Informed Consent Form

Study on the Relationship Between Pathological Features of Achalasia and Prognosis of Per-oral Endoscopic Myotomy

Main research institute: Beijing Friendship Hospital, Capital Medical University

Study Director: Fandong Meng,

Date: April 1st, 2021

Informed Consent Form

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Central Contact Person: Fandong, Meng

Sponsor: Beijing Friendship Hospital, Capital Medical University

Dear participants:

We invite you to participate in the study on the relationship between pathological features of achalasia and prognosis of Per-oral Endoscopic Myotomy. You can read this informed consent form carefully and carefully make the decision whether to participate in this study. When your doctor or researcher discusses informed consent with you, you can ask him or her to explain to you what you don't understand. We encourage you to discuss this thoroughly with your family and friends before making any decision to participate in this study. If you are participating in another study, please inform your study physician or investigator. The purpose, background, research content and other important information of this study are as follows:

Background

Achalasia is a motility disorder of the esophagus, characterized by disorders of the lower esophageal sphincter (LES). Normal peristalsis of the esophagus is eliminated and replaced by synchronous or ineffective contraction. Based on high-resolution manometry (HRM), the patients with achalasia were categorized into 3 subtypes, type I: achalasia with minimum esophageal pressurization, type II: achalasia with esophageal compression and type III: achalasia with spasm.

Previous studies have found that the pathological features of the esophageal muscular layers in patients with achalasia are degeneration of nerve plexus, reduction of interstitial cells of Cajal (ICCs), muscular atrophy, fibrosis and infiltration of different inflammatory cells. Different subtypes of achalasia have different clinical characteristics and esophageal motility. Studies have found that ganglion cells in type I patients are significantly reduced compared with type II patients, but the pattern is similar, which may

indicate that type I achalasia represents the progression of type II achalasia. Studies have shown that ICCs are preserved in type III achalasia compared with type I and II achalasia. In addition, Achalasia is related to viral infection and autoimmune disease.

Nowadays, per-oral endoscopic myotomy (POEM) is a main therapy for patients with achalasia. Most studies have focused on the relationship between pathological features and motility characteristics of achalasia, but there are few studies on the relationship between pathological features and therapeutic effect of POEM.

This study will evaluate the pathological characteristics of full-thickness esophageal muscle in patients with achalasia in order to discover the relationship between different pathological characteristics and prognosis of POEM.

Research objective

The purpose of this study is to determine whether the prognosis of POEM is different in patients with achalasia in different pathological characteristics.

Research Content

1. How many people will participate in this study?

About 50 people will participate in this study at Beijing Friendship Hospital, Capital Medical University.

2. Research procedures

If you agree to participate in this study, please sign this informed consent form.

Inclusion criteria: 1) Patients with achalasia treated in Beijing Friendship Hospital, Capital Medical University. 2) Age 18-80, no gender limitation. 3) Fit and agree to receive POEM. 4) Signed informed consent.

Exclusion criteria: 1) the previously received treatment of achalasia, Barrett's esophagus lesions, esophageal stricture, liver cirrhosis, and/or esophageal varices, the digestive tract tumor, active esophagitis, connective tissue disease, allergic disease, blood or blood coagulation patients and hiatal hernia. 2) Use of nonsteroidal anti-inflammatory drugs, corticosteroids, or other immunosuppressive drugs 6 months prior to examination.

The experimental procedure of this study is that patients are admitted to the

department of Gastroenterology in our hospital, and examination including endoscopy and high-resolution manometry need to be done. Patients will receive routine POEM, and full-thickness esophageal muscle biopsy will be performed from LES, distal esophagus (about 5cm above EGJ) and middle esophagus (about 10-20cm above EGJ) during the operation. Intraoperative biopsy to take pathological tissue depends on the patient's condition, and the collection method is to use biopsy forceps to take tissue and take 1 piece at one place. After the completion of pathological staining, the patients will be followed up at 1-, 3-, 6- and 12-months post-poem, and the improvement of symptoms and postoperative reflux will be inquired.

Baseline data were collected including gender, age, symptom score (Eckardt score), length of history, past history, results of esophagography, endoscopy, esophageal manometry, surgical information (such as operative time, myotomy length, and myotomy depth, etc.).

Follow-up data will be collected, including symptom score (Eckardt score), reflux symptom score (GerdQ score), gastroscopy, reflux esophagitis, esophagography, esophageal manometry, and PPIs treatment. Follow-up collection time is 1 month, 3 months, 6 months and 12 months after POEM.

3. How long will the study last?

The study lasted two years, with one year of data collection and one year of follow-up up after POEM for the last patient enrolled in the study.

You can opt out of the study at any time without penalty or loss of any benefits to which you are entitled. If you decide to withdraw from the study, we encourage you to talk to your doctor first. Considering your security concerns, it is possible that a relevant check will be performed after you exit.

Risks and Benefits

1. What are the risks or adverse reactions of participating in this study?

The risks you may incur by participating in this study are as follows:

Discuss these risks with your doctor who takes care of you. You may experience

some, all, or none of these adverse events during the study period. In this study, the bleeding risk of biopsy is similar to that of endoscopic biopsy. However, since 1-2 additional biopsy tissues need to be taken in this study, the bleeding risk of 1-2 sites will be increased, and the treatment measures are endoscopic hemostasis.

2. What are the benefits of participating in the study?

If you agree to participate in this study, you have the following benefit: through this research, we will provide you with esophageal muscular biopsy pathology results, and combine with HRM to assess the severity of achalasia and find the relationship between prognosis of POEM and pathology. In addition, we will provide you with 3 follow-up consultations at 3, 6 and 12 months after POEM, so that you can consult your condition, medication, treatment and matters. We hope that the information gained from your participation in this study will benefit you in the future. We hope to study the difference of prognosis of POEM in participants with different pathological characteristics, so as to clarify the efficacy of POEM and provide evidence support for patients to choose treatment methods in the future.

Confidentiality

Results of studies conducted through this program may be published in medical journals with your understanding. However, we will keep your research records confidential as required by law. Personal information will be kept strictly confidential. Your personal information will not be disclosed unless required by relevant laws. If necessary, government administrative departments, hospital ethics committees and other relevant researchers can access your data according to regulations.

Research expenses and related compensation

1. Fees for related examinations

Participants in this study need to undergo muscle layer biopsy, and biopsy specimens will need to undergo relevant pathological staining items. In addition to conventional pathological staining, we will provide additional pathological staining costs for participating in this study.

2. Compensation

In the event of any injury related to this study, you may obtain necessary medical care provided by Beijing Friendship Hospital and be compensated in accordance with relevant laws and regulations after being recognized by the relevant institution in accordance with laws and regulations of China.

Subject rights

Your participation in the study is voluntary throughout the entire process. If you decide not to participate in this study, it will not affect other treatments you should receive. If you decide to participate, you will be asked to sign this written informed consent. You have the right to withdraw from the study at any time without discrimination or unfair treatment, and your medical treatment and rights will not be affected. No biopsy specimens will be taken during the study after you drops out.

If you experience a serious adverse reaction, or if your study physician feels it is not good for you to continue in the study, he or she may decide to withdraw you from the study. The sponsor or regulatory authority may terminate the study at any time without your consent, while massive intraoperative bleeding. If this happens, you will be notified and your physician will discuss other options available to you.

Subject responsibility

You are required to provide true information about your medical history and current medical condition. You need inform the study physician of any discomfort observed during the study. You need tell the doctor if you have recently participated in or are currently participating in other studies.

Contact us if you have any questions or difficulties.

If you have any questions related to this study, please contact Fandong, Meng on weekdays at 63138738.

If you have any questions related to your rights or interests, or if you would like to report your difficulties, dissatisfaction or concerns during the process of participating in this study, or if you would like to provide comments and suggestions related to this study,

please contact the Bioethics Committee of Beijing Friendship Hospital, Capital Medical University at 010-63139017.

Researcher notification Statement

"I have informed the subject of the background, purpose, procedure, risk and benefit of the study on the relationship between different pathological features of achalasia and the prognosis of POEM. I have given him/her enough time to read the informed consent, discuss with others, and answer his/her questions about the study. I have told the subject to contact Dr. Fandong Meng whenever he encounters problems related to the study, and to contact the Bioethics Committee of Beijing Friendship Hospital, Capital Medical University whenever he encounters problems related to his own rights and interests, and provided accurate contact information. I have informed the subject that he/she can withdraw from the study; I have advised the subject that he/she will receive a copy of this informed consent form with my and his/her signatures."

Researcher Signature: _____ Date: _____

Subject informed consent Statement:

I have been informed of the background, purpose, procedure, risk and benefit of the study on the relationship between different pathological features of achalasia and postoperative outcome of POEM. I had plenty of time and opportunity to ask questions, and I was satisfied with the answers. I was also told who to contact when I had questions, wanted to report difficulties, concerns, suggestions for research, or wanted further information, or to help with research. I have read this informed consent and agree to participate in this study. I know that I can withdraw from the study at any time without any reason. I was told that I would be given a copy of the informed consent, with my signature and the investigator's.

Subject Signature: _____ Date: _____

Subject Contact Number: _____

(When the subject's informed consent ability is deficient or inadequate, the following methods will be added or replaced :)

Signature by legal representative: _____ Date: _____