Informed Consent Form

A Secondary Mitral Regurgitation Assessment Using Three-dimensional Transesophageal Echocardiography: A Multicenter Clinical Study

Protocol ID	SMR-3DTEE-01
Document Version	Version 2.0
Document Date	22 July 2026

Dear Participant,

You are invited to participate in this multicenter study of three-dimensional transesophageal echocardiography for secondary mitral regurgitation. The study will be conducted at 93 hospitals across China. Approximately 2,400 volunteers are expected to participate.

The Medical Scientific Research Ethics Committee of the First Hospital of China Medical University has reviewed and approved this study. Please read the following information carefully before deciding whether to participate. Your doctor will answer any questions. You may also discuss participation with your relatives or friends.

1. Study Background

Secondary mitral regurgitation (SMR) occurs in a structurally normal mitral valve when left ventricular or left atrial dilatation or dysfunction prevents complete leaflet closure. Associated conditions include ischemic cardiomyopathy, heart failure, atrial fibrillation, and atrial cardiomyopathy.

SMR results from left ventricular (LV) and/or left atrial (LA) remodeling, altered geometry, annular dilatation, leaflet tethering, mechanical dyssynchrony, and papillary muscle displacement. Its global prevalence is approximately 1-2%, with a higher prevalence among older adults and patients with heart failure. SMR can worsen cardiac function and heart failure, increase hospitalization and mortality, and independently predict adverse cardiovascular outcomes.

Conventional echocardiography, including transthoracic echocardiography, has limitations in assessing SMR severity, mechanisms, and contributing factors. It may incompletely characterize three-dimensional structural changes, including mitral annular geometry.

Three-dimensional transesophageal echocardiography (3D-TEE) provides high-resolution imaging and enables non-invasive, precise quantification of regurgitant volume and mitral annular remodeling. This information supports clinical decision-making. Existing studies are predominantly small, single-center investigations. Multicenter data supporting SMR prediction models and individualized treatment strategies remain limited.

This study will use the Liaoning Provincial Clinical Research Center for Medical Imaging platform to coordinate participating imaging centers across China. It will combine 3D-TEE and transthoracic echocardiography for multimodal assessment. The study will characterize SMR and examine its associations with clinical outcomes. Findings will inform treatment, including mitral valve repair and medical therapy.

2. Study Objectives

1. To assess the severity of SMR and its contributing factors using 3D-TEE.
2. To compare mitral valve structure and left ventricular functional parameters between patients with SMR and healthy controls.
3. To investigate predictors of adverse events in patients with SMR. Events of interest include atrial fibrillation recurrence, heart failure rehospitalization, catheter-based or surgical mitral valve treatment, and cardiovascular death.

3. Inclusion and Exclusion Criteria

3.1 Patient Group: Secondary Mitral Regurgitation

Inclusion criteria

1. Age 18 years or older.
2. At least mild atrial secondary mitral regurgitation (A-SMR), meeting all of the following criteria:
   - Structurally normal mitral valve without primary mitral valve disease.
   - Left ventricular ejection fraction at least 50%, without regional wall motion abnormalities or mitral leaflet tethering.
   - Normal or mildly enlarged left ventricle, meeting either of the following sex-specific criteria. The end-diastolic diameter must be below 56 mm in women or 63 mm in men. Alternatively, the end-diastolic volume index must be below 71 mL/m² in women or 79 mL/m² in men.
   - Mitral annular dilatation, with an anteroposterior diameter above 35 mm, together with left atrial enlargement. Left atrial enlargement is defined by either of two criteria. The volume index must be above 34 mL/m². Alternatively, the anteroposterior diameter must be above 37 mm in women or 39 mm in men.
3. Undergoing both transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE), with standardized images retained.

Exclusion criteria

1. Primary mitral regurgitation caused by organic mitral valve disease, including degenerative changes, rheumatic involvement, congenital mitral valve abnormalities, or vegetations.
2. Moderate or greater aortic valve disease.
3. Previous cardiac valve surgery, including surgical or catheter-based procedures.
4. Congenital heart disease.
5. Inadequate three-dimensional TEE image quality that prevents reliable assessment of mitral valve structure and motion.
6. Contraindications to TEE or inability to tolerate the examination.
7. Refusal to sign the informed consent form.

3.2 Control Group

Inclusion criteria

1. Age 18 years or older.
2. Undergoing TEE for clinical indications, such as suspected patent foramen ovale or infective endocarditis.
3. TTE showing no substantial abnormalities in cardiac structure or function, with less than mild regurgitation of all cardiac valves.

Exclusion criteria

Individuals will be excluded if they do not meet the control-group inclusion criteria or meet any exclusion criterion specified for the patient group.

4. Study Content and Procedures

This is a prospective multicenter clinical study conducted in the People's Republic of China. The study will begin in February 2026 and last for 23 months. It will include 93 participating centers and 2,400 participants: 1,600 patients and 800 controls.

1. Participants will be screened strictly according to clinical findings and echocardiographic results. They must meet all inclusion criteria and have none of the exclusion criteria.
2. Participants will sign the informed consent form.
3. Participants will undergo TTE using ultrasound equipment currently used in routine hospital practice. No prohibited medications or procedures will be used.
4. Participants will undergo TEE using ultrasound equipment currently used in the hospital. The examination is required for clinical diagnosis or treatment. No additional TEE examinations will be performed solely for this research.

5. Your Cooperation During the Study

5.1 Before the Examination

TTE does not require fasting or restriction of food or water. Before TEE, you must fast for eight hours, without food or water. Wear loose clothing to facilitate the examination. Avoid strenuous exercise and rest quietly for 5-10 minutes beforehand. This helps stabilize your condition and reduce the effects of breathing and cardiac motion on image quality.

Tell your doctor accurately about your medical history, any existing illnesses, and whether you are pregnant.

5.2 During the Examination

Adjust your position as instructed by your doctor. You may need to tilt your body, turn your shoulders, or raise your head to allow examination of specific areas. Remain quiet and avoid talking, unnecessary movement, or frequent changes of position. These movements can affect image clarity and stability. If you need to cough or sneeze, or feel uncomfortable, tell the doctor beforehand.

5.3 After the Examination

Do not eat or drink for at least four hours after TEE. Eating or drinking too early may cause swallowing difficulties, aspiration, or choking. Your doctor will assess your cardiac function and explain the findings. Please cooperate if further information is needed to clarify the examination results.

6. Possible Risks

This study involves non-invasive ultrasound examinations. Placement of the probe may cause mild discomfort during the examination. This discomfort will not cause harm.

7. Study Costs

You will not be required to pay any fees to participate in this study. You will not receive financial compensation for participation.

8. Your Rights and Potential Benefits

If you meet the eligibility criteria and choose to participate, you may receive the following benefits:

- Information about your current cardiac structure and hemodynamics will be provided free of charge. No financial compensation will be provided.
- Doctors will be available to answer questions about the relevant medical information during the study.

9. Voluntary Participation and Withdrawal

Participation is voluntary. You may decline participation or withdraw at any time without discrimination, unfair treatment, or retaliation. Your medical care and rights will not be affected.

10. Confidentiality

All information collected during the study will remain confidential and will be retained by the investigators. Investigators, ethics committee members, and relevant administrative authorities may review your records as permitted by law. Your personal information will not be individually disclosed in study reports or publications.

11. Contact Information

You may ask questions about the study at any time and may contact your doctor. If you have complaints about participation, contact the ethics committee at +86-24-83282837.

Consent Declaration

1. I have carefully read the information about this study and have had the opportunity to discuss it with a doctor and ask questions. My questions have been answered satisfactorily.
2. I understand that participation is voluntary. I have had sufficient time to consider participation and understand the following:
   - I understand the study procedures and their purpose.
   - I may ask the doctor for further information at any time.
   - I may withdraw at any time without discrimination or retaliation. My medical care and rights will not be affected.

I agree to participate in this study and to cooperate with the doctor in accordance with the study protocol.

Participant signature: _____ Date: _____

Telephone: _____

A guardian must also sign if the participant is a minor or has limited legal capacity.

Guardian signature: _____ Date: _____

Telephone: _____

I have fully explained the study purpose, procedures, potential risks, and benefits to this participant. I have answered all questions about the study satisfactorily.

Investigator signature: _____ Date: _____

Telephone: _____