatment of diversion colitis with SCFA or butyrate has shown inconsistent results. Harig successfully improved symptoms and endoscopic inflammatory change by SCFA. Komorowski et al reported similar results in four patients with diversion colitis with SCFA irrigation. However, Guillmot et al failed to demonstrate either histological or endoscopic improvement. The differences in response may be partially accounted for by disease groupings. In recent years, several studies on the usefulness of SCFA, including of butyrate, are reported. Cristina et al proposed that butyrate enemas may prevent the atrophy of the diverted colon/rectum, thus improving the recovery of tissue integrity.

**5-aminosalicylic acid**

Usefulness of 5-aminosalicylic acid (5-ASA) enemas in diversion colitis was reported for the first time by Trianantafilidis et al in 1991. Tripodi et al has also reported similar results in 1992. Calitabiano et al reported that 5-ASA enema reduces oxidative DNA damage in colonic mucosa and reduces mucosal damage using rats in a diversion colitis model. It is considered that the mucosal disorder may be improved by protective action against oxidative DNA damage and the anti-inflammatory action of SASA.

**Corticosteroids**

Glotzer reported on several patients with diversion colitis treated by steroid enemas in 1984. Lim and Jowett also reported the efficacy of the steroid enemas in 2000. Corticosteroids are first-line agents for symptomatic diversion colitis, with varying effectiveness.
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Table 3 Summary of pharmacologic treatments

| Treatment                              | Ref.                        | Procedure/standard dosage                                                                 | Efficacy                                                                 | Complications/main side effects                          |
|----------------------------------------|-----------------------------|------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|----------------------------------------------------------|
| Surgical anastomosis                   | [2,3,10,21,25,39,42]        | Mobilization of both ends of the bowel with either sutured or stapled anastomosis.         | The most effective method of eliminating the signs and symptoms          | Bleeding, infection, anastomotic leak, anastomotic stricture, anesthetic risks |
| Corticosteroids                        | [2,32,33]                  | Hydrocortisone (100 mg per 60 mL bottle) enema is administered once daily for up to 3 wk. | Response to treatment is generally seen in 3 to 5 d.                     | Local pain and burning, occasionally rectal bleeding.     |
| 5-aminosalicylic acid (5-ASA) enemas   | [31,43,63,64]              | 4 g of mesalazine in 60 mL suspensions, administered rectally once-daily dose for 4 to 5 wk. | Varying effect                                                           | Occasionally produces acute intolerance manifested by cramping, acute abdominal pain, bloody diarrhea, fever, headache, and rash. |
| Short-chain-fatty acid (SCFA) enemas   | [5,10,13,18,19,26,27,61,62] | SCFA enema rectally twice a day for 2 wk, and then tapered according to response over 2 to 4 wk. | Varying effect                                                           | None                                                     |
| Irrigation with Fibers                 | [65,66]                    | Solution containing 5% fibers (10 g/d) for 7 d.                                            | The endoscopic score which is used to quantify the intensity of the inflammation at the mucosa of the diverted colon diminished after treatment. | Probably none                                             |
| Leukocytapheresis                      | [44]                       | Leukocytapheresis, at flow rate of 40 mL/min for 60 min, once weekly for 5 wk, following low dose of metronidazole and ciprofloxacin, another set of weekly leukocytapheresis was added. | Significant improvement in her pouchitis disease activity index (PDAI) from 14 to 1. | The common side effects were nausea, vomiting, fever, chills, and nasal obstruction. |
| Autologous fecal transplantation       | [45]                       | Feces were collected from the colostomy bag, diluted with 600 mL of sterile saline (0.9 %), stirred and filtered three times using an ordinary coffee filter, irrigation endoscopically. This procedure was repeated 3 times within 4 wk (on day 0, day 10 and day 28). | All symptoms improved dramatically within 5 d after the first treatment. Colonoscopy 28 d after the first treatment showed no major signs of inflammation in the colonic stump | None, patient’s tolerance required.                      |
| Dextrose spray (hypertonic glucose)    | [29]                       | Endoscopically sprayed with 150 mL 50% dextrose via a catheter.                            | Follow-up pouchoscopy 2 wk after the dextrose spray showed normal pouch mucosa with no evidence of bleeding or mucosal friability. | It has a very low chance of causing transient hyperglycemia because there is no direct injection of the hypertonic solution into blood vessels. |

SCFA: Short chain fatty acids; 5-ASA: 5-aminosalicylic acid.

Irrigation with fibers
Resolution of diversion colitis, based on endoscopic and histologic examination, has been reported following irrigation of the diverted segment of the colon with fibers. Joaquim et al. investigated the effect of irrigating the colorectal mucosa of patients with a colostomy using a solution of fibers. In 11 patients with loop colostomies, the diverted colorectal segment was irrigated with a solution containing 5% fibers (10 g/d) for 7 d. Irrigation with fibers improves inflammation within the defunctionalized colon, so this therapy may play a role in the preoperative management of colostomies, potentially decreasing the high incidence of diarrhea after reestablishment of the intestinal transit.

Leukocytapheresis
Watanabe et al. reported successful treatment of leukocytapheresis in a patient with chronic antibiotic-refractory diversion pouchitis following IPAA for UC with diverting ileostomy. The mucosa of the diverted pouch is less exposed to the fecal stream and pathogens. Therefore, altered immunity likely plays a major role in the maintenance of diversion pouchitis. Leukocytapheresis to address the altered immunity would seem a reasonable approach for antibiotic-refractory pouchitis following IPAA for UC with diverting ileostomy, and its effectiveness in the case suggests that altered immunity may be a key contributing factor compared with dysbiosis, bacterial pathogens, and ischemia.

Autologous fecal microbiota transplantation
Fecal microbiota transplantation (FMT), which consists of transferring stool from a healthy donor to the patient’s colon, is an effective treatment for some diseases of the
colostomy closure. However, those patients with significant symptoms or histories of colitis or diarrhea should undergo a complete proximal and distal colonic evaluation prior to stoma closure, and some treatments need not be delayed in these patients. Patients with permanent diversions should undergo periodic pharmacologic treatment. This review of various treatments for diversion colitis will hopefully be useful for determining future treatments.

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