Project Source and Registration Number：**A Multicenter, Randomized Controlled Study on the Evaluation of Functional Impairment and the Promotion of Exercise Rehabilitation Standards in Maintenance Hemodialysis (MHD) Patients KFKT-1023-005**

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Project Title：A Multicenter, Randomized Controlled Study on the Evaluation of Functional Impairment and the Promotion of Exercise Rehabilitation Standards in Maintenance Hemodialysis (MHD) Patients

Sponsoring Institution： The First People's Hospital of Yunnan Province

Department： Department of Nephrology

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I. Study Introduction

Maintenance hemodialysis (MHD) is the primary renal replacement therapy for patients with end-stage renal disease (ESRD). The therapeutic goal has gradually shifted from simply prolonging survival to improving quality of life. However, MHD patients commonly exhibit impaired physical function, with a reduction of more than 50% in physical activity compared to the general population. Prolonged bed rest or lack of exercise leads to muscle weakness, functional impairment, reduced quality of life, and significantly increased hospitalization and mortality rates. This not only imposes a heavy economic and caregiving burden on families but also places enormous pressure on healthcare resources. How to improve physical function, reduce complications, and enhance quality of life in MHD patients has become a major focus in nephrology research worldwide.

In recent years, the application of rehabilitation medicine in nephrology has gained increasing attention. Based on available evidence, Chinese experts have proposed the "Standards for Rehabilitation Services in Chronic Kidney Disease Patients" (hereinafter referred to as "the Standards"), which define the core objectives, technical procedures, and safety requirements for exercise rehabilitation in MHD patients. The Standards emphasize that scientific rehabilitation interventions can improve functional impairment, enhance overall health, and reduce hospitalization and mortality. Building on these Standards, this study will employ a multicenter, randomized controlled trial (RCT) to verify the clinical effectiveness of implementing the Standards in improving functional impairment among MHD patients, and to evaluate the feasibility and effectiveness of promoting exercise rehabilitation techniques (ERT).

The central concept of this study is to integrate individualized exercise rehabilitation into routine hemodialysis sessions, providing a safe, controlled, and cost-effective intervention. The ERT consists of three phases: warm-up, core exercise, and relaxation. Warm-up includes simple stretching and limb movements to prepare patients for exercise; the core phase involves upper-limb resistance training and bedside cycling to progressively improve muscle strength and endurance; relaxation activities relieve post-exercise tension and improve comfort and compliance. The study will primarily evaluate the effects of ERT on physical function, psychological health, nutritional status, cognitive function, and overall quality of life in MHD patients, while also recording hospitalization and mortality as key clinical endpoints.

II. Study Objectives

The objective of this study is to evaluate functional impairment in MHD patients in

accordance with the Standards, and to promote exercise rehabilitation practices. The study aims to determine whether standardized rehabilitation interventions can improve functional impairment, reduce hospitalization and mortality, and enhance clinical prognosis in MHD patients.

III. Study Design and Methods

1) Study Population:

Eligible participants are MHD patients meeting the following criteria: undergoing regular dialysis for >3 months, three sessions per week, Kt/V ≥ 1.2, clinically stable, aged 18–74 years, and able to provide written informed consent. Exclusion criteria include NYHA class IV heart failure, recent unstable angina, severe peripheral arterial disease or musculoskeletal disorders, walking distance <200 meters, or oxygen saturation <90%. These criteria ensure participants can tolerate exercise interventions and complete follow-up.

2) Interventions:

The intervention is based on the Standards for rehabilitation services in CKD patients. The intervention group will receive structured ERT in addition to routine hemodialysis. The program includes:

1. Warm-up (e.g., stretching, leg raises),
2. Core exercise (e.g., upper-limb resistance training, bedside cycling),
3. Relaxation (e.g., whole-body stretching).

Each session lasts 20–60 minutes, three times weekly, for two years. The control group receives only routine hemodialysis without additional exercise. All sessions will be supervised by trained healthcare staff, and individualized prescriptions will be adjusted according to patient conditions to ensure safety and feasibility.

3) Sample Collection:

This study will recruit 800 MHD patients across 15 hemodialysis centers in China, with 40 participants planned at The First People's Hospital of Yunnan Province. Eligible patients will be randomized to intervention or control groups using sealed envelopes. Baseline assessments will include demographics, medical history, laboratory tests (hemoglobin, albumin, electrolytes, inflammatory markers, etc.), and functional impairment evaluations. Follow-ups will occur every 6 months (5 times total), with an additional 5 mL blood sample collected at each visit for metabolomics and proteomics analyses.

During the intervention, patient functional outcomes (e.g., 6-minute walk test, muscle strength) and endpoints (hospitalization, mortality) will be recorded. All

samples and data will be anonymized, coded, and managed securely to ensure quality and confidentiality. At study completion, samples and data will be handled per regulatory requirements, and findings will provide scientific evidence for clinical adoption of ERT.

IV. Inclusion and Exclusion Criteria

Inclusion Criteria:

1. On MHD ≥3 months,
2. Age 18–74 years,
3. Three sessions per week, Kt/V >1.2,
4. Adequate standard medical management.

Exclusion Criteria:

1. NYHA class IV heart failure,
2. Uncontrolled unstable angina,
3. Severe peripheral arterial disease or musculoskeletal disease,
4. Walking distance <200 m,
5. Resting SpO_2 <90%,
6. Amputation or other conditions preventing exercise.

Endpoint Events:

1. Cardiovascular events: acute myocardial infarction, other acute coronary syndromes, hospitalized congestive heart failure, severe arrhythmia (e.g., complete AV block, cardiac arrest).
2. Cerebrovascular events: intracerebral hemorrhage, subarachnoid hemorrhage, ischemic stroke (including cardioembolic stroke).
3. Exercise-related hospitalizations and mortality.

Withdrawal Criteria:
Participants will be withdrawn if any of the following occur (recorded in “Clinical Event Form”):

1. Major changes in dialysis modality (frequency, switch to high-flux dialysis, additional blood purification techniques),
2. Pregnancy,
3. Switch to peritoneal dialysis,
4. Kidney transplantation,

5. Withdrawal of informed consent,
6. Loss to follow-up (including transfer to another hospital),
7. Completion of scheduled follow-up.

Withdrawn cases will be censored in data analysis.

V. Participant Protection Measures

1. Participant Management

①. **Recruitment:**
Patients will be screened from the Department of Nephrology, Hemodialysis Center, The First People's Hospital of Yunnan Province, based on inclusion and exclusion criteria. Assessment will be conducted by qualified physicians to ensure no additional risk of disease progression from study participation.

②. **Informed Consent:**
Trained staff will explain study objectives, procedures, potential risks, and benefits. Participants will be assured that their routine treatment will not be affected. Written informed consent will be obtained from participants with full decisional capacity. Privacy and information security will be ensured during the consent process.

③. **Confidentiality:**
Personal information will be strictly protected. Data will be anonymized or coded and used only for statistical purposes. All procedures will comply with the Personal Information Protection Law and ethical standards.

④. **Compensation:**
At each follow-up visit (every 6 months, total 5 visits), an additional 5 mL blood sample will be collected. All procedures will follow clinical and ethical standards. Participants will receive financial compensation of 50 RMB per sample, settled in a lump sum at study completion.

2. Data Safety and Monitoring

①. **Data Management:**
Data will be stored in an electronic management system with integrity, security, and audit traceability. Regular backups will be performed.

②. **Statistical Analysis:**
After data collection, descriptive and inferential statistics will be conducted using SPSS. Analyses will include measures of central tendency and dispersion, correlation tests, and multivariate regression to explore relationships between variables.

③. **Ethics Committee Reporting:**
A final summary report will be submitted upon study completion, including baseline characteristics, analysis results, and study conclusions.

3. Biological Samples:

Collection and use of biological samples (e.g., blood) will be restricted to the purposes defined in informed consent. Storage and disposal will comply with regulatory requirements.