Taichung Veterans General Hospital

Informed Consent Form

Dear Participant,

You are being invited to participate in this human research study or clinical trial. This document provides you with important information about the study. The principal investigator or authorized research personnel will explain the details of the study to you and answer any questions you may have. Please do not sign this consent form until all of your questions have been answered to your satisfaction.

You are not required to decide immediately whether to participate in this study. Please take sufficient time to carefully consider your decision before signing this consent form. You may participate in this study only after signing the consent form.

If you agree to participate, this document will serve as a record of your consent. Even after you have given your consent, you are free to withdraw from the study at any time without providing any reason. If you wish to withdraw, you may notify the research team at the study institution by any means.

IRB certification：CF25881A

Title：**Patent foramen ovale–related stroke management and outcome: age-dependent risk prediction and atrial cardiopathy study:**

SENIOR: Stroke prevention in the elderly by patent foramen Ovale closuRe vs anticoagulation

Affiliation：Taichung Veterans General Hospital

Correspondence: Chi-Sheng Wang

Tel. +886 933375721

e-mail: sam7227632@gmail.com

Participant Name:

Gender：□Male □Female Birthday：

Chart number：

Phone number：

Date：2025/10/16

Emergency Contact Person： Phone number：

Name of Legally Authorized Representative:

Relationship to the Participant:

Gender：□Male □Female Birthday：

Phone number：

Background of the Study

Acute ischemic stroke is a leading cause of disability worldwide. However, approximately 25% of patients are classified as having an embolic stroke with undetermined source (ESUS), meaning that no definite cause of the stroke can be identified. Patent foramen ovale (PFO) has been recognized as an important mechanism underlying ESUS. Current international treatment guidelines recommend transcatheter PFO closure for patients younger than 60 years with ESUS and high-risk PFO, as this treatment has been shown to be significantly more effective than standard medical therapy, such as antiplatelet medication.

However, the optimal treatment strategy for patients older than 60 years remains uncertain. In particular, the comparative effectiveness between transcatheter PFO closure and novel oral anticoagulants in this population is still under debate. In addition, there is currently a lack of longitudinal cohort studies evaluating cardiac physiological parameters in this patient population.

Study Aims

To optimize an age-inclusive risk prediction system for the causal attribution of PFO related stroke across all age.

To compare the effectiveness and safety of transcatheter PFO closure versus medical therapy alone (direct oral anticoagulants [DOAC] or antiplatelet agents if protocol-defined DOAC ineligibility) for prevention of recurrent stroke among patients aged ≥60 years with high-risk PFO.

To investigate the role of atrial cardiopathy (AC) in PFO-related stroke, and to further analyze changes in cardiac physiological parameters—such as left atrial (LA) compliance and LA strain—before and after PFO closure and medical therapy alone (optional nested substudy).

Recruitment of Participants

Individuals who are identified as potential candidates for this study will be approached by the research team. The study objectives and procedures will be explained to them, and they will be invited to participate. Only those who voluntarily agree and provide written informed consent will be enrolled in the study. A total of approximately 400 participants are expected to be prospectively enrolled in this study.

Study Procedures and Related Examinations

From October 1, 2025 to October 1, 2029, all patients admitted with acute ischemic stroke or transient ischemic attack (TIA) will be prospectively registered according to the study's inclusion and exclusion criteria. For each enrolled participant, the treatment strategy will be determined by the principal investigator or co-investigators at each participating center. Treatment options may include transcatheter patent foramen ovale (PFO) closure, novel oral anticoagulant therapy, or antiplatelet therapy if the patient is unable to receive novel oral anticoagulants.

Patients who meet the eligibility criteria and provide written informed consent will be registered in a secure, encrypted research registry established by the Department of Neurology at Taichung Veterans General Hospital. Participants will be followed up every three months by telephone or during outpatient clinic visits until a study outcome occurs, including recurrent stroke or transient ischemic attack. In addition, transthoracic echocardiography will be performed at the sixth month of follow-up.

This study will also include genetic testing results for research analysis. Genetic testing will be performed using a blood sample obtained during routine blood tests for stroke evaluation. The purpose of this analysis is to investigate whether genetic factors influence the risk of stroke associated with patent foramen ovale.

After signing the consent form, participants will undergo a single additional peripheral venous blood draw related to this study during routine stroke-related blood testing. Approximately 10 mL of blood will be collected.

Possible Risks, Side Effects, and Management

This study is an observational study and does not involve experimental interventions; therefore, no additional clinical adverse effects are expected as a result of participation in the study. Medical staff will provide appropriate care for any needle puncture wounds related to blood sampling, as well as for complications that are inherent to transcatheter patent foramen ovale (PFO) closure when such procedures are clinically performed.

Possible effects related to blood sampling include temporary bruising, swelling, or infection at the puncture site.

Complications inherent to transcatheter PFO closure may include approximately 5% risk of cardiac arrhythmia, approximately 5% risk of minor complications (such as bruising or bleeding at the puncture site, or pericardial effusion), and less than 0.5% risk of serious complications (such as cardiac tamponade or device displacement). If any of these complications occur, appropriate medical treatment will be provided immediately by healthcare professionals.

Alternative Treatments

This study is observational and involves only the collection of clinical data. Participation in this study will not interfere with any medical treatments, examinations, or clinical management determined by your treating physician. Your clinical care will be provided according to standard medical practice, and your physician will determine the most appropriate treatment based on your medical history and clinical condition.

Expected Outcomes and Potential Benefits to Participants

This study is an observational study designed to evaluate the clinical outcomes and complication rates associated with two treatment strategies for patent foramen ovale (PFO)-related stroke. The study aims to compare the effectiveness and safety of transcatheter PFO closure and medical therapy in the prevention of recurrent stroke.

In addition, the study will place particular emphasis on patients older than 60 years of age. Clinical characteristics, imaging findings, cardiac examination results, biomarkers, and genetic data will be analyzed to identify factors associated with prognosis and to better understand changes in cardiac physiology related to stroke risk.

You may not receive any direct benefit from participating in this study. However, the information obtained from this research may contribute to improvements in future stroke treatment and may help provide better care for patients with stroke in the future.

Participant Responsibilities, Restrictions, and Required Cooperation During the Study

All enrolled participants will undergo routine evaluations for stroke causes and risk factors. These examinations may include blood tests, cerebrovascular ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI), transthoracic echocardiography, and 24-hour electrocardiography monitoring. In addition, a microbubble test using either transcranial Doppler ultrasound or transesophageal echocardiography may be performed to detect the presence of a patent foramen ovale (PFO).

Within two months after the onset of stroke, your physician will discuss your medical condition and treatment options with you. Based on this discussion, the treatment decision may include transcatheter PFO closure, treatment with a novel oral anticoagulant, or treatment with antiplatelet medication.

Because this study is observational in nature, participation in this study will not interfere with any treatments, examinations, or medical decisions made by your physician. Your clinical management will be determined by your physician based on your medical history and clinical condition to ensure the most appropriate care.

Compared with patients who do not participate in this study, there are no additional restrictions or prohibitions during the study period. However, this study will collect your clinical data and will follow your clinical outcomes and medication use through outpatient visits or telephone follow-up. The study uses an event-driven follow-up approach, with follow-up conducted approximately every three months until a study outcome occurs, such as recurrent stroke or transient ischemic attack.

Handling and Storage of Collected Specimens and Data

Genetic specimens collected in this study will be de-identified and coded so that they cannot be directly linked to your personal identity. These coded specimens will be stored in the Taichung Veterans General Hospital Biobank (or the Precision Medicine Center of Taichung Veterans General Hospital) and will be kept under the supervision of the principal investigator. The specimens will be stored for a period of three years.

Other clinical data and laboratory results collected during the study will be coded but not fully de-identified. These data will be entered into a secure, encrypted registry platform established

by the Department of Neurology at Taichung Veterans General Hospital. The Department of Neurology at Taichung Veterans General Hospital will be responsible for maintaining these data, which will be used only for the purposes of this research. The data will be retained for a period of ten years.

Withdrawal or Termination from the Study

Your participation in this study is entirely voluntary. You are free to decide whether or not to participate in this study. During the course of the study, you may withdraw your consent and discontinue participation at any time without providing any reason. Your decision to withdraw will not cause any inconvenience or affect the medical care you receive from your physicians in the future.

If you withdraw from the study or if the study is terminated, you may choose how your stored specimens and identifiable data will be handled.

I agree that my specimens will be handled as follows:
They will be destroyed by Taichung Veterans General Hospital.

Signatures

(1) Investigator's Statement

I confirm that I, or a member of the research team, have explained the details of this study to the above-mentioned individual, including the purpose of the study, the study procedures, the potential risks and benefits associated with participation, and the currently available alternative treatment options. All questions raised by the participant have been answered to their satisfaction.

Signature of Principal Investigator: _____
Date: _____ / _____ / _____

Signature of Person Obtaining Consent: _____
Date: _____ / _____ / _____

(2) Participant

After the explanation provided by the principal investigator, I fully understand the information described above and agree to participate in this study. I will receive a copy of this consent form. I also understand that:

1. During the course of the study, any significant new findings that may affect my willingness to continue participation will be provided to me.
2. I have the right to refuse participation or withdraw from this study at any time without affecting the medical care to which I am entitled.

Signature of Participant: _____
Date: _____ / _____ / _____

Legally Authorized Representative (if applicable):
Signature: _____
Date: _____ / _____ / _____
Relationship to Participant: _____

(3) Witness

Witness (1) Signature: _____
Date: _____ / _____ / _____
National ID Number: _____
Contact Phone Number: _____
Address: _____

Witness (2) Signature: _____
Date: _____ / _____ / _____
National ID Number: _____
Contact Phone Number: _____
Address: _____