

**Informed Consent Form**  
**Randomized Controlled Clinical Study on**  
**Fecal Microbiota Transplantation for**  
**Elderly Patients with HFpEF**

Lead Institution: The First Affiliated Hospital of Air Force Medical University

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## **Informed Consent–Information Page**

Dear Patient:

You have been diagnosed with **Heart Failure with Preserved Ejection Fraction (HFpEF)**. We invite you to participate in a randomized controlled clinical study on fecal microbiota transplantation (FMT) for elderly patients with HFpEF. This study plans to enroll 50 participants. We will compare standard therapy combined with FMT versus standard therapy combined with placebo, analyzing improvements in quality of life, cardiac function, cardiac structure, nutritional status and other related indicators in elderly HFpEF patients. The study aims to explore the role and mechanism of gut microbiota in elderly HFpEF patients, providing new insights for the prevention and treatment of HFpEF in the elderly. This study protocol has been reviewed and approved by the Ethics Committee of The First Affiliated Hospital of Air Force Medical University (Xijing Hospital).

Before deciding whether to participate in this clinical study, please read the following information carefully. It will help you fully understand the purpose, procedures, duration, potential benefits, risks and discomforts of participation. You may discuss this with your relatives and friends, and consult the study physician, who will explain any questions you may have and assist you in making your final decision.

### **Study Background**

HFpEF is a common cardiac disease in which the heart contracts normally (preserved ejection fraction) but fails to relax effectively, impairing blood return. It is prevalent in the elderly and often accompanied by obesity, diabetes, hypertension and other comorbidities. Currently, there are no specific effective drugs, and existing treatments mainly target comorbidities without improving long-term prognosis. Recent studies have found that gut microbiota imbalance may exacerbate cardiac dysfunction. Our preliminary research indicates that modulating gut microbiota (e.g., probiotic supplementation) may improve cardiac function and activities of daily living in HFpEF patients. FMT, which transfers gut microbiota from healthy donors to patients, has shown therapeutic potential in obesity, diabetes and other conditions. Basic research suggests FMT may improve cardiac function by regulating gut microbiota and reducing inflammation.

Based on current evidence and the limitations of HFpEF treatment, we aim to investigate the efficacy of adding FMT to standard anti-heart failure therapy for HFpEF. Positive results from this study may provide a new treatment option for HFpEF patients, benefiting a broader population.

### **Study Objectives**

To explore the role and mechanism of gut microbiota in elderly HFpEF patients and provide evidence for the prevention and treatment of HFpEF in the elderly.

### **Study Design**

1. Informed Consent and Screening: You may voluntarily sign the informed consent form prior to enrollment. The physician will collect your medical history, previous medication records and auxiliary examination results (e.g., echocardiography, blood biochemical tests). Eligible participants may enroll voluntarily. Refusal to participate

will be fully respected.

2. Study Procedures for Enrolled Participants: (1) Baseline Assessment (1–2 weeks before intervention): We will collect your medical history, perform physical examinations, routine laboratory tests (blood routine, liver and renal function), cardiac and inflammatory biomarker tests, 12-lead electrocardiogram, echocardiography, and assessments of frailty, sarcopenia, body composition, nutrition, physical activity and quality of life. Fecal and blood samples will be collected for gut microbiota analysis, gut microbiota metabolite testing and intestinal barrier function assessment. (2) Intervention and Follow-up: Eligible participants will receive free FMT or placebo intervention (placebo capsules made of starch, identical in appearance to FMT capsules but containing no viable bacteria). Bowel preparation with polyethylene glycol or lactulose will be administered before transplantation. FMT/placebo capsules (4 capsules per dose, within 1 hour after breakfast and lunch) will be taken orally for 6 consecutive days. Comprehensive reassessments (identical to baseline) will be conducted at Week 4 and Week 20 of treatment.

3. Required Cooperation: (1) Strictly adhere to the prescribed medication regimen to ensure data validity. (2) Truthfully report clinical data to study physicians for accurate efficacy analysis. (3) Attend all scheduled follow-up visits for efficacy evaluation and treatment guidance.

### **Inclusion and Exclusion Criteria**

Inclusion Criteria:

1. Aged  $\geq 60$  years old;
2. Meeting the diagnostic criteria for HFpEF:
  - (1) Consistent with the epidemiological and demographic characteristics of HFpEF patients;
  - (2) Presence of clinical symptoms and/or signs of heart failure;
  - (3) Cardiac imaging examination indicating LVEF  $\geq 50\%$ ;
  - (4) In sinus rhythm: BNP  $\geq 35$  pg/ml and/or NT-proBNP  $\geq 125$  pg/ml;  
In atrial fibrillation: BNP  $\geq 105$  pg/ml and/or NT-proBNP  $\geq 365$  pg/ml;
  - (5) Meet at least one of the following conditions:
    - a. LVMI  $\geq 115$  g/m<sup>2</sup> (male) or  $\geq 95$  g/m<sup>2</sup> (female);
    - b. LAVI  $> 34$  ml/m<sup>2</sup>;
    - c. Relative wall thickness  $> 0.42$ , or left ventricular free wall thickness  $> 12$  mm;
    - d. Septal  $e' < 7$  cm/s, or lateral  $e' < 10$  cm/s, or average  $E/e' \geq 14$ ;
    - e. Tricuspid regurgitation velocity  $> 2.8$  m/s, or pulmonary artery systolic pressure  $> 35$  mmHg;
3. NYHA functional class II–III;
4. Complicated with metabolic diseases such as hypertension, diabetes and obesity;
5. Accompanied by gastrointestinal symptoms;
6. Well-tolerated to current anti-heart failure regimens with stable medication for at least 1 month;
7. Stable heart failure condition without acute exacerbation;
8. Basically normal cognitive function, capable of understanding scale assessment contents;

- 9. Able to perform daily activities independently;
- 10. Fully understanding the purpose of this clinical trial, voluntary participation and signing of written informed consent.

**Exclusion Criteria:**

- 1. Symptoms caused by non-cardiac diseases;
- 2. Patients with any contraindication to Fecal Microbiota Transplantation (FMT):
  - (1) Patients with severe intestinal barrier damage induced by various causes, such as sepsis, active massive gastrointestinal bleeding, intestinal perforation;
  - (2) Patients diagnosed with fulminant colitis or toxic megacolon;
  - (3) Patients unable to tolerate enteral nutrition meeting 50% of calorie requirements due to severe diarrhea, significant fibrous intestinal stenosis, severe gastrointestinal hemorrhage, high-output intestinal fistula and other conditions;
  - (4) Patients with congenital or acquired immunodeficiency diseases;
  - (5) Patients receiving high-risk immunosuppressive or cytotoxic drugs recently, such as rituximab, doxorubicin, or moderate-to-high dose steroids (prednisone  $\geq 20$  mg/d) administered continuously for more than 4 weeks;
  - (6) Severely immunosuppressed patients with neutrophil count  $< 1500/\text{mm}^3$ ;
- 3. History of myocardial infarction, coronary artery bypass grafting, or any event that may reduce LVEF within 6 months before enrollment (unless LVEF  $\geq 50\%$  was confirmed);
- 4. Received valve replacement surgery within 6 months before enrollment;
- 5. Poorly controlled blood pressure (SBP  $\geq 180$  mmHg or DBP  $\geq 100$  mmHg);
- 6. Current acute decompensated heart failure requiring intervention;
- 7. Resting heart rate  $> 120$  beats per minute, or complicated with malignant arrhythmia;
- 8. Significant coronary artery disease requiring PCI revascularization;
- 9. Severe renal insufficiency (serum creatinine  $> 442 \mu\text{mol/L}$ ) or patients on dialysis;
- 10. Pre-existing gastrointestinal diseases, including ulcerative colitis, Crohn's disease, irritable bowel syndrome, chronic diarrhea;
- 11. Current malignant tumors requiring anti-tumor treatment;
- 12. Complicated with acute diseases or acute exacerbation of chronic diseases at present;
- 13. Participation in other interventional clinical trials or oral intake of probiotic preparations within the past 3 months.

**Study Procedures**

This is a **randomized, double-blind, controlled study**. Eligible participants will be randomly assigned to either the FMT group or the placebo group. You will receive **free FMT or placebo capsules**. After bowel preparation with polyethylene glycol or lactulose, you will take FMT/placebo capsules (4 capsules per dose, within 1 hour after breakfast and lunch) for 6 consecutive days, in addition to your standard anti-heart failure medication. Comprehensive assessments (medical history, physical examination, laboratory tests, fecal/blood samples, electrocardiogram, echocardiography, quality of life assessment, etc.) will be performed at baseline, Week 4 and Week 20.

Please contact the study team with any questions.

## **Risks and Discomforts**

This study adds FMT or placebo to standard anti-heart failure therapy. Placebo capsules (starch-based) are inert and have no adverse effects. FMT capsules use stool from healthy donors with high *Ruminococcus* content, screened for infectious and genetic diseases to minimize risks. Common FMT adverse effects include gastrointestinal symptoms (nausea, vomiting, abdominal pain, bloating, diarrhea) and rare systemic symptoms (fever, aspiration-related pneumonia). Interventions will be performed by experienced staff following standardized protocols. Close monitoring will be provided post-intervention to promptly manage adverse events.

Please notify the study physician immediately of any discomfort, new symptoms or unexpected events during the study, regardless of causality.

## **Management of Emergencies During Treatment**

For adverse events or emergencies related to the study intervention, or serious adverse events due to disease progression:

- If you are at the hospital, emergency treatment will be provided immediately.
- If you are at home, seek local emergency care and contact the study team promptly (or report directly to our hospital if feasible).

All adverse events will be reported to the hospital Ethics Committee to protect your safety and rights.

## **Potential Benefits of Participation**

Direct Benefits:

- Possible improvement in heart failure symptoms, cardiac function and quality of life.
- Access to personalized study results for better disease understanding and early prognosis prediction.

Indirect Benefits:

- Individual: Reduced disease burden, improved quality of life and enhanced medical care during the study.
- Societal: Insights into gut microbiota's role in HFpEF, advancing prevention and treatment strategies for elderly HFpEF patients and improving therapeutic adherence.

## **Study Costs**

Routine HFpEF-related tests (blood routine, liver/renal function, lipids, glucose, NT-proBNP, echocardiography, electrocardiogram) are at your own expense. All study-specific costs (FMT, inflammatory biomarkers, gut microbiota analysis, metabolite testing, intestinal barrier function assessment, 6-minute walk test, frailty/sarcopenia/body composition/nutrition/quality of life assessments) are covered by the study. No additional compensation is provided for participation.

## **Compensation for Study-Related Harm**

In the event of study-related harm, necessary medical treatment will be provided, with costs and compensation covered in accordance with national laws and regulations.

## **Confidentiality of Personal Information**

All study data will be stored securely at the hospital. Your identity will be protected using unique identifiers instead of names. Identifiable information will be removed from all datasets to prevent linkage to individual participants.

The Ethics Committee and regulatory authorities may access your original medical records for study verification (sponsors have no access). Your signature on the

informed consent form authorizes this access. Study results may be published or shared for scientific purposes, but your personal identity will never be disclosed.

**Withdrawal from the Study**

Participation is voluntary. You may refuse enrollment or withdraw at any time **without penalty or loss of benefits**, and your subsequent medical care will not be affected. Please notify the study physician if you plan to withdraw, who will conduct a final health assessment for your safety. The study team will inform you of any new information affecting your participation.

**Contact Information**

You may request study updates or report adverse events/concerns at any time via:

- Investigator Phone: [\_\_\_\_\_]
- Investigator Name: [\_\_\_\_\_]

**Ethics Committee Contact**

This study is approved by the hospital Ethics Committee. Report any protocol violations to the Xijing Hospital Ethics Committee at:

- Phone: 029-84771794

## Informed Consent Signature Page

**Study Title:** Fecal Microbiota Transplantation for Elderly Patients with HFpEF: A Randomized Controlled Trial

**Ethics Approval No.:** [\_\_\_\_\_]

### 1. Participant Consent Statement

I have read and understood the study information, had the opportunity to discuss the study with the physician and ask questions, and all my questions have been answered satisfactorily.

I understand the potential risks and benefits of participation. I confirm that my participation is voluntary, I have sufficient time to consider my decision, and I understand:

- I may request additional information at any time.
- I may withdraw from the study at any time without discrimination or penalty, and my medical care and rights will not be affected.
- If I withdraw (especially due to study-related issues), disclosing changes in my condition and completing follow-up assessments will benefit myself and the study.
- I will consult the study physician before starting any new medications during the study, or report such use truthfully afterward.
- I authorize access to my study data by regulatory authorities, the Ethics Committee or sponsor representatives.

I voluntarily agree to participate in this study and will comply with medical advice as much as possible.

Participant Signature: \_\_\_\_\_ Date: // \_\_\_\_

Legal Guardian Signature (if applicable): \_\_\_\_\_ Date: // \_\_\_\_

Participant Contact Phone: \_\_\_\_\_

### 2. Investigator Statement

I confirm that I have fully explained the study details, including participant rights, potential benefits and risks, and provided a signed copy of the informed consent form to the participant.

Investigator Signature: \_\_\_\_\_ Date: // \_\_\_\_

Investigator Contact Phone: \_\_\_\_\_