Safety and Efficacy of Endoscopic Cardial Constriction Ligation （ECCL） With a Novel Disposable Endoscope: A Multicenter Randomized Controlled Trial

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Informed Consent Form for Participants

Project Title: Safety and Efficacy of Endoscopic Cardial Constriction Ligation （ECCL） With a Novel Disposable Endoscope: A Multicenter Randomized Controlled Trial

Project Source/Lead Institution: Shenzhen Hospital of Southern Medical University

Study Institutions: Shenzhen Hospital of Southern Medical University, Army Medical Center, 964th Hospital of the Joint Logistics Support Force

Dear Participant,

We invite you to participate in a research study that has been reviewed and approved by the Medical Ethics Committee of Shenzhen Hospital of Southern Medical University. Before making a decision, we hope you will understand the purpose of this study and what your participation will involve. Your participation in this study is entirely voluntary, meaning you are free to choose whether or not to participate. The study team will explain this informed consent document to you and address any questions you may have.

You are welcome to discuss this study and the information in this document with your partner, family, friends, or doctor.

After you have considered all the information related to this study and all your questions have been answered, if you agree to participate, the study team will ask you to sign and date this informed consent form (at the end of this document) before any study-related procedures are conducted.

I. Study Background

Currently, traditional endoscopes are reusable, requiring cleaning and disinfection after each use before they can be reused. However, the inability to achieve complete sterilization with traditional endoscopes has garnered increasing

attention. In contrast, disposable endoscopes eliminate the risk of cross-infection, bypass the cumbersome cleaning and disinfection processes, and reduce the incidence of surgical instrument-related infections. Furthermore, disposable endoscopes are comparable to standard endoscopes in terms of functionality and operability.

Gastroesophageal reflux disease (GERD) can be classified based on endoscopic findings into non-erosive reflux disease (NERD), reflux esophagitis (RE), and Barrett's esophagus (BE). Typical symptoms include heartburn and regurgitation, while atypical symptoms encompass chest pain, epigastric pain, abdominal bloating, belching, and extraesophageal symptoms. Epidemiological surveys in China indicate a prevalence of heartburn occurring at least once weekly ranging from 1.9% to 7.0%. Chronic, recurrent GERD significantly impairs patients' quality of life and may increase the risk of Barrett's esophagus, esophageal mucosal dysplasia, and esophageal adenocarcinoma. The pathogenesis and progression of GERD involve multiple factors, including increased esophageal acid exposure, lower esophageal sphincter (LES) relaxation, low esophagogastric junction (EGJ) pressure, impaired esophageal clearance, hiatal hernia, damage to the mucosal barrier by cytokines (e.g., IL-6, IL-8, platelet-activating factor PAF), and heightened reflux sensitivity.

The first-line treatment for GERD currently involves lifestyle modifications and oral acid-suppressive medications, such as proton pump inhibitors (PPIs) and potassium-competitive acid blockers (P-CABs). However, some patients with refractory GERD require long-term acid-suppressive therapy, and studies suggest that prolonged PPI use may increase the risk of *Clostridioides difficile* infection, community-acquired pneumonia, gastric cancer, and chronic kidney disease, while short-term P-CAB use may lead to hypergastrinemia. According to the *2020 Chinese GERD Expert Consensus*, for patients with refractory GERD who fail medical therapy, endoscopic or surgical treatment may be considered after thorough evaluation to rule out other causes and confirm evidence of reflux, with careful consideration of risks and benefits.

Endoscopic cardia constriction ligation (ECCL), first performed by Professor Linghu Enqiang in 2013, operates on principles similar to esophageal and gastric variceal ligation. Specifically, under direct endoscopic visualization, the mucosa and partial muscle layer above the dentate line are ligated to form folds. Post-ligation, the local mucosa undergoes ischemic necrosis and heals to form scar tissue, reducing the cardia diameter, increasing LES pressure, and alleviating reflux symptoms. This method is characterized by simple operation and minimal invasiveness, making it safer than traditional surgical or laparoscopic procedures. Related complications, such as bleeding after ligation band detachment and retrosternal pain, have a low incidence and rapid recovery, with no severe adverse events reported to date. However, the long-term efficacy of ECCL requires further validation through prospective, large-scale studies.

In recent years, endoscopic treatments for refractory GERD have continued to evolve, but there are currently no studies on the efficacy and adverse event rates of ECCL performed using disposable endoscopes. Therefore, this study aims to conduct a randomized controlled trial to compare the effectiveness, safety, flexibility, and imaging clarity of ECCL guided by disposable versus traditional endoscopes in a large sample. The ultimate goal is to optimize treatment strategies, provide scientific evidence for personalized GERD treatment, and inform the development of future GERD treatment guidelines.

II. Study Objectives

- **Primary Objective**

To compare the efficacy of endoscopic cardia constriction ligation (ECCL) using disposable endoscopes versus traditional endoscopes in the treatment of refractory gastroesophageal reflux disease (GERD).

- **Secondary Objectives**

① To evaluate the observation clarity, flexibility, and compatibility of

disposable endoscopes with surgical consumables.

② To assess the incidence of device failures and complications related to disposable endoscope-guided ECCL, such as mucosal injury, bleeding, and perforation.

III. Study Population

The study population consists of patients with refractory GERD.

- **Diagnostic Criteria**: Patients diagnosed with refractory GERD in accordance with the 2023 Chinese Guidelines for the Diagnosis and Treatment of Gastroesophageal Reflux Disease.

- **Inclusion Criteria**:

(1) Age 18–80 years;

(2) Disease duration ≥6 months, with typical symptoms such as acid regurgitation and heartburn, and a confirmed diagnosis of GERD;

(3) GERD patients whose symptoms are not relieved after 8 weeks of continuous double-dose acid-suppressive therapy;

(4) Willing to participate in the study and have signed the informed consent form.

- **Exclusion Criteria**:

(1) Patients with precancerous lesions such as early esophageal cancer or Barrett's esophagus >3 cm, or advanced upper gastrointestinal cancer identified on endoscopy;

(2) Patients with hiatal hernia ≥2 cm, severe reflux esophagitis (LA-C or LA-D grade), esophageal or gastric varices, esophageal ulcer or stenosis, or a history of esophageal or gastric surgery;

(3) Patients with esophageal motility disorders such as achalasia or diffuse esophageal spasm, rheumatic diseases such as systemic sclerosis or Sjögren's syndrome, or eosinophilic esophagitis;

(4) Patients with a history of endoscopic or surgical anti-reflux procedures;

(5) Patients with coagulation disorders, severe cardiopulmonary diseases, or inability to tolerate anesthesia, endoscopy, or treatment;

(6) Women in the puerperium.

IV. Introduction to Study Product (or Medical Technology)

The experimental group will undergo endoscopic cardia constriction ligation (ECCL) using disposable endoscopes, while the control group will undergo ECCL using traditional endoscopes. The procedure involves sequentially suctioning and ligating one band each on the lesser curvature, posterior wall, and greater curvature of the cardia, capturing the mucosal and muscular layers, with a hemostatic clip securing the base of the ligated tissue on the greater curvature. Six hours post-procedure, participants may consume lukewarm liquid or semi-liquid diets and continue acid-suppressive therapy for two weeks. Vital signs and any surgery-related serious adverse events will be recorded during the procedure.

V. Study Process

1. How Many People Will Participate in This Study?

Approximately 46 participants will take part in this study conducted at Shenzhen Hospital of Southern Medical University.

2. Study Procedures

■ Before the Study Begins (Screening Period)

To determine your eligibility for participation, the following procedures will be conducted during the screening phase:

- Collection of demographic characteristics and vital signs.
- Physical examination, primarily including cardiopulmonary auscultation and abdominal palpation.
- Inquiry into your medical history and concomitant medications.

- Blood collection for laboratory tests.
- If you are a woman of childbearing potential, a pregnancy test will be conducted. The pregnancy test result must be negative for you to participate in this study.

The results of these screening tests and/or related inquiries will help researchers determine whether you can proceed with the study. If the tests indicate that you are eligible, researchers will notify you to proceed with the visit as soon as possible. If you do not meet the relevant criteria, you cannot continue participating in the study, and researchers will inform you of the results promptly.

■ **Baseline Period**

If researchers confirm your eligibility for this trial, you will be enrolled and randomly assigned (similar to drawing lots) to receive ECCL treatment with either disposable or traditional endoscopes. The following procedures will be conducted during this visit:

- Reconfirmation of your eligibility to participate in the study.
- Assignment to the randomized study treatment group (disposable endoscope group or traditional endoscope group).
- Assignment of a unique study identification number.
- Allocation to either the disposable endoscope group or the traditional endoscope group based on randomization (if applicable).
- Physical examination and collection of vital signs data.

■ **Treatment Period**

(If this is a randomized design, you will be informed that you will be randomly assigned to receive ECCL treatment with either disposable or traditional endoscopes, similar to drawing lots for one of two options.) During this period, researchers will observe the actual effects of the different treatment approaches. To ensure accurate

recording and evaluation of the treatment effects, you are required to cooperate with the following procedures:

- **Disposable Endoscope Group**: ECCL will be performed using disposable endoscopes, involving sequential suction and ligation of one band each on the lesser curvature, posterior wall, and greater curvature of the cardia, capturing the mucosal and muscular layers, with a hemostatic clip securing the base of the ligated tissue on the greater curvature. Six hours post-procedure, participants may consume lukewarm liquid or semi-liquid diets and continue acid-suppressive therapy for two weeks.

- **Traditional Endoscope Group**: ECCL will be performed using traditional endoscopes, following the same procedure as above: sequential suction and ligation of one band each on the lesser curvature, posterior wall, and greater curvature of the cardia, capturing the mucosal and muscular layers, with a hemostatic clip securing the base of the ligated tissue on the greater curvature. Six hours post-procedure, participants may consume lukewarm liquid or semi-liquid diets and continue acid-suppressive therapy for two weeks.

- Physical examination and collection of vital signs data.

- For both groups, vital signs, procedural success, and any device-related adverse events during ECCL will be evaluated and recorded.

■ **Follow-up Period**

After completing the visits for this phase, you will generally be considered to have completed the entire study. During this period, researchers will perform the following procedures:

All participants will be followed up until 6 months post-procedure. At 3 months post-procedure, participants will undergo GERD-Q scoring and be queried about GERD-related symptoms and complications via telephone or WeChat. At 6 months post-

procedure, participants will continue to undergo GERD-Q scoring and be queried about GERD-related symptoms and complications via telephone or WeChat. Participants experiencing symptoms such as bleeding, fever, or chest pain during the follow-up period must return to the hospital within 24 hours for blood tests, chest CT, or endoscopic examination to determine the cause of complications.

3. What Tests and Assessments Will Be Conducted in This Study?

After providing written informed consent, you will undergo several tests, examinations, and procedures during this study. If you have any concerns about any of these tests, please discuss them with the study doctor.

We would like to explain the tests and procedures involved in this study as follows:

• **Medical History**: The study doctor will ask you questions to understand any current or past medical conditions, as well as your medication history, surgical history, menstrual history, etc.

• **Demographic Information**: The study doctor will collect personal information about you, such as your date of birth and ethnic background.

• **Physical Examination**: The study doctor will perform a medical examination to assess all or part of the following body systems: head, eyes, ears, nose, throat, chest, lungs, heart, abdomen, bones, skin, neck, anus, and nervous system.

• **Height and Weight**: Your height and weight will be measured.

• **Vital Signs**: The study doctor will measure your blood pressure, heart rate, body temperature, and respiratory rate.

• **Blood Tests**: You will have blood drawn multiple times during the study. Blood samples will be collected for the following tests:

Complete blood count, liver function, kidney function, coagulation profile (four items), infectious disease panel (eight items).

• **Routine Urine Test**.

• **Questionnaires**.

4. How Long Will This Study Last?

This clinical study will last approximately 6 months, including two follow-up visits. At 3 months and 6 months post-procedure, we will evaluate and record your treatment outcomes and any complications.

You may choose to withdraw from the study at any time without any penalty or loss of benefits to which you are entitled. However, if you decide to withdraw from the study midway, we encourage you to discuss this with your doctor first. For safety reasons, a follow-up examination may be conducted after your withdrawal.

VI. Risks and/or Discomforts

The primary goal of the study team is to ensure your safety at all times. However, endoscopic procedures and medications used in treatment may cause side effects, including rare or currently unknown side effects. During this study, we will closely monitor your heart, kidney, liver function, and other body systems through blood and urine tests, physical examinations, and electrocardiograms (ECGs).

If you experience any worsening of your health or unexpected or unusual symptoms, you should immediately contact the study team, even if you believe these issues are not caused by the study procedures or medications used during the procedure.

1. **Anesthesia Complications** (See also the anesthesia informed consent form).

2. **Post-ECCL Complications**: Possible adverse reactions include chest pain, abdominal bloating, and, in rare cases, serious complications such as gastrointestinal bleeding, thoracic or mediastinal infection, fever, or gastrointestinal perforation. Unsatisfactory treatment outcomes or disease recurrence post-procedure may require additional or repeated endoscopic treatments. If repeated endoscopic treatments are ineffective, reliance on acid-suppressive medications may continue. The operating surgeons have extensive experience in related procedures, and with the use of post-procedure adjuvant medications (e.g., acid-suppressive drugs, mucosal protectants, antibiotics),

the occurrence and severity of these complications can be minimized to achieve the most satisfactory outcomes possible.

3. **Intraoperative or Postoperative Complications** involving the heart, brain, kidneys, lungs, or adverse outcomes due to the progression of the underlying disease.

4. **Risks and Discomforts Associated with Study Procedures**:

• **Blood Collection**: Blood samples will be collected by inserting a small needle into a vein in your arm or hand. You may experience discomfort and/or soreness during needle insertion or removal, and small bruises may occur. In very rare cases, the vein may become blocked, or minor nerve damage may occur, leading to numbness or pain. If this happens, it will resolve over time.

• **Electrocardiogram (ECG)**: During an ECG, small adhesive patches will be placed on various parts of your body. Wires connected to these patches will transmit information about electrical activity to a device for recording and measurement. This test takes only a few minutes and is painless. However, the adhesive used on the patches may cause mild skin irritation.

VII. What Are the Benefits of Participating in This Study?

Your participation in this study may help control or alleviate your condition, but this cannot be guaranteed. The endoscopic cardia constriction ligation (ECCL) procedure offers advantages such as short operation time, quick recovery, fewer complications, mild pain, and lower costs. It also significantly reduces patients' fear of postoperative pain associated with surgical procedures and decreases the need for long-term medication use. We hope that the information gained from your participation will contribute to identifying optimal treatment strategies for patients with this condition in the future.

VIII. Alternative Treatment Options

In addition to participating in this study, you have the following treatment options:

- **Surgical Treatment**: Advantages include thorough treatment, typically requiring no additional surgeries; disadvantages include significant pain and high costs.

- **Oral Acid-Suppressive Medication**: Advantages include being non-invasive and painless; disadvantages include the need for long-term medication use and potential adverse drug reactions.

You may discuss your condition and its potential outcomes with the study doctor at any time to determine the best treatment option for you.

IX. Use of Study Results and Confidentiality of Personal Information

At the conclusion of the study, we will prepare a report and submit it to regulatory authorities, such as the National Medical Products Administration. The study results may also be published in journals or presented at conferences, but no information that could identify you will be included.

To protect your privacy, records or samples released for research purposes will not include your name or other identifying information. Instead, your information will be identified only by a code. Only the study doctor and authorized personnel will have access to a list linking this code to your name, and this list will be securely stored at the research center.

If necessary, to ensure the study is conducted correctly at the research center, the sponsor, ethics committee, and government regulatory authorities may review your records in accordance with regulations. These parties are bound by confidentiality obligations and will not violate your privacy.

You have the right to control the use and disclosure of your personal information. To the extent permitted by national law, you may request access to your medical information at any time. You have the right to review all information collected about you through the study doctor and request corrections if applicable.

X. New Information Related to the Study

During the study, if there are changes to the study procedures, newly identified side

effects, or significant circumstances that may affect your health or willingness to participate, the study team will notify you. The study doctor will inform you immediately and discuss with you whether you wish to continue participating in the study. If you decide not to continue, the study doctor will make arrangements to ensure your ongoing medical care. If you choose to remain in the study, the study doctor may ask you to sign a new informed consent form.

XI. Study Costs, Compensation, and Damages

1. Costs of Medical Devices and Related Examinations

During your participation in this study, you will be responsible for the costs of endoscopic examinations and treatments, anesthesia, medications, and pre- and post-procedure tests.

2. Compensation for Damages

If you suffer harm as a result of participating in this study, you will receive free treatment provided by the Department of Gastroenterology at Shenzhen Hospital of Southern Medical University, and compensation will be provided in accordance with the law.

XII. Participant Rights and Responsibilities

1. Your Rights

Your participation in this study is entirely voluntary throughout the entire process. If you choose not to participate, this will not affect your access to other treatments you are entitled to. If you decide to participate, you will be asked to sign this written informed consent form. You have the right to withdraw from the study at any stage without facing discrimination or unfair treatment, and your medical care and rights will not be affected.

2. Your Responsibilities

You are required to provide accurate information about your medical history and current health condition; inform the study doctor of any discomfort you

experience during the study; and, as experimental treatments may pose risks to you or your fetus, you and your partner should avoid any activities that could lead to pregnancy during the study. If you become pregnant during the study, you must immediately notify your study doctor.

XIII. Contact Information

If you have any questions regarding your rights or interests, or if you wish to report difficulties, dissatisfaction, or concerns encountered during participation in this study, or to provide opinions and suggestions related to the study, please contact the Medical Ethics Committee of Shenzhen Hospital of Southern Medical University.

Contact Phone: 0755-23360060

Email: nfszyyec@163.com

Participant Signature Page

Informed Consent Statement

I have been informed about the purpose, background, procedures, risks, and benefits of this study. I have had sufficient time and opportunity to ask questions, and I am satisfied with the responses provided.

I have also been informed about whom to contact if I have questions, wish to report difficulties, concerns, or suggestions regarding the study, or seek further information or assistance related to the study.

I understand that I can choose not to participate in this study or withdraw from it at any time during the study without providing any reason. Furthermore, the investigators have not used deception, inducement, coercion, or any other means to compel me to participate in this study.

I have been informed that if my condition worsens, I experience serious adverse reactions, or my study doctor determines that continuing in the study is not in my best

interest, they may decide to withdraw me from the study. Without my consent, the sponsor or regulatory authorities may also terminate the study during its course. If this occurs, the study doctor will promptly notify me and discuss my other options.

I have read this informed consent form and agree to participate in this study.

I will receive a copy of this informed consent form, which includes my signature and that of the investigator.

Participant Signature Page

Participant Signature: _____ **Date**: _____

Contact Phone: _____

Legal Representative Signature: _____

Relationship: _____ **Date**: _____

Contact Phone: _____

(Note: If the participant lacks or has limited capacity to consent, such as in cases involving mental disorders or unconsciousness, the legal representative must sign in the designated section below for the legal representative.)

Impartial Witness Signature: _____ **Date**:

_____

Contact Phone: _____

(Note: An impartial witness signature is required only when participants who are capable of providing informed consent but unable to read the document (e.g., due to illiteracy or visual impairment) are included. It is preferable for the investigator to retain video evidence of the informed consent process as proof.)

I have accurately explained this document to the participant, and he/she has thoroughly read this informed consent form and confirms that the participant had the opportunity to ask questions and has voluntarily agreed to participate.

Investigator Signature: _____ **Date**: _____

Contact Phone: _____