Informed Consent Form

Double-Blind, Randomized Parallel Contrast Clinical Study of

Yiqi Lishui Formula on Sepsis-Induced Myocardial Dysfunction

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Information for Clinical Research Participants

Dear Madam/Sir:

You are invited to participate in a clinical study titled "A Double-Blind, Randomized Controlled Clinical Trial of Yiqi Lishui Formula in the Treatment of Sepsis-Induced Myocardial Dysfunction."This study aims to evaluate the efficacy and safety of Yiqi Lishui Formula in the treatment of sepsis-induced myocardial dysfunction.

Before you decide whether to agree to participate in this study, please read the following information carefully. It will help you understand the study, why it is being conducted, the procedures and duration, as well as the potential benefits, risks, and discomforts associated with participation. If you wish, you may discuss this with your relatives or friends, or ask your doctor for further explanation to help you make a decision.

I. Study Overview

1. The study you are invited to participate in is an interventional research study.
2. Study Title: Double-blind randomized parallel contrast clinical study of Yiqi Lishui formula on sepsis-induced myocardial dysfunction

   Principal Investigator: Guo Nan
3. Study Objective: To evaluate the efficacy and safety of Yiqi Lishui Formula in the treatment of sepsis-induced myocardial dysfunction.
4. Study Procedures: This study is a two-center, prospective, parallel-group, double-blind, randomized controlled trial. A total of 80 participants with sepsis-induced myocardial dysfunction (SIMD) who meet the inclusion and exclusion criteria will be recruited from the ICUs of Tongzhou District Traditional Chinese Medicine Hospital and Dongzhimen Hospital, Beijing University of Chinese Medicine. Participants will be randomly assigned in a 1:1 ratio to either the experimental group or the control group (50% probability of being assigned to each group). Both groups will receive standard SIMD treatment. The experimental group will receive

Yiqi Lishui Formula granules orally or via nasogastric tube, while the control group will receive a placebo orally or via nasogastric tube. The treatment duration is 7 days, with a follow-up period of 28 days. The primary outcome measure is brain natriuretic peptide (BNP). Secondary outcome measures include echocardiography, cardiac biomarkers, inflammatory markers, severity of illness scores, ICU length of stay and costs, and 28-day survival rate. These will be used to evaluate the clinical efficacy and safety of Yiqi Lishui Formula in SIMD.

5. Study Drugs:

(1) Yiqi Lishui Formula Composition: Astragalus Root 30g, Angelica sinensis 30g, Honeysuckle Flower 30g, Capillary Artemisia Herb 15g, Giant Knotweed Rhizome 15g, Lepidium Seed 30g, Sichuan Lovage Rhizome 15g, Salvia Root 15g, Jujube Fruit 15g. The trial granules are provided by Beijing Kangrentang Pharmaceutical Co., Ltd. from a single batch.

(2) Placebo Composition: 5% Yiqi Lishui Formula granules + 95% dextrin. The placebo is provided by Beijing Kangrentang Pharmaceutical Co., Ltd. from a single batch. The placebo is packaged identically to the active granules, with the same appearance, color, taste, and quality, distinguishable only by the external packaging serial number.

(3) Drug Storage: The granules and placebo will be stored in a cool, dry place under the supervision of designated personnel after retrieval.

(4) Drug Administration: Study medication (active or placebo) must be administered within 24 hours of enrollment, twice daily (8:00 AM and 4:00 PM), dissolved in 100 mL of warm water for oral administration or via nasogastric tube. The study drug is not a substitute for standard medical treatment for SIMD; standard Western medical care must be provided concurrently.

(5) Treatment Regimen:

Standard Western Medical Treatment: In accordance with the 2022 Expert

Consensus on the Diagnosis and Treatment of Sepsis-Induced Cardiomyopathy in Integrated Traditional Chinese and Western Medicine, treatment includes infection control, fluid management, lactate monitoring, vasoactive agents, inotropic agents, recombinant human brain natriuretic peptide, rate-lowering drugs, and non-pharmacological treatments such as intra-aortic balloon pump (IABP) and extracorporeal membrane oxygenation (ECMO).

Experimental Group: Standard Western medical treatment + Yiqi Lishui Formula granules orally or via nasogastric tube (twice daily).

Control Group: Standard Western medical treatment + Yiqi Lishui Formula placebo orally or via nasogastric tube (twice daily).

6. Diagnostic Criteria:

(1) Sepsis Diagnostic Criteria: According to the 2016 Sepsis-3 criteria, sepsis is defined as infection or suspected infection with an increase in the Sequential Organ Failure Assessment (SOFA) score of ≥ 2 points from baseline.

(2) Diagnostic Criteria for Sepsis-Induced Myocardial Dysfunction: According to the 2022 Expert Consensus on the Diagnosis and Treatment of Sepsis-Induced Cardiomyopathy in Integrated Traditional Chinese and Western Medicine, SIMD is diagnosed in patients with sepsis who present with cardiac dysfunction or hemodynamic abnormalities, accompanied by abnormal echocardiographic findings, elevated cardiac biomarkers (cTnI/cTnT), and/or elevated cardiac function markers (BNP/NT-proBNP), after excluding acute coronary syndrome.

(3) Diagnostic Criteria for Qi Deficiency and Water Overflow Pattern: According to the Guiding Principles for Clinical Research of New Chinese Medicines (Trial) and the third edition of Diagnostics in Traditional Chinese Medicine edited by Chen Jiaxu, the diagnosis requires meeting two primary symptoms or one primary symptom with two secondary symptoms. Primary Symptoms: Shortness of breath, facial and limb edema, oliguria and abdominal distension, with or without pleural effusion or ascites. Secondary Symptoms: Sweating, cyanotic lips, dizziness,

spontaneous sweating, worsening of symptoms with activity. Tongue and Pulse: Dark tongue with pale coating and white slipperiness; weak, thready, or intermittent pulse.

7. Inclusion Criteria:

(1) Patients hospitalized in the ICU of Tongzhou Traditional Chinese Medicine Hospital or Dongzhimen Hospital, Beijing University of Chinese Medicine between January 2024 and December 2026.

(2) Meet the diagnostic criteria for sepsis-induced myocardial dysfunction with Qi Deficiency and Water Overflow pattern.

(3) Age between 50 and 85 years (inclusive).

(4) SOFA score between 2 and 12 (inclusive).

(5) Enrollment within 24 hours of meeting SIMD diagnostic criteria.

(6) Signed informed consent form by the participant or their legal representative.

8. Exclusion Criteria:

(1) Diagnosis of acute coronary syndrome, old myocardial infarction, or history of coronary revascularization.

(2) Cardiac dysfunction due to cardiomyopathy (e.g., hypertrophic, dilated, amyloid, diabetic, or hypothyroid cardiomyopathy).

(3) Cardiac dysfunction due to structural heart disease, arrhythmia, cor pulmonale, or cardiorenal syndrome.

(4) Severe primary diseases affecting survival, including uncontrolled metastatic malignancy, hematologic diseases, and HIV.

(5) Liver or kidney dysfunction with a SOFA score ≥ 3 in either organ.

(6) Continuous use of immunosuppressants within the past 6 months, or history of organ transplantation.

(7) Use of corticosteroids within 7 days prior to enrollment at a dose equivalent to ≥ 20 mg/day of methylprednisolone.

(8) Use of Chinese herbal medicines with Qi-tonifying, blood-activating, or diuretic effects within 14 days prior to enrollment.

(9) Inability to take oral or nasogastric medications as determined by the clinical physician.

(10) Pregnant or breastfeeding women.

(11) BMI <18.5 or >30.

(12) Participation in another clinical trial within 30 days.

(13) Judgment by the investigator that the participant is unable to complete or unsuitable for participation (e.g., expected death within 48 hours, refusal of active treatment).

9. Withdrawal Criteria:

(1) Development of complications or changes in condition requiring alternative treatments that preclude continued participation.

(2) Drug allergy.

(3) Request by the participant or their family to withdraw.

10. Discontinuation Criteria:

(1) Study drug not administered within 24 hours of enrollment.

(2) Missing data affecting the evaluation of drug efficacy or safety, or inability to complete scheduled follow-up visits.

11. Termination Criteria:

(1) Serious adverse events requiring study termination as judged by the investigator.

(2) Severe complications involving the cardiovascular, cerebral, pulmonary,

hepatic, renal, digestive, or hematopoietic systems.

(3) Major protocol deviations (e.g., poor adherence) that compromise the evaluation of the study drug.

(4) Participant voluntarily requests to withdraw from the study.

Meeting any of the above criteria will result in termination, but all study records will be retained.

12. Exclusion from Analysis:

(1) Misdiagnosis; participant does not meet SIMD diagnostic criteria.

(2) Loss to follow-up (e.g., transfer to another hospital).

Participants meeting either criterion will be excluded from analysis, with reasons documented and original data retained.

13. Study Suspension or Early Termination Criteria:

(1) Significant policy or regulatory risks requiring termination.

(2) Unacceptable risk to participants.

(3) Enrollment rate below 50% of the planned rate for six consecutive months.

II. Study Site and Investigator Qualifications

The Department of Critical Care Medicine at Dongzhimen Hospital, Beijing University of Chinese Medicine, is a National Administration of Traditional Chinese Medicine (TCM) Clinical Base for Emergency Medicine, a Key Discipline in TCM Emergency Medicine, a Key Clinical Specialty of the Ministry of Health, and a Beijing TCM Emergency Specialty Treatment Center. It houses the Sepsis Research Institute and Febrile Disease Research Institute, both Class III research institutions affiliated with Beijing University of Chinese Medicine. The department has extensive experience in managing sepsis and has developed distinctive approaches, achieving a leading position in the treatment of sepsis with multiple organ dysfunction syndrome in China. It has

undertaken numerous national and provincial-level research projects and possesses first-class research capabilities. The principal investigator, Guo Nan, is a Chief Physician and Associate Professor with extensive experience in treating sepsis-induced myocardial dysfunction. Laboratory analyses for this study will be conducted at the Key Laboratory of Chinese Internal Medicine, Ministry of Education/Beijing Key Laboratory, Beijing University of Chinese Medicine, with adequate facilities to ensure the successful implementation of this study.

III. Potential Benefits of Participation

1. Benefits to Society: This study may demonstrate that Yiqi Lishui Formula improves clinical outcomes, shortens hospital stays, and increases survival rates in patients with sepsis-induced myocardial dysfunction.
2. Benefits to Participants: Participation may help alleviate symptoms, shorten the disease course, and improve prognosis.

IV. Potential Discomforts and Risks

(1) Local Injury: Blood collection may cause local pain, bleeding, or arterial injury.

(2) Blood or Needle Phobia: Some individuals with anxiety or physical sensitivity may experience vasovagal reactions during blood collection.

V. Alternative Treatments If Not Participating

You may choose not to participate in this study, which will not affect your access to standard treatment. Standard care for your condition follows the 2022 Expert Consensus on the Diagnosis and Treatment of Sepsis-Induced Cardiomyopathy in Integrated Traditional Chinese and Western Medicine, including infection control, fluid management, lactate monitoring, vasoactive agents, inotropic agents, recombinant human brain natriuretic peptide, rate-lowering drugs, and non-pharmacological therapies such as IABP and ECMO.

VI. Study-Related Costs

All study-related costs will be covered by the project, and participants will not incur any charges. These include:

(1) Relevant laboratory tests and examinations at enrollment and during follow-up, such as echocardiography, electrocardiogram, cardiac biomarkers, and complete blood count.

(2) Disease assessment scales, such as SOFA score and APACHE II score, at enrollment and during follow-up.

(3) Chinese herbal granules or placebo during the intervention period.

VII. Compensation and Indemnity

If a trial-related injury occurs, the project will cover the associated treatment costs. If severe adverse reactions require treatment, additional financial compensation will be provided. Any losses resulting from participation will be addressed with necessary medical care, and compensation will be provided through the hospital's medical risk fund.

VIII. Confidentiality

All information related to you, including identity, medical history, condition, physical examinations, and laboratory results, will be kept strictly confidential to the extent permitted by law. The investigators, ethics committee, and regulatory authorities may access your study-related medical records to verify the accuracy and authenticity of the data collected, but personal identifiers will not be disclosed. Your name will not appear in any public reports or publications related to this study.

IX. Participant Rights

Participation is entirely voluntary. You have the right to withdraw at any stage without penalty or loss of benefits, and your medical care will not be affected. If you decide not to participate or withdraw after enrollment, please contact your doctor.

Your doctor may terminate your participation without your consent under the following circumstances:

A. For your medical well-being.B. Failure to follow study procedures, such as not taking medication as instructed or missing scheduled assessments.C. Study termination.

X. Contact for Concerns

If you have any concerns regarding your participation, please contact the study investigator at 15600089226, the principal investigator at 13810227635, or the Ethics Committee Office at 010-84012709.

Signature Page

Participant Confirmation

I have read the participant information for the study "A Double-Blind, Randomized Controlled Clinical Trial of Yiqi Lishui Formula in the Treatment of Sepsis-Induced Myocardial Dysfunction"and fully understand the purpose, content, methods, potential benefits, and risks of participation. The doctor has explained all relevant medical terms clearly, and all my questions have been answered in an understandable manner. I understand that I may refuse to participate or withdraw at any time without affecting my medical care or rights.

My participation is voluntary and based on my own consideration. I understand the potential therapeutic effects and risks associated with the study and have received complete and truthful information. I voluntarily agree to participate and will cooperate with the study team.

I consent to the inspection of my medical records by national drug regulatory authorities, clinical research auditors, and monitors as necessary.

I will receive a signed and dated copy of this informed consent form.

Participant (Signature): _____ Date: _____

Legal Representative (Signature): _____

Relationship to Participant: _____ Contact Number: _____

Investigator Confirmation

I have explained the content, procedures, potential risks, and benefits of this study to the participant. I have answered all questions raised by the participant, and the participant has understood the information and provided consent.

Investigator (Signature): _____ Date: _____

Contact Number: _____