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# Washed Microbiota Transplantation Using Ileocolic Transendoscopic Enteral Tubing Versus Basic Treatments for Intestinal Inflammatory Obstruction in Crohn's Disease: A Multicenter Concurrent Controlled Trial

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## ABSTRACT

**Background:** Surgical intervention becomes necessary when conservative treatments fail in patients with Crohn's disease (CD) complicated by intestinal obstruction. Given the limited therapeutic alternatives, this study aimed to evaluate the efficacy of washed microbiota transplantation (WMT) compared with conventional basic treatment in managing intestinal inflammatory obstruction in CD.

**Methods:** In this multicenter, nonrandomized, and concurrent controlled trial, patients with active CD and radiologically confirmed intestinal inflammatory obstruction were enrolled. The WMT group underwent WMT following basic treatment during hospitalization, whereas the non-WMT group underwent basic treatment alone. Propensity score matching (1:2) was used to balance baseline characteristics. The primary outcome was the obstruction improvement rate at 28 days, with follow-up continuing until surgery or 3 months post-discharge.

**Results:** Between March 2018 and March 2024, 48 patients were analyzed after matching, with 16 in the WMT group and 32 in the non-WMT group. The 28-day obstruction improvement rate was significantly higher in the WMT group (93.8% vs. 65.6%, $p = 0.021$). For secondary outcomes, the WMT group showed more favorable trends in 14-day improvement, as well as in clinical remission and surgery rates assessed at 1 and 3 months after discharge, respectively. In contrast, the obstruction remission rate at 1 month post-discharge was slightly higher in the non-WMT group. However, none of these differences reached statistical significance. No severe adverse events occurred in the WMT group.

**Abbreviations:** AEs, adverse events; CD, Crohn's disease; CDOS, Crohn's disease obstruction score; EEN, exclusive enteral nutrition; FMT, fecal microbiota transplantation; GMP, Good Manufacturing Practice; HBI, Harvey–Bradshaw Index; IBD, inflammatory bowel disease; IQR, interquartile ranges; PSM, propensity score matching; SD, standard deviation; SIBO, small intestinal bacterial overgrowth; TET, transendoscopic enteral tubing; WMT, washed microbiota transplantation.

You Yu, Xinlu Jin, and Zhaoyang Zhao share co-first authorship.

**Conclusion:** WMT using ileocolic transendoscopic enteral tubing (TET) offers a safe and effective option bridging surgical intervention and conservative treatments in the management of CD with complicated intestinal inflammatory obstruction.
**Trail Registration:** ClinicalTrials.gov NCT01793831, February 2013

## 1 | Introduction

Crohn's disease (CD) is a chronic relapsing inflammatory disorder of the gastrointestinal tract. Among its complications, strictures are the most common structural abnormality, developing in approximately one-third of patients within 5 years of diagnosis [1]. Strictures can be symptomatic or asymptomatic, depending on clinical presentation [2]. Symptomatic strictures may progress to intestinal obstruction, a life-threatening condition that often requires urgent intervention [3, 4].

According to the latest European Crohn's and Colitis Organization (ECCO) guidelines, the preoperative improvement of the conditions of CD patients from emergency to elective therapies is crucial to improve short-term and long-term postoperative outcomes [5]. Elective surgery is preferred over emergency surgery due to lower surgical risks and fewer adverse events (AEs), especially in cases where patients have preoperative immunosuppression and malnutrition [6, 7]. Accordingly, medical therapy and therapeutic endoscopy have been used to relieve obstructive symptoms and defer surgery [8]. However, when medical management and endoscopic interventions fail, or when endoscopic therapy is contraindicated, surgery becomes unavoidable [5, 9]. More than half of patients with CD will undergo at least one surgical procedure during their lifetime [10]. Significantly, elective surgery in CD has notably lower postoperative mortality rates compared to emergency surgery (0.6% vs. 3.6%) [11]. Therefore, advancing new approaches that defer surgery until patients reach optimal health and nutritional status is essential [5].

Gut microbiota plays a key role in the initiation, progression, and treatment response of CD [12–14]. However, the mechanisms and efficacy of fecal microbiota transplantation (FMT) in CD remain controversial [15], likely due to the heterogeneity in FMT protocols and the clinical complexity of the disease. Washed microbiota transplantation (WMT) is a new method of FMT, incorporating an automated washing process that reduces protocol variability and AEs [16]. WMT was released by the consensus statement from the FMT-standardization Study Group in 2019 [17]. In our previous cohort study, WMT induced and maintained clinical response in CD patients with inflammatory masses, suggesting that microbiota reconstruction may attenuate extraintestinal inflammation [18]. For patients with intestinal obstruction, upper gastrointestinal delivery should be avoided because newly introduced luminal contents may aggravate obstructive symptoms. Ileocolic transendoscopic enteral tubing (TET) [19] provides an alternative route, as the catheter can be fixed distal to the obstructed segment and enables repeated WMT without crossing the obstruction site.

We hypothesized that WMT delivered using ileocolic TET could alleviate intestinal inflammatory obstruction in patients with CD and thereby delay surgical intervention. The comparator in this study was standard basic treatment for intestinal obstruction, including fasting, intravenous fluids, and gastrointestinal decompression when necessary, because it remains the most commonly used approach in clinical practice. Given the limited treatment options and substantial surgical risk faced by CD patients with inflammatory obstruction, we conducted a nonrandomized concurrent controlled trial with propensity score matching (PSM) to assess the effectiveness of WMT.

## 2 | Materials and Methods

### 2.1 | Study Design and Patient Recruitment

This nonrandomized concurrent controlled trial was conducted at the Second Affiliated Hospital of Nanjing Medical University and the Affiliated Huai'an No.1 People's Hospital of Nanjing Medical University since March 2018. This study was designed according to TREND guidance [20].

Eligible participants were adults aged ≥ 18 years with active CD, defined as a Harvey–Bradshaw Index (HBI) > 4, and confirmed intestinal inflammatory obstruction through imaging. Patients were eligible only if they did not respond after 3 days of basic obstruction treatment, including fasting, intravenous fluids, and gastrointestinal decompression when indicated. This 3-day window was used as a predefined threshold for initial assessment of treatment response in intestinal obstruction [21]. Exclusion criteria were poorly controlled cardiovascular diseases, including severe heart failure, coronary artery disease, cardiomyopathy, or significant arrhythmia; hemodynamic instability or unstable vital signs at enrollment associated with foreseeable treatment risk; active severe infection exceeding grade 2 per NCI-CTCAE version 5.0, including intestinal fungal, viral, or tuberculous infections; breastfeeding; other serious conditions considered by the investigators to make participation unsuitable; and absent or limited legal capacity.

Patients in the WMT group received WMT using ileocolic TET following basic treatment, and antibiotics were discontinued when WMT was initiated. Patients in the non-WMT group underwent basic treatment alone during hospitalization. Participants were enrolled between March 2018 and March 2024, and chose WMT or continued basic treatment based on preference. PSM at a 1:2 ratio was employed to balance baseline characteristics between groups. As this study was a pilot trial, no formal sample size calculation was conducted.

The primary outcome was the 28-day obstruction improvement rate. Obstruction improvement was defined as the ability to achieve sufficient energy intake of 25 kcal/kg × body weight (kg) from exclusive enteral nutrition without worsening obstructive symptoms. This definition enables clinicians to objectively assess the patient's condition. Secondary outcomes included the 14-day obstruction improvement rate; the proportion of patients achieving an HBI ≤ 4 and a CD obstruction score [22] (CDOS) ≤ 2 at 1 month after discharge; and the surgical intervention rate

**Key Points**

- Ileocolic TET is a novel technique for transanal retrograde intervention in treating CD complications.
- Microbiota transplantation and medication delivery using the ileocolic TET route can effectively treat inflammatory obstructive CD.
- Ileocolic TET can be used to bridge emergency surgery with elective surgery/nonsurgical management in CD.
- Therapies based on transcolonic TET enrich the spectrum of interventional IBD techniques.

within 3 months post-discharge. Clinical remission was defined as HBI ≤ 4, and obstruction remission was defined as CDOS ≤ 2, consistent with prior studies [22]. Safety outcomes included AEs of WMT and TET. Follow-up ended at surgical intervention or at 3 months after discharge, whichever occurred first.

AEs were categorized according to the Common Terminology Criteria, as previously reported [16]. AE severity was graded as mild, moderate, severe, life-threatening, or fatal. AEs potentially associated with WMT were adjudicated as definitely related, probably related, possibly related, or unrelated.

The study protocol was approved by the Institutional Ethical Review Board of the Second Affiliated Hospital of Nanjing Medical University (2012-KY-015) and the Affiliated Huai'an No. 1 People's Hospital of Nanjing Medical University (KY-2017-004-01). This study is part of a registered clinical trial (ClinicalTrials.gov, NCT01793831), approved in February 2013. Participation was voluntary, with all participants providing written informed consent for the treatment. The study was conducted in accordance with the principles of the Declaration of Helsinki. In China, WMT and manual FMT are legal medical therapies for *Clostridioides difficile* infection and other conditions in hospital settings [23, 24].

## 2.2 | Donors and Washed Microbiota Preparation

Donors were college students screened using criteria described previously [17]. Washed microbiota was prepared using an automated purification system (GenFMTer, FMT Medical, Nanjing, China) in a dedicated Good Manufacturing Practice (GMP) laboratory separated from other experiments [16, 17]. Briefly, donor stool was collected in a disposable container, homogenized in normal saline, and centrifuged, after which the supernatant was discarded. The pellet was resuspended in sterile saline and the washing procedure was repeated three times. After the final centrifugation, a vector solution was added to generate washed microbiota for immediate use at a volume ratio of 1:2. A single unit dose of washed microbiota (10 $cm^3$ of microbial cell pellet) was delivered using ileocolic TET once daily at 37°C.

## 2.3 | Ileocolic TET Placement

The ileocolic TET tube with a guide wire used in this study had outer diameters of 2.7 mm (FMT Medical, Nanjing, China). The soft tube was secured to the intestinal wall using endoscopic clips. The distal segment contains three loops designed for fixation to the colonic or ileal wall. The first loop site was fixed to the intestinal wall with one or two disposable endoscopic clips (ROCC-D-26-195-C, ≥ 10 mm, Nanjing Microtech, China). At the second and third loop sites, zero to two clips were used at the discretion of the endoscopist. After removing the guide wire, the extended portion of the tube was separated and the distal external end was secured to the left hip using medical tape. This TET tube was then used for on-demand infusion of microbiota suspension. If the tube needed to pass through a stricture to enable drug delivery, microbiota transplantation, or proximal luminal drainage, the first loop or both the first and second loops could be snipped before insertion. Under endoscopic visualization, the second or third loop was then fixed at the anal-side opening of the stenotic segment.

## 2.4 | WMT Delivery Using Ileocolic TET

Patients were informed about the donor source and microbiota preparation procedures. Antibiotics were discontinued for 12–48 h before WMT and withheld thereafter. If abdominal pain or distension occurred, air and fluid were aspirated using a 20-mL syringe. Patients were generally placed in a Trendelenburg position at a 10° tilt if they could tolerate. One or two units of fresh washed microbiota suspension were prepared at 37°C for infusion using the ileocolic TET. The tube was flushed with 5 mL of normal saline. Following consensus recommendations, the recumbent position was maintained for at least 2 h to extend fluid retention [17]. In severe cases, patients were maintained in a supine position during and after delivery.

## 2.5 | Data Collection and Monitoring

Baseline medications administered before transfer were extracted from discharge records. Imaging was performed on admission for all patients unless completed prior to transfer. Symptoms and medications were recorded daily during hospitalization. Physicians assessed disease activity and obstruction severity using HBI and CDOS at admission and again at 1 month after discharge. Patients were typically scheduled for an outpatient visit 1 month after discharge, with additional follow-up by telephone as needed. All clinically collected data were curated by the investigators and cross-verified against medical records before analysis. Data on WMT delivery and safety evaluation were provided by the China Microbiota Transplantation System. Because this was a pilot nonrandomized study, no formal data monitoring committee was established. The Second Affiliated Hospital of Nanjing Medical University served as the primary coordinating center, and its ethics committee conducted continuing review according to study progress. Faming Zhang possesses complete access to the final trial dataset.

## 2.6 | Statistical Analysis

Analyses were performed using SPSS Statistics (Version 26, IBM Corp., Armonk, NY, USA) and Python (Version 3.9). Normally distributed continuous variables are expressed as mean ± standard deviation (SD), and non-normally distributed continuous variables are presented as median with interquartile ranges (IQR).

PSM was employed to reduce confounding. Propensity scores were estimated using predefined covariates, specifically age and sex, and patients were matched at a 1:2 ratio using nearest-neighbor matching. Balance after matching was assessed using the standardized mean difference (SMD). Sensitivity analysis was conducted to compare the primary outcome before and after matching. Additionally, Firth logistic regression was employed to address variables that remained imbalanced post-matching. Perianal disease was not included as a covariate because it occurred in only one patient in the non-WMT group, which could lead to separation and unstable estimates in multivariable models.

Categorical variables were compared using the $\chi^2$ test or Fisher's exact test, as appropriate. Continuous variables were analyzed using the independent *t*-test for normally distributed data and the Wilcoxon Mann–Whitney test for non-normally distributed data. Associations between variables were evaluated using chi-square tests with Cramer's *V* for nominal–nominal pairs, *F*-tests with $\eta^2$ for nominal–continuous pairs, and Spearman correlation analysis for ordinal or continuous data. A *p*-value of $< 0.05$ was considered statistically significant.

## 3 | Results

### 3.1 | Patients

From March 2018 to March 2024, 94 patients were screened and 74 were enrolled, with follow-up completed for all participants in August 2024. Fifteen patients discontinued for the following reasons: therapeutic endoscopic intervention for intestinal obstruction during hospitalization; administration of anti-TNF-α therapy during hospitalization, which could confound efficacy assessment; resolution of intestinal obstruction before WMT in the WMT group; or diagnosis of other concurrent diseases causing intestinal obstruction (Figure 1). After matching, the SMD for age, gender, and propensity score were all below 0.2 (Figure 2A). The final analytic cohort comprised 16 patients in the WMT group and 32 in the non-WMT group, of whom 41 completed the 3-month follow-up.

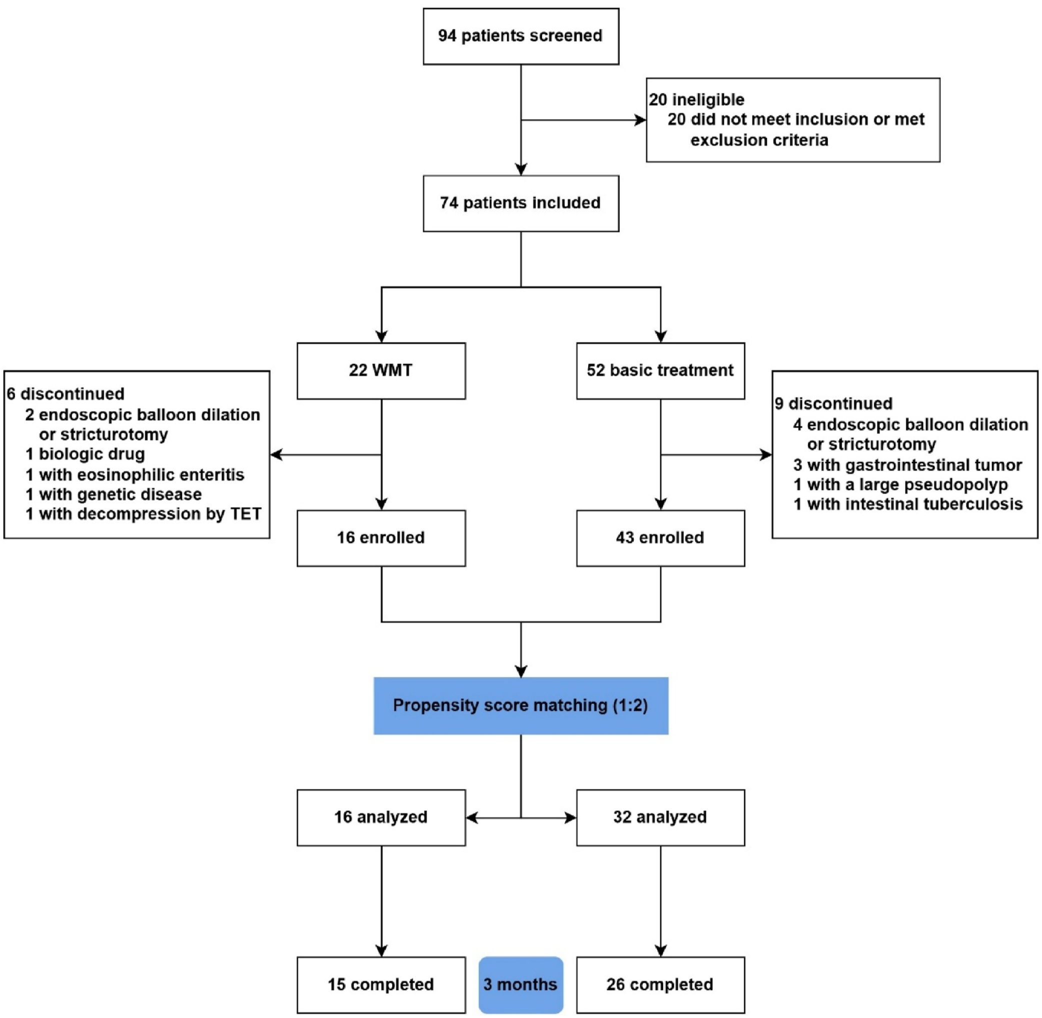


**FIGURE 1** | Flow chart.

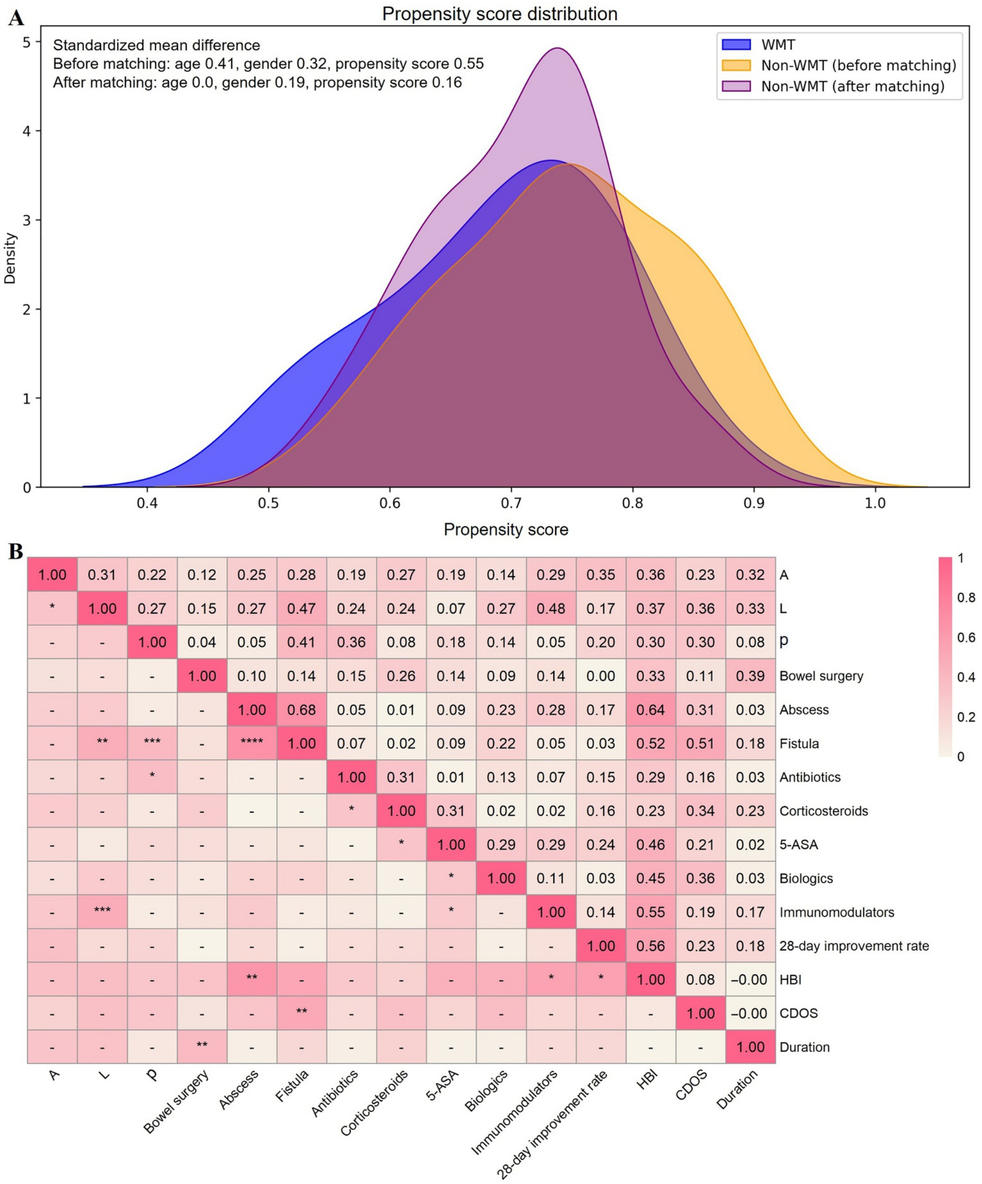


**FIGURE 2** | Propensity score matching and correlation analysis. (A) The distribution of propensity scores and standardized mean differences before and after matching. (B) Analysis of the association between baseline characteristics and primary outcomes after matching. Spearman correlation analysis is presented for ordinal/continuous–ordinal/continuous variables, reporting the absolute values of the correlation coefficients. Chi-square test is presented for nominal–nominal variables and reported the Cramer's *V* values. *F*-test is presented for nominal–continuous variables and reported the $\eta^2$ values. The color intensity reflecting the strength of the correlation. 5-ASA, 5-aminosalicylic acid; A, age at diagnosis; CDOS, Crohn's disease obstruction score; HBI, Harvey–Bradshaw Index; L, location; p, perianal disease. Statistical significance is denoted by asterisks: $*p < 0.05$, $**p < 0.01$, $***p < 0.001$, $****p < 0.0001$.

The baseline characteristics of the two groups were generally comparable (Table 1). Differences in disease duration, perianal disease, and fistula prevalence were observed; however, these variables showed no association with the primary outcomes (Figure 2B). According to the Montreal classification [25], all patients had the stricture phenotype (B2). Notably, 25% of patients in both groups had previously undergone intestinal surgery for CD-related strictures. Detailed baseline characteristics are provided in Table S1. Patients in the WMT group received a median of 6 days of basic treatment (Table S2). Overall, patients in the WMT group had a longer disease duration and a higher prevalence of perianal disease or fistulas than those in the non-WMT group.

Given the severity and urgency of intestinal obstruction, the clinical protocol for the WMT group was designed to maximize clinical applicability, integrating diagnostic evaluation, treatment allocation, and efficacy assessment (Figure 3). A cleansing enema was used for bowel preparation to avoid exacerbation of obstruction by oral laxatives, providing a feasible option for patients with limited oral intake.

## 3.2 | Primary Outcomes

At day 28, the obstruction improvement rate was 93.8% in the WMT group and 65.6% in the non-WMT group ($p$ = 0.021,

**TABLE 1** | Baseline characteristics of the patients.

| Characteristics | WMT group ($n$ = 16) | Non-WMT group ($n$ = 32) | $p$ |
|---|---|---|---|
| Age (years), mean ± SD | 40.6 ± 12.0 | 40.6 ± 13.2 | 1.000 |
| Male, $n$ (%) | 6 (37.5) | 15 (46.9) | 0.537 |
| Disease duration (years), median (IQR) | 7 (4.5–11.0) | 2.5 (0.4–8.0) | 0.027 |
| Crohn's disease phenotype (Montreal classification), $n$ (%) | | | |
| A (age at diagnosis, year) | | | 0.934 |
| A2 (> 16, and ≤ 40) | 10 (62.5) | 20 (62.5) | |
| A3 (> 40) | 4 (25.0) | 9 (28.1) | |
| L (location) | | | 0.233 |
| L1 (ileal disease) | 6 (37.5) | 20 (62.5) | |
| L3 (ileocolonic disease) | 9 (56.3) | 10 (31.3) | |
| B2 (stricturing disease) | 16 (100) | 32 (100) | — |
| p (perianal disease) | 4 (25.0) | 1 (3.1) | 0.023 |
| Bowel surgery[a], $n$ (%) | 4 (25.0) | 8 (25.0) | 1.000 |
| CRP, median (IQR) | 13.8 (6.9–60.3) | 17.4 (3.5–28.9) | 0.710 |
| Additional complications, $n$ (%) | | | |
| Abdominal abscess | 4 (25.0) | 3 (9.4) | 0.160 |
| Fistula | 8 (50.0) | 5 (15.6) | 0.013 |
| Medications, $n$ (%) | | | |
| Antibiotics | 13 (81.3) | 26 (81.3) | 1.000 |
| 5-ASA | 11 (68.8) | 15 (46.9) | 0.152 |
| Systemic corticosteroids | 7 (43.8) | 7 (21.9) | 0.121 |
| Immunomodulators | 5 (31.3) | 8 (25.0) | 0.648 |
| Biologics[b] | 4 (25.0) | 7 (21.9) | 0.809 |
| HBI, median (IQR) | 8.0 (6.0–10.0) | 7.0 (6.0–8.0) | 0.211 |
| CDOS, median (IQR) | 6.0 (3.0–6.0) | 4.0 (4.0–6.0) | 0.363 |

Abbreviations: 5-ASA, 5-aminosalicylic acid; CDOS, Crohn's disease obstruction score; CRP, C-reactive protein; HBI, Harvey–Bradshaw Index; IQR, interquartile range; SD, standard deviation.
[a]Appendectomy is not included.
[b]It indicates that the patient was on regular biologic therapy but did not receive it during the current hospitalization.

Figure 4A). In the WMT group, the duration of WMT following basic treatment until obstruction improvement was combined, as these were considered sequential therapies within the same hospitalization. In the non-WMT group, basic treatment before admission and during hospitalization were combined to represent similar continuous management before and after transfer to our hospitals. This approach ensured comparable treatment periods between the two groups, enabling a more accurate assessment of therapeutic efficacy. The robustness of the matching strategy was evaluated by comparing primary outcomes before and after matching. Prior to matching, the 28-day obstruction improvement rates were 93.8% in the WMT group and 65.1% in the non-WMT group ($p$ = 0.015; Figure S1). We further conducted Firth logistic regression to examine the sensitivity of the results. Both the unadjusted model and the model adjusted for covariates that remained imbalanced after baseline matching ($p$ = 0.034 and 0.047, respectively; Figure S2) yielded results consistent with the post-matching chi-square test, supporting the robustness of the results.

### 3.3 | Secondary Outcomes

At day 14, the obstruction improvement rate was 62.5% in the WMT group compared to 53.1% in the non-WMT group ($p$ = 0.537; Figure 4A). At discharge, 21.9% of patients in the non-WMT group still had intestinal obstruction, whereas all patients in the WMT group had improved (Figure 4B). One month after discharge, 18.8% of patients in the WMT group and 21.9% of those in the non-WMT group achieved a CDOS ≤ 2, indicating obstruction remission without food restriction ($p$ = 0.800; Figure 4C). Further analysis of detailed baseline characteristics (Table S1) revealed that among the seven patients with obstruction remission in the non-WMT group, five (71.4%) had a disease duration of ≤ 1 year, whereas all patients with obstruction remission in the WMT group had a disease duration > 1 year. An HBI score of ≤ 4 typically indicates clinical remission of CD. At 1 month, the remission rates were 75.0% in the WMT group and 56.3% in the non-WMT group ($p$ = 0.206; Figure 4D). For patients who experienced symptom recurrence during the 4-week follow-up, such as patient 8 in the

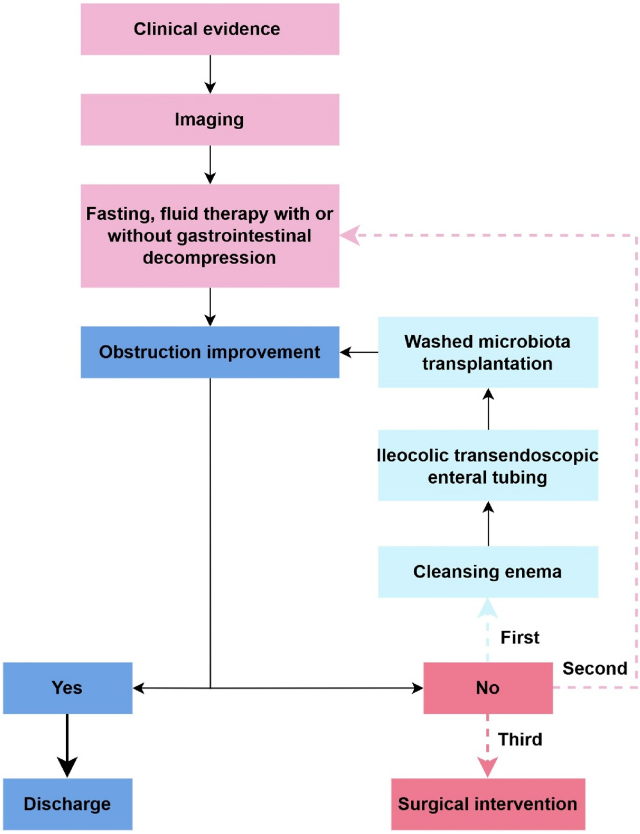


**FIGURE 3** | Clinical protocol for Crohn's disease with intestinal obstruction. The initial diagnosis of intestinal obstruction should be based on persistent clinical symptoms and clinical assessment. Subsequent imaging studies should be performed. If obstructive symptoms do not improve significantly after basic treatment, WMT using ileocolic TET should be considered. EEN should be initiated at 20 mL/h and advanced gradually based on patient tolerance. Patients who tolerate EEN and meet the caloric target (weight × 25 kcal/kg/day) are classified as improved. For those who do not, a second round of basic treatment is recommended. If obstructive symptoms persist, surgery should be considered.

WMT group, the highest HBI and CDOS scores at admission were used for analysis. Sensitivity analyses yielded results consistent with the primary analyses (Figure S2).

Compared to the non-WMT group, the WMT group exhibited a trend towards reduced surgery within 3 months, though the difference did not reach statistical significance ($p = 0.219$; Figure 4E). Sensitivity analysis produced consistent findings (Figure S2). Specifically, 18.8% (6/32) of patients in the non-WMT group underwent surgery, compared with 6.3% (1/16) in the WMT group. In the WMT group, three patients underwent endoscopic balloon dilation or endoscopic stricturotomy within 3 months after discharge, whereas no patients in the non-WMT group underwent therapeutic endoscopic procedures. Paired representative images from two WMT-group patients who completed 3-month follow-up imaging illustrate radiologic changes before and after treatment. Baseline imaging at admission demonstrated significant intra-abdominal inflammatory exudation in both patients (Figure 4F,H), identified as an extra-intestinal factor contributing to obstruction. During follow-up, both patients reported symptomatic improvement, with imaging confirming resolution of the previously observed inflammatory exudation (Figure 4G,I).

The ileocolic TET tube could be flexibly positioned to target inflammatory lesions throughout the colon and terminal ileum (Figure 5). During colonoscopy, scope advancement was frequently limited by inflammatory polyps or intestinal strictures. In cases of severe segmental strictures that precluded passage of the colonoscope, the TET tube was placed distal to the obstruction to deliver WMT. For less severe strictures allowing endoscopic passage, the TET tube was positioned proximal to the narrowed segment, which generally represented a less affected area. Deeper tube placement potentially enhanced post-WMT microbial retention and colonization, as exemplified by patient 3 (Figure 5). Ileocolic TET was successfully performed in all patients without any TET-related AEs. Among the 36 WMTs performed, two AEs (5.6%) were reported, both presenting as mild diarrhea (Table S2). One event was deemed probably related to WMT (patient 6) and the other was deemed possibly related to WMT (patient 11). Both cases resolved spontaneously within 2 days and 2 h, respectively. No serious AEs were observed during the follow-up, indicating favorable safety of WMT using ileocolic TET in patients with intestinal obstruction.

## 4 | Discussion

This study investigated patients with CD presenting with intestinal inflammatory obstruction, a population often excluded from FMT-related CD research, thereby addressing an important evidence gap. WMT delivered using ileocolic TET was proposed as a feasible therapeutic option for intestinal inflammatory obstruction and showed superior efficacy compared with conventional basic treatment. Furthermore, the findings provide valuable insights into the potential of microbiota reconstruction as a strategy for managing complex CD. According to the Preferred Reporting Items for Microbiotherapy (PRIM) guidelines 2024, the present study reported 10 of the required reporting items and 18 specific key points [26].

The inclusion criterion requiring failure of 3 days of basic treatment was selected to minimize the influence of self-limiting obstruction on outcome assessment. In the WMT group, the contribution of initial basic treatment was accounted for by combining the days of basic treatment and WMT when calculating the obstruction improvement rate, and patients whose obstruction resolved before WMT were excluded to avoid confounding. A significant difference in obstruction improvement emerged at 28 days but not at 14 days, likely because patients in the WMT group received a median of six additional days of basic treatment, prolonging the overall treatment course and attenuating early between-group differences. The relatively small sample size ($n = 48$ after matching) also limited statistical power for secondary endpoints. Furthermore, the lack of a guideline-endorsed standard for evaluating obstruction improvement is noteworthy. The present study used a stringent definition of obstruction improvement (exclusive enteral nutrition (EEN) at 25 kcal/kg/day), which may not fully reflect radiologic or functional improvement. A more permissive threshold (e.g., 15 kcal/kg/day) might show a short-term advantage of WMT. Longer

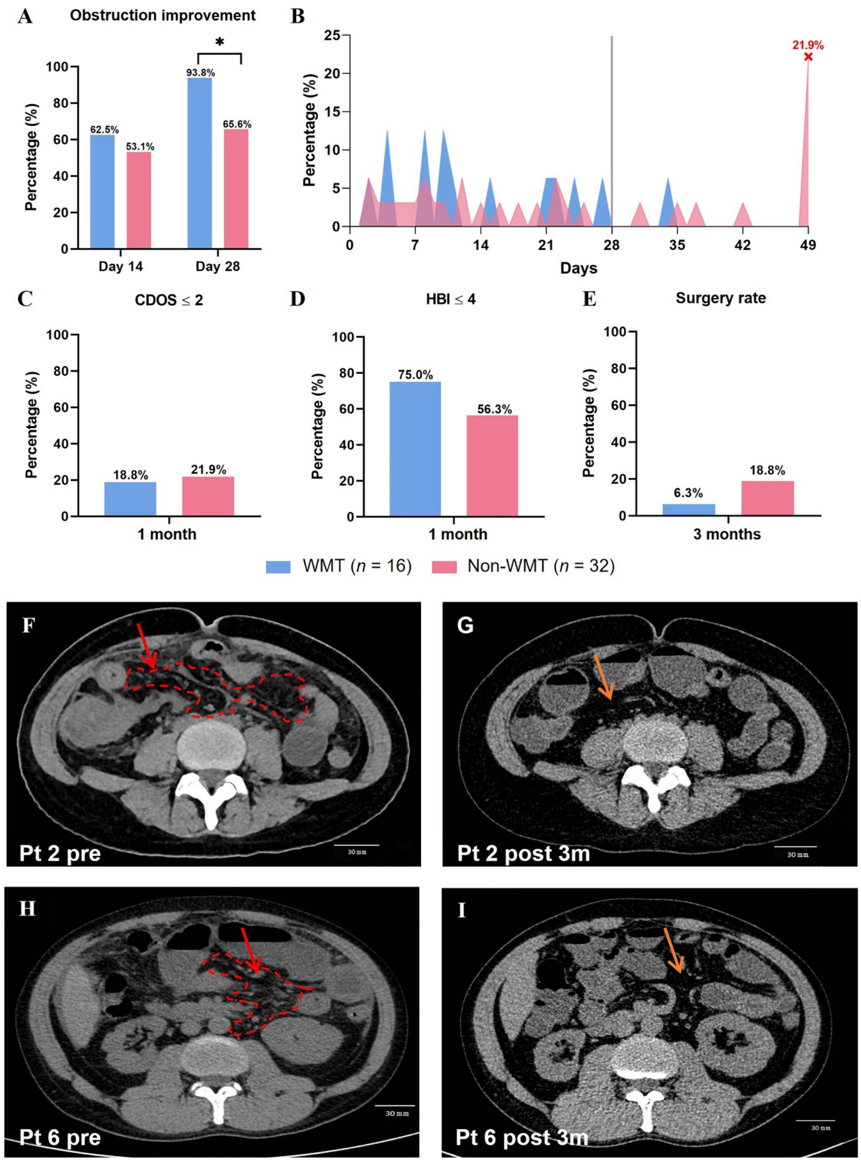


**FIGURE 4** | Outcomes. (A) Comparison of obstruction improvement rate at 14 and 28 days. (B) The percentage of patients with obstruction improved during hospitalization. Red crosses indicate that patients' intestinal obstruction did not improve upon discharge. (C–E) Comparison of obstruction remission rate, clinical remission rate, and 3-month surgery rate between the two groups. Blue represents the WMT group, and red represents the non-WMT group. (F–I) Imaging before and after WMT. Both patients (patinet 2 and patient 6) demonstrate improvement in obstruction signs and intra-abdominal inflammatory exudation on imaging. The red arrow with a red dashed circle indicates the most prominent areas of intra-abdominal inflammatory exudation. The yellow arrow indicates the absorption of inflammatory exudation at approximately the same level on follow-up images. Pt 2 pre: patient 2 before treatment; Pt 2 post 3m: patient 2, 3 months after treatment; Pt 6 pre: patient 6 before treatment; Pt 6 post 3m: patient 6, 3 months after treatment. Significance levels are indicated by asterisks, with *$p < 0.05$.

disease duration and the presence of perianal disease are known to be associated with delayed responses [27], and in these difficult-to-treat cases, WMT clearly increased 28-day obstruction resolution, providing a practical alternative to basic treatment.

Although clinical remission rates (HBI ≤ 4) did not differ statistically between groups with limited sample size, the WMT group demonstrated better trends towards remission. Our previous study reported a lower clinical remission rate of 58.7% (64/109) following FMT [28]. This may reflect differences in disease characteristics: patients in the current study suffered from acute inflammatory obstruction, leading to rapid HBI improvement once obstruction resolved, whereas the previous cohort primarily had chronic inflammatory disease requiring longer recovery. Additionally, HBI has limited applicability for patients with intestinal obstruction because it overemphasizes diarrhea, whereas severe obstruction typically presents with constipation. Nevertheless, as HBI remains a guideline-recommended measure for CD remission, it was retained for completeness in our analysis.

To overcome the aforementioned limitation, we employed the CDOS, an index established in 2017 for CD patients with stricture [22], to provide a more thorough assessment of severity. Although the non-WMT group exhibited a slightly higher rate of obstruction remission (CDOS ≤ 2) compared to the WMT group,

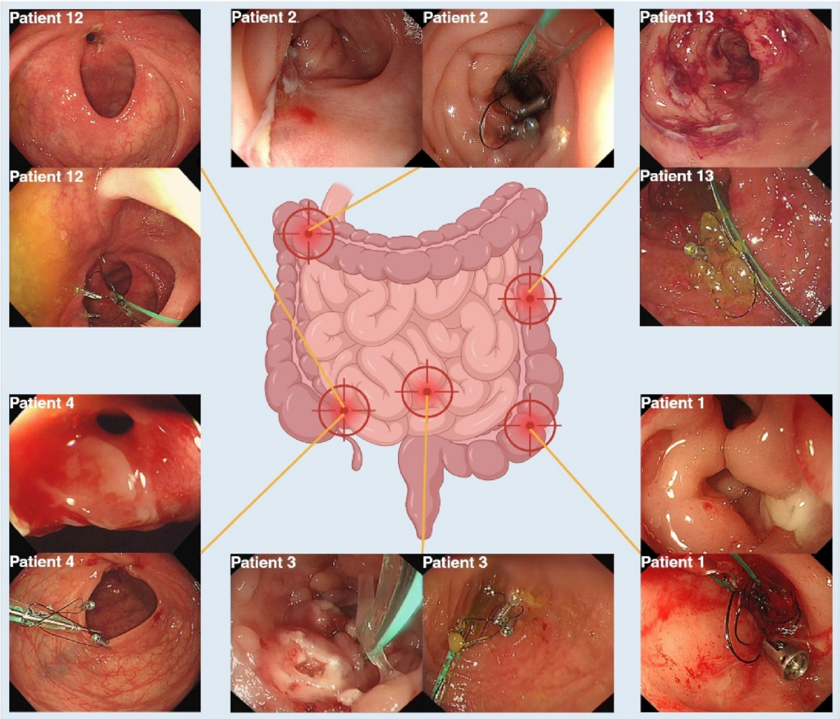


**FIGURE 5** | Ileocolic TET placement according to individual patient conditions. Patient 1: TET tube fixed in the sigmoid colon due to obstructive inflammatory polyps and strictures. Patient 2: TET tube fixed in the transverse colon due to obstruction caused by inflammatory stricture of the ascending colon. Patient 3: TET tube successfully fixed onto the terminal ileum despite obstacles from inflammatory polyps and strictures in the colorectal anastomosis. Patient 4: TET tube fixed in the ileocecal valve due to inflammatory stricture causing obstruction in the intestine. Patient 12: TET tube fixed at the colorectal anastomosis due to inflammatory stricture causing obstruction in the intestine. Patient 13: TET tube fixed on the descending colon due to inflammatory polyps and strictures causing obstruction in the intestine.

this was likely driven by their shorter disease duration: five of seven responders in the non-WMT group had disease for ≤ 1 year, whereas the WMT group had significantly longer disease courses. This observation reveals a limitation of CDOS, namely its insensitivity to duration-dependent disease heterogeneity. Evaluation using the recently proposed 14-day obstructive symptom score may better reflect obstruction severity in future studies [29, 30], though both indices still require extensive validation across diverse CD populations. Although positive outcomes underscore the effectiveness of WMT using ileocolic TET in managing CD with intestinal inflammatory obstruction, the overall low obstruction remission rate (18.8%) illustrates the persistent challenge of treating symptomatic strictures [31]. Interventional inflammatory bowel disease (IBD), which encompasses therapeutic endoscopic techniques bridging medical and surgical approaches, offers an evolving paradigm for managing complex IBD complications [32]. Conventional interventions, such as endoscopic balloon dilation or stricturotomy, are often unsuitable for inflammatory obstruction. Selection of patients ineligible for or contraindicated to conventional interventional IBD procedures allowed for a clear evaluation of WMT efficacy.

Although the pathogenesis of CD remains incompletely understood, compelling evidence supports a key role of gut dysbiosis [33]. Alterations in gut microbial composition affect mucosal immunity and inflammatory status [34]. For example, reductions in *Bifidobacterium*, *Blautia*, and *Lachnospiraceae*, along with enrichment of *Escherichia*/*Shigella*, exacerbate colitis in mice through regulatory T (Treg) cell depletion and M1 macrophage polarization [35]. *Clostridium innocuum*, found within mesenteric adipose tissue, promotes local tissue remodeling through M2 macrophage activation, contributing to the expansion of "creeping fat", a hallmark of CD-related strictures [36, 37]. Other bacteria, such as *Ruminococcus*, are also linked to stricture formation, although mechanisms remain unclear [38, 39]. These insights suggest that WMT may alleviate inflammatory obstruction by reshaping host–microbiota immune interactions. However, few studies have explored microbiota-based therapy specifically in CD with intestinal obstruction, likely because of the difficulty in obtaining samples and the confounding effects of extensive antibiotic exposure [40]. In this study, antibiotics were administered in 81.3% of cases as part of basic treatment. Close collaboration between medical and surgical teams to acquire postoperative specimens may help elucidate the underlying mechanisms of WMT in future work.

Patients with intestinal strictures also face elevated risks of small intestinal bacterial overgrowth (SIBO) [41]. Delivering microbiota through the upper gastrointestinal tract may aggravate this risk and worsen obstruction symptoms. Indeed, one patient (patient 4, WMT group) whose obstruction worsened after gastroscopic FMT before transfer to our hospital underscores this concern. Delivering WMT using ileocolic TET offers a safer alternative by introducing microbiota distal to the obstruction in a bottom-up direction, thereby avoiding luminal stagnation and upper-tract bacterial overgrowth. This approach minimizes passage through the small intestine and associated microbial burden. Emerging ecological evidence further supports the use of region-specific microbial interventions to reduce post-transplant ecological mismatch between donor microbiota and the recipient intestinal niche [42]. The absence of severe AEs in our study supports the safety of this route and aligns with emerging perspectives positioning ileocolic TET as an important advancement in microbiota medicine, representing a concept that extends beyond conventional microbiome research and clinical practice [43]. In complex clinical settings, the favorable safety profile of ileocolic TET supports its integration into a broader microbiota–medicine technological ecosystem, enabling delivery of diverse therapeutic agents, such as corticosteroids, bacteriophages, and traditional Chinese medicine formulas, and thereby facilitating the adaptation to and development of novel therapeutic technologies [44].

Avoiding or postponing surgery remains a central objective in the management of CD-related complications [45]. Previous works have shown that ileocolic TET can help avoid surgery by enabling decompression and local delivery of agents such as corticosteroids [46, 47]. The present study suggests that WMT delivered using ileocolic TET can also contribute to this goal. Although the surgery rate did not differ statistically, only patients in the WMT group underwent subsequent endoscopic therapeutic procedures within the 3-month follow-up, reflecting better local disease control and allowing more time for nutritional optimization before potential surgery [48]. With a larger sample size, WMT using ileocolic TET might demonstrate a significant reduction in the surgery rate within 3 months compared to basic treatment.

However, the present study has several limitations. Future randomized controlled trials with larger sample sizes and extended follow-up durations are needed to provide more solid conclusions. Integration of inflammatory marker profiling, microbiome analysis, and comprehensive imaging will help clarify mechanistic pathways and deepen understanding of obstruction improvement under WMT.

## 5 | Conclusion

WMT using ileocolic TET represents a novel therapeutic alternative for alleviating intestinal inflammatory obstruction in patients with CD, particularly in scenarios where conventional basic treatment alone is insufficient. By improving disease control under more challenging conditions, it can function as a bridge between conservative medical management and surgery, potentially extending the window for optimization before operative intervention.

### Author Contributions

Study concept and design: Y.Y., X.J., Z.Z., and F.Z. Acquisition, analysis, or interpretation of data: Y.Y., X.J., Z.Z., W.W., F.X., C.W., S.L., Q.W., B.C., H.W., and F.Z. Statistical guidance: X.X. Drafting of the manuscript: Y.Y., X.J., and Z.Z. Critical review of the manuscript: Y.Y., X.J., Z.Z., H.W., and F.Z. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.


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### Ethics Statement

The study protocol was approved by the Institutional Ethical Review Board of the Second Affiliated Hospital of Nanjing Medical University (2012-KY-015) and the Affiliated Huai'an No.1 People's Hospital of Nanjing Medical University (KY-2017-004-01).

### Consent

All of the authors agreed to submit and publish the final manuscript. Part of this study was previously presented orally at the 2024 APDW.

### Conflicts of Interest

Faming Zhang conceived the concept of GenFMTer and TET and related devices. Faming Zhang is the Editor-in-Chief of *Microbiota Medicine Research*. To minimize bias, he was excluded from all editorial decision-making related to the acceptance of this article for publication. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

### Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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## Supporting Information

Additional supporting information can be found online in the Supporting Information section.
**Figure S1:** Intestinal obstruction improvement rate at 28 days after treatment in the pre-matching cohort. Statistical significance is denoted by asterisks, with *$p < 0.05$. **Figure S2:** Post-matching Firth logistic regression. Model 1: unadjusted. Model 2: adjusted for "Duration" and "Fistula". **Table S1:** Detailed patient characteristics. **Table S2:** Endoscopy and treatments.