AGA CLINICAL PRACTICE UPDATE: EXPERT REVIEW

Management of *Clostridium difficile* Infection in Inflammatory Bowel Disease: Expert Review from the Clinical Practice Updates Committee of the AGA Institute

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This article has an accompanying continuing medical education activity, also eligible for MOC credit, on page e60. Learning Objective–Upon completion of this activity, successful learners will be able to identify and manage *Clostridium difficile* infection in patients with inflammatory bowel disease.

The purpose of this expert review is to synthesize the existing evidence on the management of *Clostridium difficile* infection in patients with underlying inflammatory bowel disease. The evidence reviewed in this article is a summation of relevant scientific publications, expert opinion statements, and current practice guidelines. This review is a summary of expert opinion in the field without a formal systematic review of evidence.

Best Practice Advice 1: Clinicians should test patients who present with a flare of underlying inflammatory bowel disease for *Clostridium difficile* infection.

Best Practice Advice 2: Clinicians should screen for recurrent *C difficile* infection if diarrhea or other symptoms of colitis persist or return after antibiotic treatment for *C difficile* infection.

Best Practice Advice 3: Clinicians should consider treating *C difficile* infection in inflammatory bowel disease patients with vancomycin instead of metronidazole.

Best Practice Advice 4: Clinicians strongly should consider hospitalization for close monitoring and aggressive management for inflammatory bowel disease patients with *C difficile* infection who have profuse diarrhea, severe abdominal pain, a markedly increased peripheral blood leukocyte count, or other evidence of sepsis.

Best Practice Advice 5: Clinicians may postpone escalation of steroids and other immunosuppression agents during acute *C difficile* infection until therapy for *C difficile* infection has been initiated. However, the decision to withhold or continue immunosuppression in inflammatory bowel disease patients with *C difficile* infection should be individualized because there is insufficient existing robust literature on which to develop firm recommendations.

Best Practice Advice 6: Clinicians should offer a referral for fecal microbiota transplantation to inflammatory bowel disease patients with recurrent *C difficile* infection.

*C*lostridium difficile is an anaerobic, spore-forming, gram-positive bacillus.[1,2] Pathogenic strains produce 2 large protein exotoxins (toxin A and toxin B).

In 1978, *C difficile* and its toxins were first identified as causing antibiotic-associated pseudomembranous colitis.[3,4] The incidence and severity of colonic disease caused by *C difficile* have increased greatly in recent years.[5] A study of *C difficile* infection (CDI) in the United States in 2011 found that there were 453,000 incident cases and 83,000 first recurrences.[6] Of greatest concern is the estimated number of CDI-associated deaths at 29,000 per annum, a death rate that exceeds the total number of deaths attributed to both multidrug-resistant gram-negative bacteria and methicillin-resistant *Staphylococcus aureus* combined.[6,7] The ascent of *C difficile* to become the most lethal acute enteric pathogen in the United States led the Centers for Disease Control to designate it as an urgent antibiotic resistance threat in 2015, 1 of only 3 pathogens to earn this attribute (http://www.cdc.gov/drugresistance/biggest_threats.html). The substantial increases in CDI incidence and mortality appear to arise from a combination of factors including increased antibiotic use, an aging population, and the emergence of highly virulent strains such as the BI/NAP1/027/toxinotype III strain.[5,8–10] Patients with inflammatory bowel disease (IBD) commonly experience exacerbations secondary to CDI, which leads to adverse outcomes in IBD patients including increased risk of hospitalization, escalation of IBD therapy, and surgery. Current major challenges of CDI include increasing incidence, frequent recurrences, and progression to severe, or even fatal, disease.[6] These complications are even more problematic when CDI arises against a background of IBD with

Most current article

colitis. Dilemmas for management in these patients include the choice of antibiotic therapy, and timing and need for change in immunosuppressants for IBD. This review summarizes the existing literature and provides management recommendations.

Methods

This article is not based on a formal systematic review but instead seeks to provide practical advice based on the best available evidence, including existing clinical studies, systematic reviews, and practice guidelines. The focus is on the management of both CDI and IBD in patients with underlying IBD who are infected by CDI.

Epidemiology of Clostridium difficile Infection in Inflammatory Bowel Disease

In the late 1970s, toxigenic C difficile was identified as a causative agent in antibiotic-associated colitis and pseudomembranous colitis.[3,4] Shortly thereafter, an increased risk for colonization with toxin-producing C difficile was noted in individuals with IBD, leading to an active debate as to whether C difficile toxins may be a cause for IBD or IBD flares.[11] In more recent years, as the incidence and severity of CDI has increased in the general population, even greater increases have been described in patients with IBD.[12–14] In 2004, 7% of CDI cases diagnosed at one institution occurred in patients with underlying IBD; in 2005, this proportion had increased to 16% (Figure 1A).[15] During the same time period the overall rates of CDI in hospitalized IBD patients increased from 1.8% to 4.6%. Almost all patients with CDI had a prior history of IBD with colitis (91%).[15] Similar trends have been seen in other studies (Figure 1B).[13] The increasing incidence of CDI mainly afflicts patient with ulcerative colitis, increasing from 2.4% of admissions in 1998 to 3.9% in 2004; rates were lower in patients with Crohn's disease (0.8% increasing to 1.2%).[16] In another study, the overall rates of CDI were higher in patients with ulcerative colitis than Crohn's disease, and nearly 8 times greater overall in IBD than in non-IBD patients (Figure 2).[17] These differences may reflect the lower incidence of colitis in Crohn's disease and hence less widespread colonic dysbiosis.

It is important to note that CDI arising in patients with IBD may have several atypical features (Table 1). Patients with IBD who present with symptoms or signs suggesting a colitis flare should be evaluated for the presence of toxigenic C difficile in their stool. A history of recent antibiotic use is not a requirement for testing.

Pathogenic Mechanisms

The potential first step in the pathogenesis of CDI consists of disruption of the normal colonic bacterial
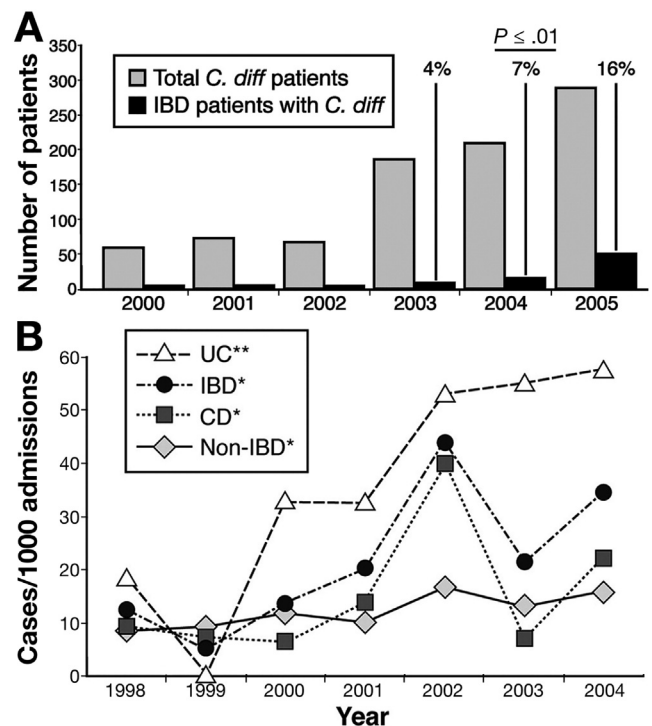

Figure 1. (A) Increasing proportion of IBD patients with C difficile (C diff) infection compared with the total number of C difficile–infected patients at a single referral hospital from 2000 to 2005. Published with permission from Elsevier.[15] (B) C difficile infection incidence at Barnes–Jewish Hospital increased from 1998 to 2004; ulcerative colitis (UC) patients appear primarily to account for the increase observed in the IBD population as a whole. *P < .001 and **P = .08 comparing the first and last 3 years of data. Published with permission from Elsevier.[13]

populations by antibiotic therapy (Figure 3).[1,18] This interferes with the colonization resistance against CDI that naturally is conferred by the gut microbiome. If exposure to C difficile spores then occur, as is common in
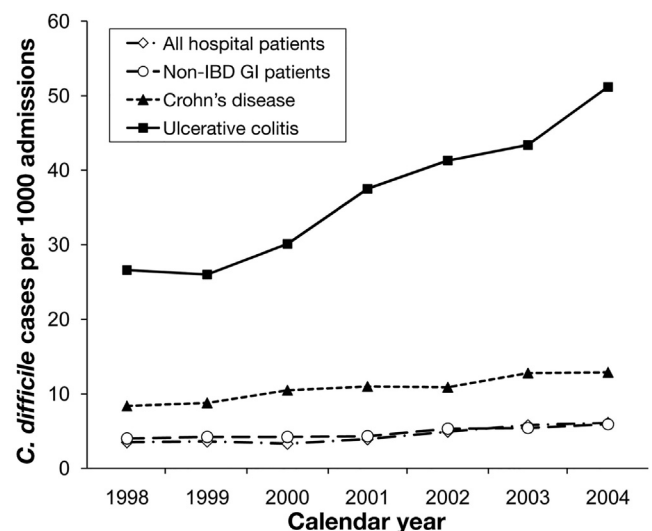

Figure 2. Increasing rates of C difficile infection among hospitalized IBD patients compared with non-IBD gastrointestinal (GI) patients, and a representative sample of all hospital discharges. Published with permission from Elsevier.[17]

Table 1. Atypical Features of C difficile Infection Complicating Inflammatory Bowel Disease

May develop without antimicrobial use
Younger age
More often community-onset
Lack typical colonoscopic features
Simple colonization without infection also is more common
Symptom presence or resolution is an unreliable marker

Data from Issa et al,[15] Ananthakrishnan et al,[16] Clayton et al,[22] Issa et al,[62] and Epple.[63]

nosocomial settings, colonization and disease can follow. CDI risk is age-related; the rate of infection is 7-fold higher in persons older than age 65 years compared with those aged 45 to 64 years.[7,19] Interestingly, asymptomatic carriage of toxin-producing strains of C difficile appears to be as common as CDI and has been linked to protective adaptive immunity against C difficile toxins.[20] Although a majority of cases of CDI are health care–associated, approximately one-third are community acquired and a substantial number of these cases appear not to be antibiotic-associated.[6,21]

In IBD, colonic dysbiosis and loss of resistance to bacterial colonization frequently arises from the underlying colitis, allowing CDI to develop in the absence of any recent antimicrobial therapy.[15,22–25] This predisposing dysbiosis is characterized by a reduced diversity of the colonic microbiota together with alterations in the population distributions, which leads to a loss of colonization resistance against C difficile.[22–25] A majority of CDI cases overall are hospital-acquired or hospital-associated.[1,6,16] However, CDI in IBD often is community-acquired, resulting from contact with C difficile spores that are ubiquitous in the

general environment.[13] Ingested spores germinate under the influence of body temperature, availability of key nutrients, and the presence of primary bile salts.[26,27] Conversely, secondary bile salts, resulting from the action of bacterial hydrolases, are inhibitory to C difficile growth; the balance between primary and secondary bile salts is disrupted by dysbiosis, which can facilitate C difficile colonization and persistence (Figure 3).[27]

The manifestations of CDI are a result of the action of C difficile toxins A and B, which induce colonic mucosal inflammation and injury. The host immune response to C difficile and its toxins may be both harmful and protective. In general, innate immune responses to toxins A and B exacerbate tissue injury through the production of proinflammatory cytokines and the activation and recruitment of polymorphonuclear and other inflammatory cells. Conversely, adaptive immune responses, manifest by the production of neutralizing antitoxin antibodies, protect against symptomatic CDI and against recurrence.[20,28,29]

Disease Outcomes

The combination of CDI and IBD is associated with an increased risk for multiple adverse outcomes when compared with either condition alone (Table 2). Patients with both CDI and IBD remain in the hospital for 3 days longer (95% confidence interval, 2.3–3.7 d) than those IBD patients who are not infected.[16] Concomitant CDI and IBD patients are less likely to respond to medical therapy for their CDI.[15,16,30] These patients are susceptible to frequent flares of their underlying IBD associated with a greater likelihood that their IBD therapy will need to be intensified. Colectomy or other gastrointestinal surgeries
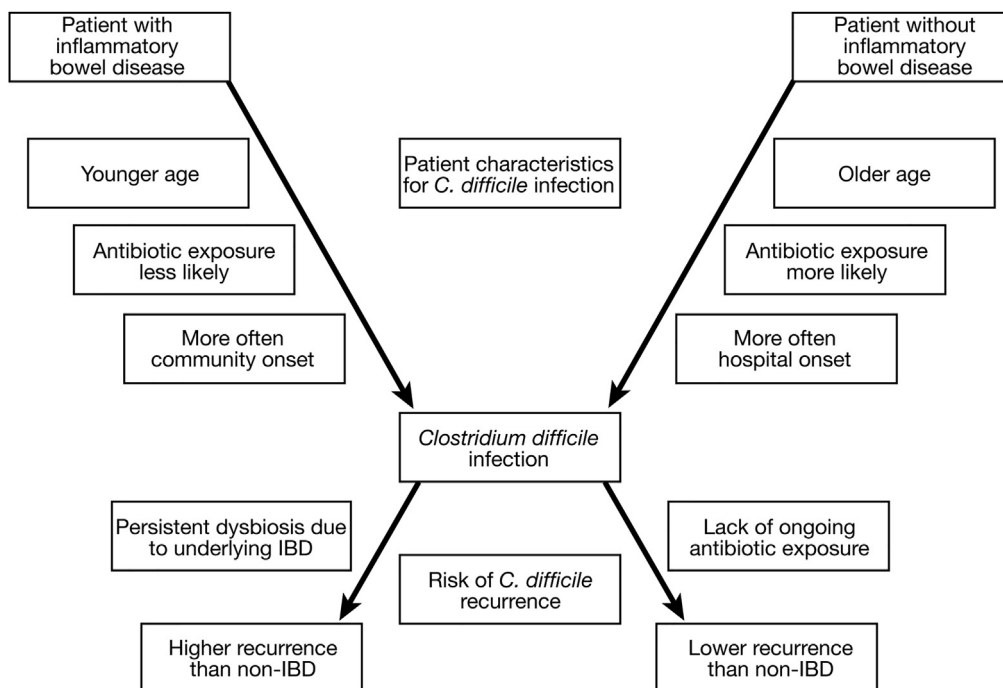

Figure 3. Differences in the pathogenesis of C difficile infection in patients with and without inflammatory bowel disease.

Table 2. Adverse Outcomes of *C difficile* Infection Complicating Inflammatory Bowel Disease

Subsequent IBD flares
More likely to fail medical therapy
More frequent need to escalate IBD therapy
Higher surgery rates
Higher mortality rate than for IBD alone
More frequent CDI recurrences
Increased emergency room visits
Longer hospital stay
Increased health care costs

Data from Rodemann et al,[13] Issa et al,[15] Ananthakrishnan et al,[16] Dubberke et al,[19] Jodorkovsky et al,[30] Khanna and Pardi,[31] and Jen et al.[53]

are required more frequently in patients with CDI complicating IBD.[15,16,30] Of greatest concern is that mortality rates are 4 times higher than in patients with IBD alone.[15,16,31] Not surprisingly, given the series of negative outcomes outlined earlier, health care costs are higher in patients with CDI and IBD compared with IBD alone.[16]

Several risk factors have been identified for recurrence of CDI after an initial response to therapy. These include the following: advancing age, prior CDI recurrence, severe underlying comorbid conditions, ongoing or recurrent exposure to antibiotics, low serum antitoxin IgG, infection with a more virulent CDI strain (eg, ribotype 027 or 078), and, possibly, use of acid antisecretory medication.[32–34] Recent studies have indicated that underlying IBD with colitis can be added to this list of risk factors for CDI recurrence.[31,35] IBD patients with recurrent CDI were more likely than those without to report recent antibiotic therapy; other predictors included mesalamine use, steroid use, biologic therapy with infliximab, and presence of Crohn's colitis.[35]

The associations between CDI in IBD with increased morbidity and mortality are clear. However, the extent to which CDI causes these events is less so. The diagnosis of CDI in a patient with IBD may act as an indicator or marker for patients who already are susceptible to develop some or most of these complications. Regardless of the cause-and-effect sequence, clinicians must recognize that a diagnosis of CDI in their IBD patient warrants close and careful attention to the management of both conditions to avert a complicated or even fatal clinical course.

Clinical Presentation and Diagnosis

The clinical presentations of CDI and of IBD with colitis overlap substantially. Diarrhea is the most prominent symptom, but is more likely to be bloody in IBD; other shared symptoms include abdominal discomfort and fever. Hence, clinical differentiation between an acute IBD flare and acute CDI complicating IBD is difficult. All patients with IBD who present with worsening of underlying diarrhea or symptoms or signs suggesting a colitis flare such as increased blood in stool should be tested for the presence of toxigenic *C difficile* in the stool. Testing methods are the same as for patients who do not have IBD and mainly

consist of nucleic acid amplification tests (NAATs) or enzyme immunoassays (EIAs).[2,36,37] The diagnostic dilemma is heightened by the phenomenon of symptomless carriage of toxigenic *C difficile*.[20,38–40] Hence, a positive stool test for *C difficile* or its toxins does not, in and of itself, absolutely diagnose CDI. This is especially the case when very sensitive assays are used to identify the organism rather than the toxin in stool (eg, NAAT or culture).[41,42] Owing to the potential of overdiagnosis with NAAT, a 2-step testing modality is being used to diagnose CDI with high sensitivity and specificity. The first step is to test for glutamate dehydrogenase using EIA, which is highly sensitive but not specific for *C difficile*. This is followed by EIA for *C difficile* toxins to confirm a diagnosis of CDI. Samples with discordant results can be confirmed with NAAT testing. This strategy potentially may identify true infection and may be the preferred modality to diagnose CDI in patients with IBD owing to nonreliability of symptoms. Although colonoscopy seldom is required to diagnose CDI in the general population, it more frequently is used in patients with possible CDI complicating IBD. However, the classic appearance of pseudomembranous colitis is not typically seen against a background of IBD with colitis, and the histopathologic changes are not differentiated easily.[15] Inflammatory or infectious biomarkers to differentiate colitis caused by CDI vs IBD have not been validated. Faced with these diagnostic challenges and limitations, the expedient approach, when caring for a symptomatic IBD patient with a positive stool test for toxigenic *C difficile*, is to treat initially for CDI and, if a clinical response is not evident, to later intensify IBD therapy (as discussed further later).

Management

Management of Clostridium difficile *Infection in Inflammatory Bowel Disease*

Management of CDI in IBD is exceptionally challenging with dilemmas including distinguishing symptoms of an active infection from an IBD flare, the choice of antibiotic therapy for CDI, and timing and need for escalation vs de-escalation of immunosuppressants for IBD. There is emerging evidence for the use of fecal microbiota transplantation (FMT) for the management of CDI in IBD. In the absence of prospective data specific for the treatment of CDI in IBD patients, evidence from the non-IBD population is used to guide management.

Management of Clostridium difficile *Infection: General Principles*

After initial fluid and electrolyte balance management, a detailed history and laboratory data must be obtained to assess for the number of prior episodes and severity, because treatment depends on these parameters. Concomitant systemic antibiotics ideally should be discontinued or de-escalated. Some experts advocate

withholding antimotility agents and opioids, but these recommendations do not have a robust evidence base. In frail or severely ill patients in whom there is a strong clinical suspicion for CDI, empiric anti-CDI antibiotic treatment may be started while stool test results are pending. Infection control measures including isolation practices, use of gloves and gowns, hand washing, and the use of chlorine-containing disinfecting agents should be strictly implemented.

Metronidazole, Vancomycin, or Fidaxomicin?

According to management guidelines from the American College of Gastroenterology or the Infectious Diseases Society of America, a first and a second episode of mild–moderate CDI is treated with metronidazole 500 mg 3 times a day for 10 to 14 days, despite this being an off-label use.[2,43] A small, single-center, randomized, controlled trial from 2007 indicated that metronidazole was similar to vancomycin for mild–moderate CDI.[44] However, CDI may be more refractory to metronidazole treatment than in the past.[45] In 1 study, from 1991 to 2002, the rate of metronidazole failure was 9.6%, but recent studies have shown that metronidazole failures have increased to as high as 22% to 26%.[45,46] The strongest data came from a post hoc analysis of 2 large, multicenter, phase III, randomized, controlled trials showing that metronidazole was less effective overall than vancomycin for CDI.[47]

Vancomycin has been approved by the US Food and Drug Administration for treatment of CDI and, according to treatment guidelines, it is the first-line therapy for severe (monotherapy) and severe complicated CDI (in combination with intravenous metronidazole).[2,43] Vancomycin is superior to metronidazole for CDI and noninferior to fidaxomicin for initial clinical response in primary or first recurrence.[48] Fidaxomicin, a narrow-spectrum antibiotic, was introduced in 2011 and is efficacious for the management of initial and first CDI recurrence; importantly, clinical trials showed fewer recurrences compared with vancomycin.[48] Patients on concomitant systemic antibiotics also may benefit from fidaxomicin instead of vancomycin in terms of reduced recurrences.[49] However, the higher cost of fidaxomicin has curtailed its widespread use.[50]

Unfortunately, most of the clinical trials investigating CDI medications have excluded IBD patients because of the inability to identify clinical end points of cure. There are limited published data from retrospective studies regarding the use of antibiotics for CDI in IBD patients. In adults with IBD, vancomycin use compared with metronidazole has been associated with a decreased colectomy rate,[15] significantly fewer re-admissions, and an approximately 50% shorter length of hospital stay.[51] An open-label study evaluating the use of fidaxomicin in 21 patients with IBD showed that all patients responded with resolution of diarrhea (81%) or improvement, but not resolution, of diarrhea and negative repeat *C difficile*

testing after fidaxomicin (19%). The rate of recurrent CDI was 19%, with a median time to recurrence of 29 days.[52]

In general, it is pertinent to treat patients with severe CDI (defined either by an increased leukocyte count, increased creatinine level, or low albumin level) aggressively to prevent adverse outcomes such as prolonged length of hospital stay, intensive care unit admission, colectomy, and mortality because these severity-defining parameters have been shown to be associated with these adverse outcomes.[15,53] Similarly, when CDI complicates the course of patients with underlying IBD, it is associated with adverse outcomes such as prolonged hospitalization, need for surgery, escalation of IBD therapy, and increased mortality.[15,53] Hence, IBD can be considered as another CDI severity marker that indicates the need for more aggressive management. In our opinion, vancomycin or fidaxomicin, but not metronidazole, should be used for the management of CDI in IBD.

Management of Recurrent Clostridium difficile Infection in Inflammatory Bowel Disease: Role of Fecal Microbiota Transplantation

The management of recurrent CDI is challenging and the presence of IBD escalates the challenge. The risk of recurrent CDI after a first CDI episode in IBD patients can be as high as 40%, which is substantially higher than the 20% to 25% risk in non-IBD patients. This suggests that perturbation of the gut microbiota in IBD with colitis is an independent risk factor for both initial and recurrent CDI.[35] As a result of adverse outcomes from CDI in IBD, patients with recurrence need to be managed aggressively. The treatment options for recurrent CDI include vancomycin pulse and taper, vancomycin followed by a rifaximin chaser regimen, and intravenous immunoglobulin. Emerging treatment options such as bezlotoxumab, a monoclonal antibody to toxin B, and nontoxigenic *C difficile* are under investigation.[54,55] There is a paucity of literature supporting the use of any of these treatment regimens for CDI management in IBD patients. However, it appears that the response rates and recurrence rates to these regimens are probably less favorable compared with non-CDI patients.

Another treatment option for recurrent CDI includes gut microbial restoration such as FMT, which has been shown to be effective in non-IBD patients with more than 80% efficacy and also in immunosuppressed patients including those with IBD on systemic immunosuppression.[56] One study suggested that IBD patients with CDI can undergo FMT with no safety concerns; response rates were lower than in non-IBD patients and were not dependent on immunosuppressive therapy. However, one quarter of patients with IBD had a clinically significant IBD flare after FMT, with some patients requiring hospital admission.[57] There is also some emerging evidence that FMT may become an adjunct therapy for IBD apart from CDI.[58] There is a lack of evidence on predictors (host or donor) of lack of response to or adverse outcomes from FMT in IBD patients
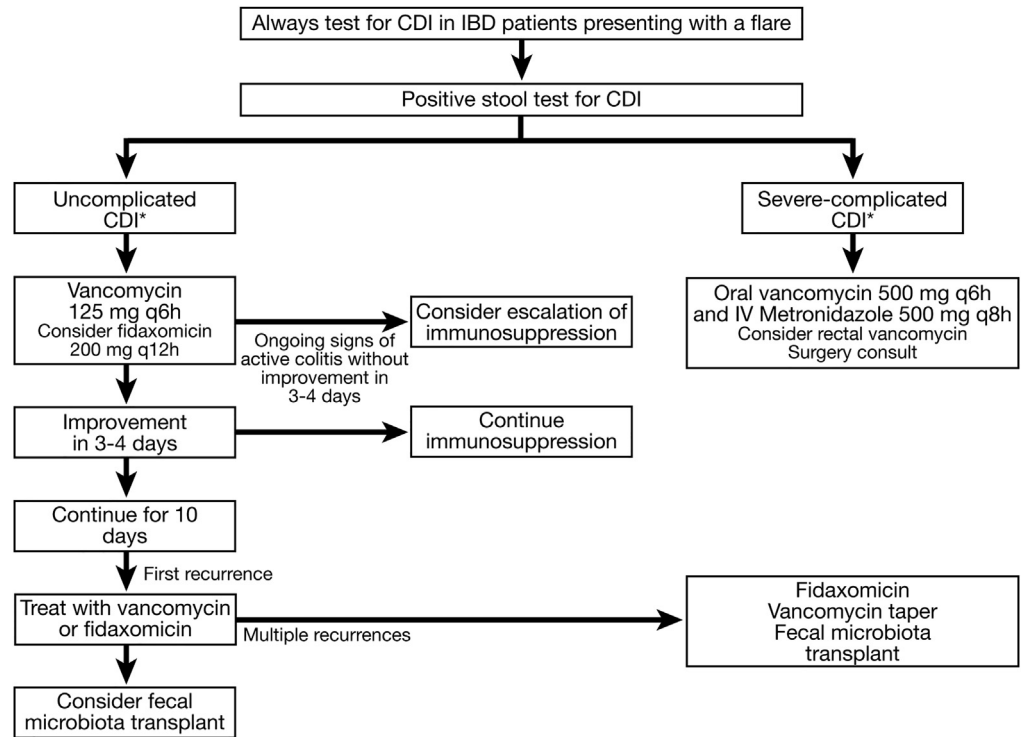
Figure 4. A proposed management algorithm for CDI in patients with inflammatory bowel disease. *Severe-complicated CDI is defined by the intensive care unit admission, hypotension, temperature higher than 38.5°C, ileus/megacolon, mental status changes, leukocyte count greater than 35,000/μL or less than 2000/μL, or lactate level greater than 2.2 mmol/L. These features are absent in uncomplicated CDI. IV, intravenously.

with CDI. FMT for CDI remains experimental and the long-term effects of FMT remain unknown. Upon discussion of risks and benefits, given the high safety and efficacy for FMT in CDI, the high complication rates for CDI in IBD patients, and the lack of data for routine antibiotic regimens for recurrent CDI in IBD patients, FMT may be considered earlier in the course of CDI in IBD such as after the first recurrence, by referring these patients to a center performing FMT for CDI (Figure 4). IBD patients with multiply recurrent CDI may be maintained on long-term suppressive oral vancomycin until FMT is available. The American Gastroenterological Association (http://www.gastro.org/patient-care/procedures/fecal-microbiota-transplant-fmt;

accessed: September 30, 2016) and Infectious Diseases Society of America (https://www.idsociety.org/FMT; accessed: September 30, 2016) provide regular updates on the emerging data and regulations for the use of FMT.

Immunosuppression in the Management of *Clostridium difficile* Infection in Inflammatory Bowel Disease

The biggest challenge in the management of CDI in IBD remains distinguishing symptoms of an IBD flare from those of superimposed CDI. Furthermore,

Table 3. Best Practice Advice

Description	The purpose of this expert review is to synthesize the existing evidence on the management of *Clostridium difficile* Infection in patients with underlying inflammatory bowel disease.
Methods	The evidence reviewed in this manuscript is a summation of relevant scientific publications, expert opinion statements and current practice guidelines.
Best Practice Advice 1	Clinicians should test patients who present with a flare of underlying inflammatory bowel disease for *C difficile* infection.
Best Practice Advice 2	Clinicians should screen for recurrent *C difficile* infection if diarrhea or other symptoms of colitis persist or return after antibiotic treatment for *C difficile* infection.
Best Practice Advice 3	Clinicians should consider treating *C difficile* Infection in inflammatory bowel disease patients with vancomycin instead of metronidazole.
Best Practice Advice 4	Clinicians should strongly consider hospitalization for close monitoring and aggressive management for inflammatory bowel disease patients with *C difficile* infection who have profuse diarrhea, severe abdominal pain, a markedly elevated peripheral blood leukocyte count or other evidence of sepsis.
Best Practice Advice 5	Clinicians may postpone escalation of steroids and other immunosuppression agents during acute *C difficile* infection until therapy for *C difficile* infection has been initiated. However, the decision to withhold or continue immunosuppression in inflammatory bowel disease patients with *C difficile* Infection should be individualized as there is insufficient existing robust literature upon which to develop firm recommendations.
Best Practice Advice 6	Clinicians should offer fecal microbiota transplantation to inflammatory bowel disease patients with recurrent *C difficile* infection.

immunosuppression may lead to worsening of the underlying infection but may be required to manage the IBD flare caused by CDI. As a result, the decision to augment immunosuppressive therapy for clinical worsening secondary to suspected IBD requires careful judgment. In clinical practice, CDI in patients with IBD frequently is treated with both antibiotics and immunosuppression. Unfortunately, there is a paucity of literature answering this very important question.

In a small retrospective cohort study from Europe, 12% of the patients treated with antibiotics and immunomodulators had an adverse outcome of death or colectomy within 3 months of admission or in-hospital megacolon, bowel perforation, shock, or respiratory failure. This compares with no adverse outcomes in those patients treated with antibiotics alone. The use of more than 1 immunomodulator further increased the risk of having an adverse outcome independent of disease severity at presentation.[59] In contrast, a retrospective study from the United States studying IBD patients with CDI showed that low serum albumin level, anemia, and increased creatinine level predicted mortality and colectomy, but the use of immunomodulators, systemic corticosteroids, or anti–tumor necrosis factor agents did not predict these adverse outcomes.[60] Interestingly, 46% of 169 gastroenterologists (25% IBD experts), when asked to comment on case management of CDI in IBD, elected to add immune suppression in combination with antibiotics, but 54% elected to treat flare with antibiotics alone. Overall, 11% elected to withdraw maintenance azathioprine upon CDI diagnosis and more IBD experts stopped azathioprine than non-IBD experts.[61]

In the absence of prospective data, withholding immunosuppression and antibiotic therapy alone for CDI occurring in patients with acute severe IBD cannot be recommended. In sick inpatients, it is reasonable to start patients on corticosteroids and even escalate immunosuppressive therapy after a few days of antibiotic therapy for CDI with vancomycin, because fidaxomicin or metronidazole have failed to improve symptoms. However, upon escalation of immunosuppression, these patients should be monitored closely for worsening symptoms and impending complications (Figure 4).

Summary and Conclusions

C difficile is a common complication in patients with IBD (Table 3). Clinicians should test all patients who present with a flare of underlying IBD for CDI. Patients should be tested for recurrent CDI if diarrhea or other symptoms of colitis persist or return after antibiotic treatment. IBD patients with CDI should be treated with vancomycin instead of metronidazole. Inflammatory bowel disease patients with CDI who have profuse diarrhea, severe abdominal pain, a markedly increased peripheral blood leukocyte count, or other evidence of sepsis should be hospitalized for close monitoring and aggressive management. Clinicians may postpone escalation of steroids and other immunosuppression agents during acute *C difficile* infection until therapy for *C difficile* infection has been established. However, the decision to withhold or continue immunosuppression in inflammatory bowel disease patients with *C difficile* infection should be individualized because there is insufficient existing robust literature upon which to develop firm recommendations. Fecal microbiota transplantation should be offered to patients with IBD with recurrent CDI.

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