

Diverticulitis Management in Complex Medical Contexts

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Abstract

Diverticulitis is a prevalent medical issue, particularly among elderly individuals in the Western world. Management is nuanced and is influenced by both disease presentation and patient factors, especially those that affect risk of septic and surgical complications. This paper reviews existing literature to explore the incidence, presentation, and management of diverticulitis in complex medical contexts—immunocompromised populations, specifically highlighting those undergoing chemotherapy, HIV/AIDS patients, transplant recipients, and individuals with autoimmune and connective tissue diseases. Not surprisingly, management of diverticulitis in these complex patient populations is associated with increased morbidity. However, even taking into consideration the risk of septic and surgical complications, more recent data and treatment recommendations suggest that both nonoperative and operative management strategies may be appropriate based on individual patient presentations, mirroring the treatment paradigm of immunocompetent patients. In addition, in discussing operative management of complex medical patients, immunosuppression alone should not be considered a contraindication to primary anastomosis. Overall, there are limited existing data on diverticulitis in immunocompromised populations and, especially, patients with autoimmune and connective tissue disorders. Further research is warranted to better understand the impact of these chronic diseases on diverticulitis severity and to best inform evidence-based practices in this complex clinical scenario.

Keywords

- diverticulitis
- operative management
- immunocompromised
- autoimmune disease

Diverticulosis is one of the most common medical problems among those over 65 years of age in the Western world, with up to 60% of the general population carrying the diagnosis.^{1–3} Of those with diverticula, up to 25% will experience acute diverticulitis, with 30% of those developing recurrent episodes.^{4–7} Diverticulitis accounts for 102 out of every 100,000 hospital admissions annually in the United States,⁴ with recent data showing an increased incidence in younger populations.^{8,9} Diverticulitis is diagnosed based on clinical presentation and computed tomography (CT) findings and can vary in presentation from uncomplicated to complicated.⁸ Uncomplicated disease is often limited to colonic wall thickening and surrounding fat stranding, while complicated

disease involves evidence of perforation, bleeding, fistula, abscess, or obstruction. Management is based on presentation and disease severity and can range from conservative management with or without antibiotics to emergent or elective surgical resection of the segment of diseased colon with end colostomy (Hartmann's procedure) or immediate reconstruction with or without diverting loop ileostomy.⁵

The pathogenesis of diverticulosis/diverticulitis is not entirely understood, but the development of diverticula has been attributed to increased intraluminal pressure due to constipation in the sigmoid colon. In this vein, high-fat, high-protein, low-fiber Western diets resulting in constipation have previously been associated with diverticular

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disease. In addition, obesity and smoking have been demonstrated as risk factors for diverticulitis, while protective factors include physical activity and high-fiber diets.^{1,5}

Various complex populations are untowardly affected by diverticulitis, and management of patients who are immunocompromised or have underlying diseases that may portend increased risk of complications (i.e., connective tissue diseases) warrant special discussion. Whether due to chronic immunosuppression, cancer and chemotherapy, HIV/AIDS, or organ transplant, 2.7% of U.S. adults are considered immunocompromised. The incidence of diverticulitis in immunocompromised patients is known to be higher than the general population at 1% compared with 0.02%.¹⁰ With the number of immunocompromised patients increasing annually in the United States, this population deserves special attention.^{8,10–13} Although 2014 American Society of Colon and Rectal Surgeons (ASCRS) guidelines recommended a low threshold for elective sigmoid colectomy in immunocompromised patients, more recent literature on the topic has led to changes in these recommendations.¹⁴ Here, we aim to examine management considerations for diverticulitis in the immunocompromised patient (chronically immunosuppressed, cancer patients undergoing chemotherapy, patients with HIV/AIDS, and posttransplant patients), as well as patients with connective tissue diseases.

Immunocompromised Patients

As previously stated, it is estimated that nearly 3% of the U.S. population is considered immunocompromised, and this number continues to rise. Given the risk of septic morbidities associated with both conservative and operative management, treatment of this complex patient population warrants special attention.

Chronic Immunosuppression

Early studies had shown more severe disease and morbidity for immunosuppressed patients presenting with diverticulitis.^{12,13,15,16} However, larger, more robust, and more recent studies have not borne out the same results. In 2023, He et al followed 122 patients over 4 years admitted to the Mayo Clinic with diverticulitis who were considered immunosuppressed for a variety of reasons, including chronic steroid use. Most of these patients presented with uncomplicated diverticulitis, and nonoperative management was successful in 93% of these presentations, with 2.3% requiring surgery during their initial admission and 4.8% subsequently presenting with new abscess or need for readmission within 30 days. In patients presenting with complicated disease, initial nonoperative management was successful in 88.9%. Surgical morbidity in patients who required operative intervention at initial presentation was 50%, and mortality rate was 18.8% with all mortality being noted in patients who presented with perforation.¹⁶ Tartaglia et al compared a larger group of immunosuppressed and immunocompromised patients extracted from the Web-based International Registry of Emergency Surgery and Trauma between January 2018 and December 2021. They found that immunosup-

pressed patients typically present with more severe diverticulitis, were more likely to undergo open sigmoid resection with end colostomy (Hartmann's procedure), and had, similar to the findings of He et al, higher rates of morbidity and mortality compared with immunocompetent patients.¹⁰

Ahmadi et al retrospectively reviewed all patients diagnosed with diverticulitis at the Royal Prince Alfred Hospital in Sydney, Australia, between 2006 and 2018. Their data found no significant difference in severity of initial presentation between the immunosuppressed and immunocompetent groups, and there was no difference in rates of failure of nonoperative management between immunosuppressed and immunocompetent patients (8% vs. 5%, respectively; $p = 0.347$). However, immunosuppressed patients with complicated disease, especially those with paracolic or pelvic abscesses, were more likely to undergo surgery at their initial admission than immunocompetent patients (13.3% vs. 5.1%, respectively; $p = 0.020$). In addition, following surgery, immunosuppressed patients were more likely to have grade III–IV Clavien–Dindo complications as compared with immunocompetent patients (30% vs. 7%, $p < 0.001$).⁵

Based on this work, it is reasonable to conclude that nonoperative management is a rational course of action for management of uncomplicated diverticulitis in the immunosuppressed patient.¹⁰ Additionally, ASCRS notably does not identify immunosuppression as a contraindication to primary anastomosis following sigmoid resection. Ultimately, these studies support that the treatment paradigm for immunosuppressed patients should mirror that for immunocompetent patients, but surgeons should be aware and cautious of increased morbidity and mortality in immunosuppressed patients, especially those who present with more severe disease.

Cancer/Chemotherapy

Medical decision-making regarding diverticulitis in the cancer patient undergoing chemotherapy must weigh the pros and cons of operative intervention, with special attention paid to the timing and side effects of individualized chemotherapy regimens. While elective sigmoid resection would decrease the risk of diverticulitis episodes, these patients often have significant morbidity associated with operations, which can delay chemotherapy in the perioperative period and have a significant impact on their overall oncologic care.

Samdani et al examined all patients over the age of 18 years between 1988 and 2004 who presented to Memorial Sloan Kettering with diverticulitis. They separated patients with their first presentation of diverticulitis into a chemotherapy group, including those that had received chemotherapy within the month prior to presentation, and a nonchemotherapy group, including both patients with and without cancer or history of previous chemotherapy. Patients who were undergoing chemotherapy presented with a significantly lower white blood cell and absolute neutrophil count and were more likely to be neutropenic ($p < 0.01$). However, even with this immunosuppressed state, there was no significant difference in the severity of disease at presentation or in the decision for nonoperative management ($p = 0.15$ and 0.98 , respectively). In addition,

failure of nonoperative management was uncommon and similar failure rates between the two groups were appreciated (13.2% in chemotherapy vs. 4.4% in no chemotherapy group, $p = 0.12$).

In patients who underwent surgery for management of their initial presentation of diverticular disease, there was surprisingly no significant difference between the groups with regard to diversion, and there was no significant difference in morbidity, overall mortality, or hospital stay. Admission for diverticulitis caused patients to pause their chemotherapy for some time, although the majority had resumed at a median of 2.1 months later. Overall mortality was significantly higher for the group receiving chemotherapy. In follow-up, although the likelihood of undergoing a subsequent resection was not significantly different between the two groups, the likelihood of complicated diverticulitis at the time of recurrence was significantly higher for the group undergoing chemotherapy (87.5% vs. 29.4%, $p = 0.01$). In addition, the group receiving chemotherapy was more likely to require emergent surgery and diversion upon recurrence ($p = 0.03$). Reassuringly, there was no significant difference in the number of patients requiring a stoma at their last follow-up visit between the two groups.¹⁷ This study highlights that decisions regarding patients undergoing chemotherapy who present with diverticulitis are nuanced and must be carefully considered. While patients undergoing chemotherapy are more likely to re-present with more severe disease, they are not more likely to recur than those not receiving chemotherapy. There is also no higher morbidity postoperatively. For uncomplicated diverticulitis, nonoperative management is reasonable and safe in these patients. For complicated disease, if immediate surgery is required, choosing not to divert can be considered; however, diversion is also an option and should be decided on a case-by-case basis. If considering elective surgery, a risk-benefit conversation should be held with the patient regarding next steps.

HIV/AIDS

In 2021, it was estimated that nearly 1.2 million people in the United States were living with HIV, with 32,100 new cases diagnosed that year.¹⁸ Given the significant improvement in antiretroviral medications in recent years, patients with HIV are living much longer with the disease with far fewer infectious complications. Following the trend that diverticulitis increases in older patients, more patients with HIV are now affected by diverticulitis, with an overall incidence similar to the general population. Management of diverticular disease in HIV positive is not well studied. In 2014, Cronley et al evaluated 2,375 patients from the Nationwide Inpatient Sample, Healthcare Cost and Utilization Project database by the Agency for Healthcare Research and Quality. This study found that patients with HIV who had diverticulitis were typically younger (49.9 vs. 60.2 years old, $p < 0.001$), had a significantly higher mortality rate (odds ratio [OR], 3.94; 95% confidence interval [CI], 1.52–10.20), and underwent fewer surgical interventions (OR, 0.74; 95% CI, 0.57–0.95) compared with patients without HIV. There was no significant difference in length of stay related to management of their diverticular disease.¹⁹ The

findings of this study differ from a smaller subsequent case-control study performed in 2018, which demonstrated similar classification of presentation of diverticulitis (complicated vs. uncomplicated disease), but no difference in need for surgery or rates of mortality between these two study populations.²⁰ Overall, there is little published literature about the management of diverticulitis in HIV patients and more research is necessary to best delineate treatment recommendations for this growing and aging population. However, based on the existing data, treatment of patients with HIV and concomitant diverticular disease should follow an algorithm similar to that of immunocompetent patients.

Organ Transplant

Transplant patients represent another unique immunosuppressed population that is increasingly affected by diverticulitis. Nearly 50,000 solid organ transplants were performed in the United States in 2022, with the United States reaching a historic milestone of its one millionth organ transplant that year.²¹ The rates of diverticulitis in this growing patient population are variable, with some studies reporting the incidence similar to that of the general population and other studies identifying a much higher incidence with a notably larger percentage of complicated diverticulitis (40.1%).^{4,22} Klos et al recently (2023) retrospectively studied a group of kidney, liver, and kidney-pancreas transplant patients at the University of Wisconsin before and after transplant. This study found similar rates of failure of nonoperative management and need for urgent colectomy between pre- and posttransplant patients presenting with diverticulitis. Higher body mass index was the only factor noted to be significant with regard to failure of nonoperative management (36 ± 5 vs. 30 ± 2 , $p = 0.02$). Although the 30-day complication rate after colectomy was higher (43% vs. 13%) in the posttransplant group, regression models did not find that posttransplant status had a significant independent effect after adjusting for sex and need for urgent colectomy. Ultimately, the data showed that disease severity at presentation correlated with failure of nonoperative management, and complication rates were higher in those requiring initial urgent colectomy, regardless of pre- or posttransplant status. Interestingly, complication rates were not significantly higher for those requiring colectomy after failure of nonoperative management as compared with those who underwent initial operative management.⁴

Overall, the literature is variable regarding morbidity rate for transplant patients with diverticulitis. Some show increased incidence of complications, particularly after operative management. Others, such as Sugrue et al, found no increased disease-specific morbidity after operative and nonoperative management in transplant recipients as compared with immunocompetent patients with diverticulitis (60% vs. 50%, $p = 0.48$). Interestingly, on multivariate analysis, the only predictor of complications was undergoing operative management.²³ In addition, Lee et al found no increased risk of complications for transplant patients undergoing operative management after recurrent disease as compared with initially at first presentation.²⁴

Available data on transplant recipients seem to echo that of other immunocompromised patients. Nonoperative management is safe for uncomplicated disease and should be managed in the same manner as for immunocompetent patients, as operative intervention is associated with higher morbidity. In complicated disease, surgical management is at times warranted; although it can lead to increased morbidity, this seems to be more so related to disease severity as opposed to immunosuppression status. In addition, there does not appear to be an advantage to elective operative intervention following a first episode of diverticulitis given the high morbidity associated with surgical management.^{4,25}

Autoimmune and Connective Tissue Disease

Very few studies examine patients with autoimmune and connective tissue disease who are also affected by diverticulitis, likely because this is a small, albeit important, population. Several case reports examine patients with Ehlers–Danlos syndrome (EDS), rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and polymyositis, among others. These patients demonstrate higher prevalence and severity of diverticulitis and require thoughtful management considerations in the setting of their chronic diseases.

Ehlers–Danlos Syndrome

Patients with EDS, a connective tissue disease affecting multiple organ systems, have been shown to have up to three times higher rates of hospitalization for diverticulitis as compared with the general population.¹ In 2016, Leganger et al showed that diverticulitis incidence and rate of hospital admission for diverticulitis are higher in EDS patients as compared with the general population (2.0% vs. 0.68% and 1.0% vs. 0.34%, respectively), but demonstrated no significant difference in severity of diverticulitis, treatment, length of stay, or 30-day mortality between the EDS and the comparison cohorts.²⁶ While case reports of successful nonoperative management of complicated diverticulitis (perforation) in a patient with EDS exist, there is a paucity of data evaluating management strategies in this complex patient population.²⁷

Rheumatoid Arthritis

RA is an autoimmune disease characterized by autoantibody formation and immune complex deposition and is often treated with tocilizumab (TCZ), a monoclonal antibody targeting the interleukin 6 (IL-6) receptor. IL-6 is known to mediate colonic contraction and increase proliferation of intestinal epithelial cells following injury. This medication has been shown to increase risk of gastrointestinal (GI) perforation and diverticulitis. As GI perforation is a known complication of RA itself, and as 80% of perforations occur in the lower GI tract, treatment with TCZ should likely be reconsidered in patients with a history of diverticulosis.^{28–30}

While this study helps guide appropriate medical management of RA in patients with known diverticulitis, there are little data to suggest that management strategies of diverticulitis in patients with RA should differ from the general population.

Systemic Lupus Erythematosus

Patients with SLE are noted to have a particularly high risk of perforation due to the pathogenesis of their disease. Similar to RA, the inflammatory process characteristic of SLE is mediated by cytokine release, autoantibody formation, and immune complex deposition. This leads to vasculitis that can cause ischemia and necrosis of any portion of the GI tract. It is likely for this reason that diverticulitis is one of the most common GI manifestations in SLE. Ahmed et al examined a group of patients with SLE and diverticulitis. This group found a female predominance (90% vs. 57.7%) and younger age (62.5 vs. 68.5 years old) among SLE patients with diverticulitis. Perforation rates for SLE patients with diverticulitis were higher (36.9% vs. 35.8%; OR, 1.05; 95% CI, 1.01–1.09); however, abscess and fistula formation rates were lower (4.4% vs. 5.1%; OR, 0.87; 95% CI, 0.80–0.94; and 0.3% vs. 0.5%; OR, 0.68; 95% CI, 0.51–0.91, respectively). This can likely be explained by the pathogenesis of the disease as outlined above. There was no difference in rates of sepsis, GI bleeding, or need for surgical intervention between patients with SLE and those of the general population, but patients with SLE were noted to have a significantly longer length of hospital stay and associated hospital costs. In addition, treatments for SLE such as nonsteroidal anti-inflammatory drugs, biologic therapies, and chronic steroids, which increase the risk of perforation in general, put these patients at a high risk of complicated diverticulitis episodes.²⁰

Other vasculitides, such as polyarteritis nodosa (PAN), also likely have an effect on diverticulitis incidence and presentation, although, due to overall low prevalence, this has not been clearly demonstrated in the literature. The mesenteric vasculitis and necrosis that can be seen with PAN could exacerbate diverticulitis, and the need for chronic steroid therapy should not be disregarded. Although there are no data to suggest that these patients should be managed differently than the general population, special consideration of treatment of underlying vasculitides with early reinitiation of chronic steroids, cyclophosphamide, or other long-term treatments should be considered so that the vasculitis does not worsen the diverticulitis presentation.³¹

Undoubtedly, more studies of these complex patient populations are necessary to better understand the effect of their chronic diseases on diverticulitis presentation and severity, as well as the treatment recommendations for management of diverticulitis in the setting of their comorbidities.

Conclusion

Diverticulitis management presents a unique challenge in the immunocompromised patient, as well as those with underlying connective tissue diseases. Questions of adjustments in management prevail amid a lack of robust research on the topic. Traditional teaching considers these patients to present with more severe disease and to be at higher risk of infectious and anastomotic complication postoperatively due to poor wound healing. Concerns for

delayed presentation and missed diagnoses due to blunted immune response and atypical clinical picture have plagued management paradigms. Previous guidelines had suggested elective colectomy in these patients after the first episode of diverticulitis due to concerns of more severe disease at representation. However, as more studies have examined disease progression and management, practice patterns have changed in the treatment of diverticulitis in the immunocompromised patient. ASCRS guidelines (2020) now state that nonoperative management with intravenous antibiotics, fluids, and bowel rest is appropriate for immunocompromised patients who present with noncomplicated disease. When considering colectomy for patients with uncomplicated diverticulitis in the elective setting, one should consider the increased morbidity associated with operative intervention and weigh this against patient symptoms and quality of life.¹⁴ A similar treatment paradigm for management of complicated diverticulitis is also recommended. As such, proceeding with elective colectomy in the immunocompromised patient, as with the immunocompetent patient, should be an individualized discussion between the provider and the patient considering all the risks and benefits. Similarly, consideration for primary anastomosis in the elective setting at the time of colectomy should be given and immunosuppression alone should not be a contraindication to restoration of intestinal continuity, although robust data on this aspect are lacking. Given the lack of data in patients with connective tissue diseases, an individualized discussion and approach in these patient populations is warranted, bearing in mind that these patients often present with more complex disease.

In general, more work needs to be done to fully understand the effect of various types of immunosuppression and connective tissue disease on the presentation and management of diverticulitis. Most current studies combine all immunosuppressed patients and do not have the power to perform subgroup analyses on each individual class, and data on connective tissue disease are minimal. Overall, treatment of diverticulitis in immunocompromised patients should account for all aspects of a specific patient's presentation, ultimately following the same treatment guidelines as for immunocompetent patients. Providers should be aware that there appears to be an increased risk of morbidity for these patients with complex medical comorbidities, but that both nonoperative and operative management are viable management strategies based on patient presentation and provider judgment.

Conflict of Interest

None declared.

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