Efficacy of Fecal Microbiota Transplantation for Recurrent *C. Difficile* Infection in Inflammatory Bowel Disease

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Background: *Clostridioides difficile* infection (CDI) is associated with poor outcomes in inflammatory bowel disease (IBD) patients. Data are scarce on efficacy of fecal microbiota transplant (FMT) for recurrent CDI in IBD patients.

Methods: We reviewed health records of IBD patients (18 years of age or older) with recurrent CDI who underwent FMT. Outcomes of FMT for CDI were assessed on the basis of symptoms and stool test results.

Results: We included 145 patients (75 women [51.7%]; median age, 46 years). Median IBD duration was 8 (range, 0–47) years, 36.6% had Crohn disease, 61.4% had ulcerative colitis, and 2.1% had indeterminate colitis. Median number of prior CDI episodes was 3 (range, 3–20), and 61.4% had received vancomycin taper. Diarrhea resolved after FMT in 48 patients (33.1%) without further testing. Ninety-five patients (65.5%) underwent CDI testing owing to post-FMT recurrent diarrhea; 29 (20.0%) had positive results. After FMT, 2 patients received empiric treatment of recurrent CDI without symptom resolution, suggesting IBD was the cause of symptoms. The overall cure rate of CDI after FMT was 80.0%, without CDI recurrence at median follow-up of 9.3 (range, 0.1–51) months. Forty-three patients (29.7%) had planned IBD therapy escalation after CDI resolution; none de-escalated or discontinued IBD therapy. Overall, 7.6% had worsening IBD symptoms after FMT that were treated as new IBD flares. No clinical predictors of FMT failure were identified.

Conclusions: Few patients had new IBD flare after FMT. Fecal microbiota transplantation effectively treats recurrent CDI in IBD patients but has no apparent beneficial effect on the IBD course.

Key Words: *Clostridioides difficile* infection, efficacy, fecal microbiota transplant, inflammatory bowel disease

INTRODUCTION

Clostridioides difficile infection (CDI) is the most common cause of in-hospital infectious diarrhea and is associated with adverse outcomes including sepsis, need for intensive care, and death.[1, 2] Risk factors for CDI include antibiotic exposure, hospitalization, comorbid conditions, immunosuppressive treatment, acid-suppressing medications, and contact with active carriers.[3–5] Inflammatory bowel disease (IBD) is an independent risk factor for CDI.[6] The proposed hypothesis, although unclear, is that CDI is secondary to persistent dysbiosis in IBD patients, thereby predisposing them to CDI. These patients can have CDI even in the absence of antibiotic exposure or hospitalization.[7, 8] *Clostridioides difficile* infection in patients with IBD is associated with increased emergency department visits, hospitalizations, IBD therapy escalation, colectomy, length of hospital stay, death, and health care costs.[9–11]

Over the last decade, the incidence rates of IBD and CDI have increased.[12, 13] Fecal microbiota transplant (FMT) has become a mainstream alternative to standard antibiotic therapy for recurrent CDI, with the aim of restoring the intestinal microbiome.[14] Studies have suggested that FMT is a safe and effective therapy, and case series and randomized controlled trials report success rates greater than 85% for patients who received 1 or more infusions.[15, 16] One study reported that FMT is safe and has few adverse events, even for immunocompromised patients[17]; however, in another study, a quarter of patients with IBD had a flare after FMT.[18] In addition, that retrospective study compared the effectiveness of using FMT to treat recurrent CDI between patients with IBD and patients without IBD, and FMT was less effective in patients with IBD (74.4% vs 92.1% of patients had CDI clearance; $P = 0.001$).[18] Another study with 20 IBD patients estimated approximately 75% efficacy in using FMT to prevent recurrent CDI in patients with IBD, and no patients had adverse events.[19] However, given the increasing incidence of CDI in patients with IBD

Received for publications April 16, 2019; Editorial Decision October 2, 2019.

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Presented at Digestive Disease Week, Washington DC, June 2–5, 2018, and published in abstract form: *Gastroenterology*, 2018;154(1):S96.

Abbreviations: CDI, *Clostridioides difficile* infection; FMT, fecal microbiota transplant; IBD, inflammatory bowel disease; PCR, polymerase chain reaction; UC, ulcerative colitis

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doi: 10.1093/ibd/izz299
Published online 9 December 2019

and the reported poor outcomes, further research in this area is necessary.

Therefore, we studied the effect of FMT on the clinical course of CDI in IBD patients to determine if FMT is an effective treatment of recurrent CDI and if FMT improves the course of IBD.

METHODS

The Mayo Clinic Institutional Review Board approved this study. We retrospectively reviewed the electronic health records of a prospectively followed cohort of patients with IBD and CDI who underwent FMT from August 1, 2012, through March 30, 2017, at Mayo Clinic in Rochester, Minnesota, and Phoenix, Arizona.

Patient Population

Adult (18 years of age or older) patients with a clinical and histopathologic diagnosis of IBD and recurrent CDI were considered for FMT. Recipients were screened with a predefined standard protocol,[20] and donors were screened with a standard donor-screening protocol.[4] Patients received education and detailed informed consent that outlined the risks and benefits of and alternatives to FMT before the procedure.

Inclusion Criteria

We included patients with recurrent CDI with underlying IBD (ulcerative colitis [UC], Crohn disease, or indeterminate colitis). All patients considered for FMT had 3 or more CDI episodes proven with a positive polymerase chain reaction (PCR) stool test result for *C. difficile* in the presence of diarrhea and had symptom improvement after prior treatment with antibiotics for CDI. Antibiotics for CDI were stopped 24 hours before FMT.

Exclusion Criteria

Patients with CDI in the ileal pouch were excluded. We also excluded any patient without a laboratory-confirmed diagnosis of recurrent CDI before FMT. Patients who were extremely sick, thus precluding colonoscopy, were excluded from the FMT program.

Clinical Characteristics and Treatment of IBD and CDI

A detailed history of IBD and CDI, which included duration of IBD and number of prior CDI episodes, was obtained from the electronic health records. Prior and concurrent treatments for IBD, including use of an immunomodulator, biologic, and corticosteroid, were recorded. Data were obtained regarding prior CDI treatments and responses. The presence of an IBD flare at the time of FMT was determined on the basis of the clinical judgment of the clinician caring for the patient. Additionally, we recorded the presence of IBD flares (defined as worsening IBD symptoms with or without IBD therapy escalation) at the time of FMT and whether patients had IBD flare after FMT. We also obtained data on the severity of IBD (inactive, mild, mild to moderate, moderate, or severe) as determined by the performing endoscopist at the time of colonoscopy.

Preparation, Stool Processing, and FMT Procedure

The methods for stool preparation and FMT have been previously described for Mayo Clinic in Rochester, Minnesota, and in Phoenix, Arizona.[20, 21] Treatment of IBD was continued according to prior dosing schedules and was not altered because of FMT unless directed by the managing physician. Antibiotic treatment of CDI was stopped 24 hours before FMT. Fecal microbiota transplantation was performed via colonoscopy, and donor stool was infused into the cecum.

Follow-up

Outcomes after FMT were assessed on the basis of patient symptoms or stool test results if symptom resolution was not documented in the electronic health records. All patients with recurrence of diarrheal symptoms were offered repeated CDI testing. The patients were contacted by a nurse via telephone calls at 1 week, 1 month, and 12 months, and symptoms and overall well-being were evaluated with a standard questionnaire.

Statistical Analysis

Statistical analysis was performed with JMP version 13.0 (SAS Institute Inc.). As applicable, data analysis included descriptive statistics, *t* tests for normally distributed continuous variables, nonparametric tests for skewed variables, and χ^2 test or analysis of variance for categorical variables. $P \leq 0.05$ was considered significant.

RESULTS

Demographic and Clinical Characteristics

Of all patients who underwent FMT, 145 patients with IBD were identified, and 75 patients (51.7%) were women. The median age was 46 (range, 19–83) years. Fifty-three patients (36.6%) had Crohn disease; 89 (61.4%) had UC; and 3 (2.1%) had indeterminate colitis.

History of CDI

The median number of prior CDI episodes was 3 (range, 3–20). The median number of prior metronidazole courses was 1 (range,1–5), vancomycin was 2 (range, 1–8), and vancomycin tapers was 1 (range, 0–5). At least 1 vancomycin taper was administered for a prolonged duration and failed in 89 patients (61.4%), and at least 1 course of fidaxomicin failed in 38 patients (26.2%).

History of IBD

The median IBD duration was 8 (range, 0–47) years. Before FMT, 14 patients (9.6%) underwent small-bowel resection, and 8 (5.5%) underwent subtotal colectomy for underlying IBD. Use of IBD medications before, at the time of, and after FMT was determined (Table 1).

CDI Outcomes After FMT

After FMT, 48 patients (33.1%) noted improved symptoms and overall well-being, with resolution of diarrhea and no recurrent CDI symptoms at a median follow-up of 9.3 (range, 0.1–51.3) months. Among the patients with complete symptom resolution, the median time to resolution of diarrhea was 6 (range, 0–10) days. Of the other 97 patients, 95 (65.5%) underwent CDI testing because of post-FMT diarrhea, and 2 received empiric treatment of recurrent CDI without confirmatory testing after FMT and did not have symptom improvement. Of the 95 patients who underwent CDI testing, 29 (30.5%) had positive test results for CDI, and the other 66 patients (69.5%) had CDI resolution confirmed with negative laboratory test results. Thus, the overall cure rate of CDI among patients who received FMT was 80.0% (116 of 145 patients), which was determined on the basis of symptom resolution, negative CDI test results, no response to antibiotics for recurrent CDI after FMT, or a combination of these findings.

Predictors of FMT Failure

Failure of FMT to treat CDI was not associated with history of more than 3 CDI episodes; number of metronidazole or vancomycin courses; ileal or colonic disease; severity of IBD (inactive, mild, mild to moderate, moderate, or severe); IBD subtype; use of a corticosteroid, 5-aminosalicylate, immunomodulator, or biologic before or at the time of FMT; IBD flare after FMT; or escalation of IBD therapy after FMT (Table 2).

IBD Outcomes After FMT

A total of 11 patients (7.6%) had worsening IBD symptoms after FMT. Their symptoms were treated as a new IBD flare, and IBD therapy was escalated after successful resolution of CDI. The median (range) duration to development of new IBD flare after FMT was 15 (range, 4–60) days. Additionally, 32 patients (22.1%) continued to have a flare that started before FMT and required planned escalation of IBD therapy. Therapy for IBD was not decreased or discontinued after FMT in any patient. Of the patients who required IBD therapy escalation, 34 (79.1%) were treated with a corticosteroid, 25 (58.1%) were treated with a biologic, and 15 (34.9%) were treated with an immunomodulator.

Serious Adverse Events

After FMT, 2 patients had severe, self-limiting abdominal pain; they were seen in the emergency department. Computed tomographic scans and emergency department evaluation were unremarkable except for worsening of IBD. One patient had transient hypotension, and because of concern for sepsis, he was admitted to the intensive care unit and required intravenous antibiotics. Symptoms resolved after intravenous fluid resuscitation, with no need for additional antibiotics because of the negative blood culture results.

Management of Recurrent CDI After FMT

Of the 29 patients with CDI recurrence after the first FMT, 17 were treated with vancomycin and 12 with fidaxomicin (Fig. 1). No patients treated with fidaxomicin had recurrence; however, 11 patients treated with vancomycin had recurrence.

DISCUSSION

In this study, FMT was an effective therapy for CDI in patients with IBD, and few serious adverse events occurred. However, FMT had no apparent beneficial effect on the course of IBD, and more than one fourth of patients required IBD therapy escalation to treat an IBD flare after clearance of the CDI infection. In our study, we also found efficacy to be slightly lower in IBD patients compared with that of non-IBD patients, as reported in the literature.[22] Dysbiotic changes that occur before FMT include overabundance of Proteobacteria species and paucity of Bacteroidetes and Firmicutes species.[23] Decreased biodiversity in the gut microbiota of patients

TABLE 1. IBD Medications Administered Before, at the Time of, and After FMT (N = 145)[a]

IBD Medication	Before FMT[b]	At the Time of FMT	After FMT
5-ASA	97 (66.9)	55 (37.9)	63 (43.4)
Biologic	71 (49.0)	56 (38.6)	69 (47.6)
Corticosteroid	108 (74.5)	57 (39.3)	56 (38.6)
Immunomodulator	63 (43.4)	36 (24.8)	46 (31.7)

[a]All values are shown as No. (%).
[b]Medications were administered at least once after IBD was diagnosed.
Abbreviation: 5-ASA, 5-aminosalicylate.

TABLE 2. Demographic, Clinical, and Treatment Characteristics of Patients With IBD and CDI Treated With FMT, Stratified on the Basis of CDI Recurrence After FMT[a]

Characteristic	No CDI Recurrence (n = 116)	CDI Recurrence (n = 29)	*P*
Age, median (range), y	43.5 (19–83)	49.0 (20–79)	0.83
Women	62 (53.4)	13 (44.8)	0.46
Irritable bowel syndrome	5 (4.3)	2 (6.9)	0.57
≥3 CDI episodes before FMT	98 (84.5)	25 (86.2)	0.28
Duration of IBD, median (range), y	7 (1–48)	8 (0.7–36)	0.99
Prior treatment			
5-ASA	75 (64.7)	22 (75.9)	0.24
Immunomodulator	53 (45.7)	10 (34.5)	0.27
Biologic	57 (49.1)	14 (48.3)	0.93
Corticosteroid	84 (72.4)	24 (82.8)	0.23
Antibiotic			
≥1 metronidazole course	17 (14.7)	6 (20.7)	0.44
≥2 vancomycin courses	71 (61.2)	18 (62.1)	0.93
≥1 vancomycin taper	39 (33.6)	8 (27.6)	0.53
≥1 fidaxomicin course	27 (23.3)	11 (37.9)	0.11
Surgery for IBD	16 (13.8)	6 (20.7)	0.89
Concurrent treatment			
5-ASA	43 (37.1)	12 (41.4)	0.67
Biologic	28 (24.1)	8 (27.6)	0.70
Corticosteroid	46 (39.7)	11 (37.9)	0.86
Immunomodulator	43 (37.1)	13 (44.8)	0.44
IBD therapy escalation after FMT			
5-ASA	51 (44.0)	12 (41.4)	0.80
Biologic	54 (46.6)	15 (51.7)	0.61
Corticosteroid	43 (37.1)	13 (44.8)	0.44
Immunomodulator	36 (31.0)	10 (34.5)	0.72
IBD subtype			
Ulcerative colitis	72 (62.1)	17 (58.6)	0.86
Crohn disease	42 (36.2)	11 (37.9)	0.90
Indeterminate colitis	2 (1.7)	1 (3.4)	0.57
Stool donor type			
Family	15 (12.9)	2 (6.9)	0.42
Standard	101 (87.1)	27 (93.1)	0.82
Disease location			
Colon	89 (76.7)	24 (82.8)	0.80
Ileum	23 (19.8)	4 (13.8)	0.58
Ileum and colon	4 (3.4)	1 (3.4)	>0.99
IBD flare	7 (6.0)	5 (17.2)	0.09
Severity of IBD disease[b]			
Inactive	46 (40.0)	11 (37.9)	0.86
Mild	20 (17.4)	6 (20.7)	0.79
Mild to moderate	17 (14.8)	3 (10.3)	0.59
Moderate	19 (16.5)	5 (17.2)	0.92
Severe	13 (11.3)	4 (13.8)	0.73

[a]Values are shown as No. (%) unless specified otherwise.
[b]1 patient was excluded owing to poor bowel preparation.
Abbreviation: 5-ASA, 5-aminosalicylate.

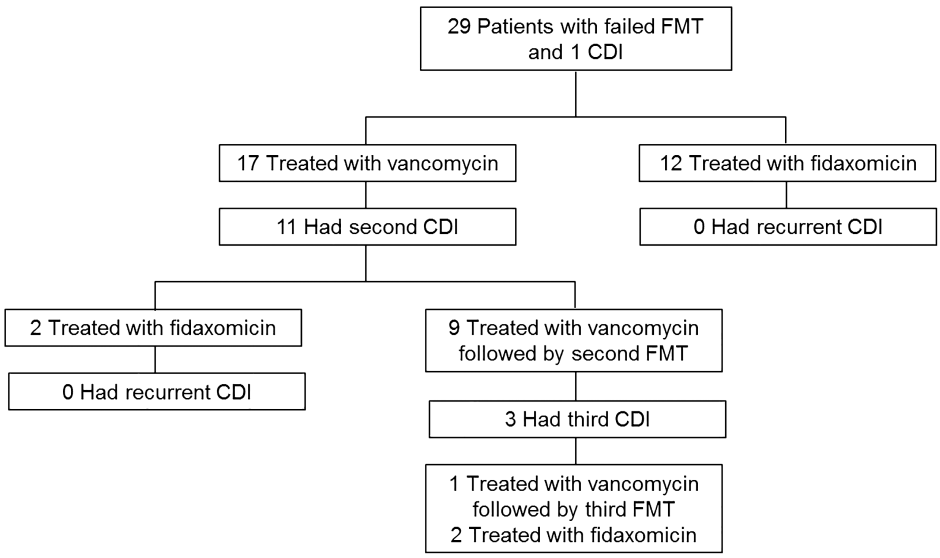

FIGURE 1. Treatment of patients with inflammatory bowel disease after failure of FMT for CDI.

with IBD has been reported, with a lower representation of Bacteroidetes and Firmicutes species and a higher representation of Actinobacteria and Enterobacteria species.[24, 25] These dysbiotic changes have been reversed after successful FMT with stool from healthy donors, resulting in symptom improvement and resolution of CDI.[15, 26, 27] Fecal microbiota transplantation results in engraftment of new species from donors and may lead to proliferation of species that were present at low levels before FMT.[28] Restoration of Bacteroidetes and Firmicutes species and a decrease in Proteobacteria species seem to be key changes after FMT. We previously showed that microbial engraftment after FMT is affected by underlying IBD,[29] which likely explains the lower rate of CDI resolution after FMT, as was also shown by our study.

In our study, we found that FMT had no apparent beneficial effect on the course of IBD, and more than one fourth of patients required IBD therapy escalation to treat an IBD flare after clearance of the CDI infection. As interest in the role of the gut microbiome in the pathogenesis of IBD increases, FMT is being studied for the management of IBD. In 1 study, FMT more often induced remission in patients with active UC (25% had remission) than patients who received a placebo (5%), with no difference in adverse events.[30] However, another randomized controlled trial did not show any benefit of using FMT to manage UC.[31] A recent trial enrolled 85 patients with UC and reported corticosteroid-free clinical remission with endoscopic remission in 27% of patients in the FMT group vs 8% of patients in the placebo group.[32] However, the trial used an intensive FMT dosing schedule (40 FMTs over 8 weeks) with stool obtained from a multidonor pool, and the results suggested that an intensive FMT protocol might be necessary for efficacious treatment of UC. The lack of improvement of IBD symptoms in our patient cohort may be partly attributable to the use of a single-dose FMT schedule, as opposed to multiple-dose schedules used in clinical trials. In summary, the results from these studies suggest that FMT or other microbial therapies may have a future role in the treatment of patients with UC. However, more research is needed on the effect of FMT on IBD.

Patients with IBD whose FMT failed were treated with vancomycin or fidaxomicin. Interestingly, no patients treated with fidaxomicin had further recurrences. A prior study has also suggested lower rates of CDI recurrence in patients treated with fidaxomicin than those treated with vancomycin.[33] However, nonresponse to CDI treatment is extremely difficult to distinguish from an ongoing IBD flare and is mostly diagnosed on the basis of clinician judgment. The risk of recurrent CDI can be as high as 40% in patients with IBD after initial treatment, unlike 20% to 25% in patients without IBD.[34, 35] This risk further increases with additional systemic antibiotics and subsequent CDI episodes.[36] Our results suggest that fidaxomicin might be a better option for patients whose FMT failed if they are not candidates of further FMT.

The strengths of our study include the large number of patients with IBD who received FMT to treat CDI. Limitations include its retrospective design and lack of microbiome profiles. Another limitation of the study was that diagnosis of CDI was based on the clinical judgment of physicians because no objective method can distinguish an IBD flare from CDI. *Clostridioides difficile* infection in IBD patients and IBD flare have similar symptoms (abdominal pain and worsening diarrhea), and testing patients with an IBD flare for CDI is recommended because CDI is a common cause of IBD flares even in the absence of antibiotic exposure.[9, 10] However, PCR is overly sensitive, and toxin detection with enzyme immunoassay has low sensitivity. As part of our program, most patients were tested with a PCR-based assay at our institution or another

location. A PCR stool assay may not distinguish between active infection and carrier state. In our FMT program, in addition to positive stool assay results, we also evaluate baseline symptoms, presence of risk factors for CDI, and response to antibiotic treatment of CDI before diagnosing recurrent CDI and considering FMT. About 20% of patients who were referred for recurrent CDI and for possible FMT received an alternative diagnosis.[37] Additionally, it is very difficult to distinguish IBD from CDI on endoscopy. In our clinical experience, and as reported in a published study,[38] the endoscopic appearance of IBD is similar to that of CDI complicating IBD. In CDI patients without IBD, treatment of CDI with antibiotics leads to remission and resolution of colonic inflammation before FMT is performed.[39] Hence, active inflammation due to CDI is rarely seen after antibiotics lead to remission.

In conclusion, FMT is a safe and effective treatment of recurrent CDI in patients with IBD. Our results may be useful for clinicians weighing the risks and benefits of using FMT to treat CDI in patients with IBD. In addition, because an active infection is usually a barrier to aggressive treatment of underlying IBD, these results may help determine the need for IBD therapy escalation for patients with CDI clearance after FMT but who continue to have worsening IBD symptoms. Although FMT did not alter the course of IBD, it allowed planned escalation of IBD therapy owing to CDI clearance. More research is needed to identify patient and donor characteristics that predict successful treatment of IBD with FMT.

REFERENCES

1. Khanna S, Pardi DS. The growing incidence and severity of Clostridium difficile infection in inpatient and outpatient settings. *Expert Rev Gastroenterol Hepatol.* 2010;4:409–416.
2. Khanna S, Pardi DS. *Clostridium difficile* infection: new insights into management. *Mayo Clin Proc.* 2012;87:1106–1117.
3. Leffler DA, Lamont JT. *Clostridium difficile* infection. *N Engl J Med.* 2015;372:1539–1548.
4. Khanna S, Pardi DS. *Clostridium difficile* infection: management strategies for a difficult disease. *Therap Adv Gastroenterol.* 2014;7:72–86.
5. Tariq R, Singh S, Gupta A, et al. Association of gastric acid suppression with recurrent *Clostridium difficile* infection: a systematic review and meta-analysis. *JAMA Intern Med.* 2017;177:784–791.
6. Rodemann JF, Dubberke ER, Reske KA, et al. Incidence of *Clostridium difficile* infection in inflammatory bowel disease. *Clin Gastroenterol Hepatol.* 2007;5:339–344.
7. Ananthakrishnan AN. Detecting and treating *Clostridium difficile* infections in patients with inflammatory bowel disease. *Gastroenterol Clin North Am.* 2012;41:339–353.
8. Issa M, Vijayapal A, Graham MB, et al. Impact of *Clostridium difficile* on inflammatory bowel disease. *Clin Gastroenterol Hepatol.* 2007;5:345–351.
9. Ananthakrishnan AN, Binion DG. Impact of *Clostridium difficile* on inflammatory bowel disease. *Expert Rev Gastroenterol Hepatol.* 2010;4:589–600.
10. Ananthakrishnan AN, Binion DG. *Clostridium difficile* and inflammatory bowel disease: more questions than answers? *Inflamm Bowel Dis.* 2010;16:1445–1446.
11. Ananthakrishnan AN, Guzman-Perez R, Gainer V, et al. Predictors of severe outcomes associated with *Clostridium difficile* infection in patients with inflammatory bowel disease. *Aliment Pharmacol Ther.* 2012;35:789–795.
12. Ananthakrishnan AN. Epidemiology and risk factors for IBD. *Nat Rev Gastroenterol Hepatol.* 2015;12:205–217.
13. Ma GK, Brensinger CM, Wu Q, et al. Increasing incidence of multiply recurrent *Clostridium difficile* infection in the United States: a cohort study. *Ann Intern Med.* 2017;167:152–158.
14. McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis.* 2018;66:e1–e48.
15. van Nood E, Speelman P, Nieuwdorp M, et al. Fecal microbiota transplantation: facts and controversies. *Curr Opin Gastroenterol.* 2014;30:34–39.
16. van Nood E, Vrieze A, Nieuwdorp M, et al. Duodenal infusion of donor feces for recurrent *Clostridium difficile*. *N Engl J Med.* 2013;368:407–415.
17. Kelly CR, Ihunnah C, Fischer M, et al. Fecal microbiota transplant for treatment of *Clostridium difficile* infection in immunocompromised patients. *Am J Gastroenterol.* 2014;109:1065–1071.
18. Khoruts A, Rank KM, Newman KM, et al. Inflammatory bowel disease affects the outcome of fecal microbiota transplantation for recurrent *Clostridium difficile* infection. *Clin Gastroenterol Hepatol.* 2016;14:1433–1438.
19. Meighani A, Hart BR, Bourgi K, et al. Outcomes of fecal microbiota transplantation for *Clostridium difficile* infection in patients with inflammatory bowel disease. *Dig Dis Sci.* 2017;62:2870–2875.
20. Tariq R, Weatherly R, Kammer P, et al. Donor screening experience for fecal microbiota transplantation in patients with recurrent *C. difficile* infection. *J Clin Gastroenterol.* 2018;52:146–150.
21. Patel NC, Griesbach CL, DiBaise JK, et al. Fecal microbiota transplant for recurrent *Clostridium difficile* infection: Mayo Clinic in Arizona experience. *Mayo Clin Proc.* 2013;88:799–805.
22. Kassam Z, Lee CH, Yuan Y, et al. Fecal microbiota transplantation for *Clostridium difficile* infection: systematic review and meta-analysis. *Am J Gastroenterol.* 2013;108:500–508.
23. Zhang L, Dong D, Jiang C, et al. Insight into alteration of gut microbiota in *Clostridium difficile* infection and asymptomatic *C. difficile* colonization. *Anaerobe.* 2015;34:1–7.
24. Kostic AD, Xavier RJ, Gevers D. The microbiome in inflammatory bowel disease: current status and the future ahead. *Gastroenterology.* 2014;146:1489–1499.
25. Manichanh C, Borruel N, Casellas F, et al. The gut microbiota in IBD. *Nat Rev Gastroenterol Hepatol.* 2012;9:599–608.
26. van Nood E, Dijkgraaf MG, Keller JJ. Duodenal infusion of feces for recurrent *Clostridium difficile*. *N Engl J Med.* 2013;368:2145.
27. Aroniadis OC, Brandt LJ, Greenberg A, et al. Long-term follow-up study of fecal microbiota transplantation for severe and/or complicated *Clostridium difficile* infection: a multicenter experience. *J Clin Gastroenterol.* 2016;50:398–402.
28. Kelly CR, Kahn S, Kashyap P, et al. Update on fecal microbiota transplantation 2015: indications, methodologies, mechanisms, and outlook. *Gastroenterology.* 2015;149:223–237.
29. Khanna S, Vazquez-Baeza Y, González A, et al. Changes in microbial ecology after fecal microbiota transplantation for recurrent *C. difficile* infection affected by underlying inflammatory bowel disease. *Microbiome.* 2017;5:55.
30. Moayyedi P, Surette MG, Kim PT, et al. Fecal microbiota transplantation induces remission in patients with active ulcerative colitis in a randomized controlled trial. *Gastroenterology.* 2015;149:102–109 e106.
31. Rossen NG, Fuentes S, van der Spek MJ, et al. Findings from a randomized controlled trial of fecal transplantation for patients with ulcerative colitis. *Gastroenterology.* 2015;149:110–118.e4.
32. Paramsothy S, Kamm MA, Kaakoush NO, et al. Multidonor intensive faecal microbiota transplantation for active ulcerative colitis: a randomised placebo-controlled trial. *Lancet.* 2017;389:1218–1228.
33. Louie TJ, Miller MA, Mullane KM, et al.; OPT-80-003 Clinical Study Group. Fidaxomicin versus vancomycin for *Clostridium difficile* infection. *N Engl J Med.* 2011;364:422–431.
34. Kelly CP, LaMont JT. *Clostridium difficile*–more difficult than ever. *N Engl J Med.* 2008;359:1932–1940.
35. Khanna S, Pardi DS, Aronson SL, et al. The epidemiology of community-acquired *Clostridium difficile* infection: a population-based study. *Am J Gastroenterol.* 2012;107:89–95.
36. Hu MY, Katchar K, Kyne L, et al. Prospective derivation and validation of a clinical prediction rule for recurrent *Clostridium difficile* infection. *Gastroenterology.* 2009;136:1206–1214.
37. Tariq R, Weatherly RM, Kammer PP, et al. Experience and outcomes at a specialized *Clostridium difficile* clinical practice. *Mayo Clin Proc Innov Qual Outcomes.* 2017;1:49–56.
38. Ananthakrishnan AN, McGinley EL, Binion DG. Excess hospitalisation burden associated with *Clostridium difficile* in patients with inflammatory bowel disease. *Gut.* 2008;57:205–210.
39. Cho JM, Pestana L, Pardi R, et al. Fecal microbiota transplant via colonoscopy may be preferred due to intraprocedure findings. *Intest Res.* 2019;17:434–437.