

STUDY PROTOCOL

Official Title: Implications of Fecal Microbiota Transplantation in Modulating the Effects of Liver Cirrhosis

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1. Background

Liver cirrhosis is associated with profound alterations of the intestinal microbiota, which contribute to systemic inflammation, disease progression and complications such as hepatic encephalopathy. The gut–liver axis plays a crucial role in the pathophysiology of cirrhosis, as microbial imbalance may promote endotoxemia, immune dysregulation and worsening liver function.

Fecal microbiota transplantation (FMT) has emerged as a promising therapeutic approach aimed at restoring microbial diversity and intestinal homeostasis. By transferring intestinal microbiota from a healthy donor to a patient, FMT may improve gut barrier integrity, reduce inflammation and potentially improve clinical outcomes in patients with liver disease.

Several studies have suggested that modulation of gut microbiota may improve hepatic encephalopathy and liver-related outcomes. However, evidence regarding its impact on liver fibrosis and cirrhosis progression remains limited. The present study investigates the potential clinical benefits of fecal microbiota transplantation in patients with alcohol-associated liver cirrhosis.

2. Study Objective

The objective of this study is to evaluate the clinical effects of fecal microbiota transplantation on liver fibrosis and hepatic encephalopathy in patients diagnosed with alcohol-associated liver cirrhosis.

3. Study Design

This study is designed as a prospective clinical investigation conducted over a three-year period between 2023 and 2025.

A total of 19 participants with alcohol-associated liver cirrhosis are included in the study and divided into two groups:

FMT group: 6 patients receiving fecal microbiota transplantation.

Control group: 13 patients receiving standard medical therapy for liver cirrhosis.

Participants are recruited from adult patients admitted primarily to the Gastroenterology Department of the County Clinical Emergency Hospital of Sibiu.

4. Study Population

Eligible participants are adult patients diagnosed with liver cirrhosis according to standard international diagnostic criteria based on clinical, laboratory and imaging evaluations.

Although gender is not a predefined selection criterion, all enrolled participants are male, which contributes to greater cohort homogeneity and reduces potential variability related to sex differences.

Some patients presenting characteristics of metabolic dysfunction associated with alcohol-related liver disease (MetALD) may be included, reflecting real-world clinical practice. However, none of the enrolled participants meet the diagnostic criteria for metabolic syndrome according to the NCEP ATP III guidelines.

5. Eligibility Criteria

Inclusion Criteria

Participants must meet the following criteria:

Age \geq 18 years

Diagnosis of alcohol-associated liver cirrhosis

Documented abstinence from alcohol at study enrollment

Ability and willingness to provide written informed consent

Exclusion Criteria

Participants are excluded if they present:

Cirrhosis of non-alcoholic etiology

Uncertain or unconfirmed diagnosis of liver cirrhosis

Age below 18 years

Concomitant malignancies

Major trauma

Hemodynamic or respiratory instability

Acute or chronic infections including HIV, tuberculosis, cytomegalovirus, multidrug-resistant Enterobacteriaceae, parasitic or fungal infections

Severe immunodeficiency

Comatose state or severely impaired consciousness

Refusal or inability to provide informed consent

6. Study Procedures

All participants undergo baseline clinical and paraclinical evaluation including:

clinical examination

laboratory tests

stool sample collection

abdominal ultrasound

liver elastography

Participants assigned to the FMT group undergo colonoscopy with fecal microbiota transplantation using stool obtained from a screened healthy donor.

Following the transplantation procedure, participants undergo a follow-up evaluation approximately one month (approximately 30 days) after the intervention.

The follow-up visit includes:

clinical examination

laboratory investigations

abdominal ultrasound

liver elastography

Patients included in the FMT group must not have received antibiotic therapy during the three months preceding transplantation.

7. Control Group Management

Patients assigned to the control group receive standard medical therapy for liver cirrhosis, which may include:

normocaloric diet

normoproteic diet

normolipidic and normoglucidic dietary regimen

beta-blockers

hepatoprotective agents

diuretics

Baseline clinical and laboratory assessments are performed at study entry.

A follow-up evaluation is conducted approximately one month (approximately 30 days) after the baseline assessment.

Alcohol consumption is prohibited throughout the study period.

8. Donor Selection and Screening

Fecal donors are selected from healthy volunteers, including both relatives of patients and unrelated individuals.

Preference is given to young donors without significant comorbidities. All donors provide written informed consent and undergo extensive screening procedures.

Screening includes:

medical questionnaire assessing epidemiological risk factors

complete blood count

biochemical and coagulation tests

screening for HIV infection

screening for viral hepatitis

stool examination for occult blood

microbiological and parasitological stool analysis

These measures are implemented to minimize the risk of infectious transmission to recipients with liver cirrhosis.

9. Preparation of Fecal Material

On the day of transplantation, fecal material is prepared according to a standardized protocol.

A minimum of 70 g of stool is mixed with 250 mL of sterile 0.9% sodium chloride solution in a sterile container and homogenized for approximately three minutes.

The mixture is filtered through sterile gauze layers to remove particulate material. The filtrate is transported to the hospital and used for transplantation within approximately six hours after preparation to ensure microbial viability.

10. Fecal Microbiota Transplantation Procedure

FMT is performed via colonoscopy following standard bowel preparation with polyethylene glycol solutions.

Sedation and analgesia are administered according to routine clinical protocols.

Following transplantation, patients are instructed to avoid defecation for approximately two hours in order to improve transplant retention.

11. Outcome Measures

Primary Outcome

Liver fibrosis assessed by measurement of liver stiffness (kPa) using transient elastography (FibroScan).

Secondary Outcome

Hepatic encephalopathy assessed using the EncephalApp Stroop Test.

Clinical staging of encephalopathy is performed according to the West Haven classification.