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Fecal microbiota transplantation as potential first-line treatment for patients with *Clostridioides difficile* infection and prior appendectomy

Zhao JW *et al.* FMT for CDI patient without appendix

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Abstract

Clostridioides difficile infection (CDI) is a global health problem. The association of appendectomy on the severity and prognosis of CDI has been reported in many literatures, but there are still contradictions. In a retrospective study entitled “Patients with *Clostridium* diffuse infection and prior appendectomy may be prone to word outcomes” published in *World J Gastrointest Surg* 2021, the author found that prior appendectomy affects the severity of CDI. Appendectomy may be a risk factor for increasing the severity of CDI. Therefore, it is necessary to seek alternative treatment for patients with prior appendectomy when they are more likely to have severe or fulminant CDI.

Key Words: *Clostridioides difficile* infection; Appendectomy; Fecal microbiota transplantation; Intestinal microbiota; Toxic megacolon; Colectomy

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Core Tip: The fecal microbiota transplantation (FMT) is a universally approved treatment plan for recurrent *Clostridioides difficile* infection (CDI). We believe that early FMT is a better choice for patients with CDI and prior appendectomy even if they are not diagnosed as recurrent CDI. FMT can change the composition of patients' intestinal microbiota in a lasting way to prevent worse outcomes.

TO THE EDITOR

We read with great interest the article by Shaikh *et al*^[1] entitled ¹patients with “*Clostridium difficile* infection and prior appendectomy may be prone to worse outcomes”. They studied the association of ²appendectomy on the severity and prognosis of *Clostridioides difficile* infection (CDI). CDI remains a major health care problem globally. Due to super virulent strains and the abuse of antibiotics, the incidence and severity of CDI have been increasing since 2000^[2].

We found that there were contradictions in the discussion of the role of prior appendectomy on CDI in the previous literature. The sample size of this article is much larger than that of previous studies, which is one of its strengths, thus providing more powerful evidence for future research on ²the relationship between prior ¹appendectomy and CDI. This study did not prove that the ²risk of CDI recurrence in patients with prior ²appendectomy was increased. However, ²appendectomy affected the severity of CDI and was also related to toxic megacolon and colectomy, which was consistent with the conclusion of Yong *et al*^[3], who stated that appendectomy may be a risk factor for the increase in CDI severity. The specific reason still needs to be determined *via* experimental and clinical research. It is speculated that the appendix is the "safe house" of normal colon bacteria^[4], and appendectomy may reduce intestinal immune reactivity, which may reduce intestinal resistance to *Clostridioides difficile* and lead to a worse outcome of CDI. To further confirm and validate the results of this paper, a larger prospective study is needed.

It is necessary to seek a new treatment plan when patients with prior appendectomy are more likely to have severe or fulminant CDI. The fecal microbiota transplantation (FMT) is a method approved by most international guidelines for recurrent CDI^[5,6]. Although FMT has been proven to be safe and effective in recurrent infections, its efficacy in severe or fulminant CDI is still unclear. A series of studies show that FMT combined with antibiotics can reduce the mortality of severe and fulminant CDI^[7] and reduces the occurrence of surgery^[8]. Early FMT can improve the survival rate of patients with severe CDI. Severe CDI patients without FMT have a serious prognosis and a very high

mortality rate (30%-60%)^[9]. FMT treatment in primary severe CDI has a very low disease recurrence rate^[10]. Tixier *et al*^[11] provided low-quality evidence to support FMT as a safe and effective treatment for adult severe and fulminant CDI. At present, some scholars believe that FMT can be used as the first-line treatment for severe and fulminant CDI^[12], but more evidence is needed.

FMT should be performed by an experienced team after a thorough risk assessment. In clinical practice, the need for FMT or even multiple FMTs can be assessed by establishing a risk assessment system that includes prior appendectomy as a risk factor. Additionally, it has been demonstrated that the presence of pseudomembranous lesions under colonoscopy and highly pathogenic CDI strains are predictors of FMT failure, so patients with severe or fulminant CDI may require multiple FMTs until the pseudomembranous lesions disappear and clinical remission is achieved^[13]. We believe that early FMT is a better option to modify the composition of the patient's gut microbiota in a durable way, prophylactically reducing the incidence of toxic megacolon as well as colectomy.

Many risk factors for CDI are immutable (such as advanced age)^[14]. The current prevention strategies mainly focus on improving hand hygiene, contact isolation, environmental purification and antibiotic management plans^[15]. These strategies have been proven to be effective but still have limitations. Shaikh made us realize that new strategies are needed to prevent CDI when dealing with specific patients. Although probiotics are not included in the guidelines for the prevention and treatment of CDI, some probiotic such as strains from *Saccharomyces*, *Bifidobacterium*, or *Lactobacillus* genera have potential protective effect against *Clostridioides difficile*^[16]. For patients who have undergone prior appendectomy, preventive improvement of intestinal flora is the key to avoid worse outcomes.

Many studies have confirmed the long-term safety of FMT for recurrent CDI^[17]. A multicenter long-term follow-up study also showed that FMT is successful and safe for patients with severe or refractory CDI^[18]. These findings all emphasize the value of FMT in avoiding the repeated use of antibiotics which may cause dysbiosis of the intestinal

microbial community permanently. FMT can restore the biological diversity of intestinal microbiota to restore the normal intestinal function. All these enlighten us that FMT has the potential to be the first-line treatment for patients with CDI and prior appendectomy.

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PRIMARY SOURCES

1	f6publishing.blob.core.windows.net Internet	45 words — 4%
2	www.ncbi.nlm.nih.gov Internet	33 words — 3%
3	Danial Haris Shaikh, Harish Patel, Rezwan Munshi, Haozhe Sun et al. " Patients with infection and prior appendectomy may be prone to worse outcomes ", World Journal of Gastrointestinal Surgery, 2021 Crossref	14 words — 1%

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