Clinical study protocol
Project proposal

Program name: A real-world registry study of multidisciplinary collaborative diagnosis and treatment model for cardioembolic stroke

Program No.:

Study type: A real world registration research

Founding source: Jiangxi Provincial Department of Science and Technology

Version No.: V 1.0

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Schema version modification history[1]

Version Number: V 1.0 Modification time:		
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chapters and sections	Summarize the change content	Change reason

[1] If the form is not enough, you can expand the page, but do not attach other irrelevant materials

1. Main participants of the project

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[2]Major members of the project should receive GCP training and obtain certificates

2. Summary of the research Plan (it shall include the research topic, research purpose, design type, research object, sample size, selection criteria, observation indicators, statistical analysis methods, etc.)

Research title: Real-world registration study of the multidisciplinary cooperative diagnosis and treatment mode of cardioembolic stroke

purpose of research:

① Main purpose: To establish a multidisciplinary assisted diagnosis and treatment mode for patients at high risk of cardioembolic stroke, and to manage and collect the diagnosis, treatment and prognosis data of patients;

② Secondary objectives: To explore the improvement of cardioembolic stroke, cardiovascular complex events, recurrent stroke and all-cause death risk, quality of life, and cardiac function in the "multidisciplinary assisted diagnosis and treatment mode" group and the "routine diagnosis and treatment model group". The conventional diagnosis and treatment mode can match the patients not adopted in the same period and "multidisciplinary assistance in diagnosis and treatment mode".

Design type: A non-intervention, prospective, observational, real-world study (at least 1.5 years). No fixed diagnosis and treatment plan is set up in advance, and only a multidisciplinary assisted diagnosis and treatment mode is established. All treatment options are completely made by the clinicians who follow the expert consensus of relevant textbooks and clinical guidelines, and they are formulated according to the patients' conditions.

Study subjects: Collect high-risk patients from the Second Affiliated Hospital of Nanchang University and various hospitals of Jiangxi Province from September 2022 to September 2023.

Selection criteria: ① met the high embolic risk (including intracardiac thrombosis, intracardiac tumor, aortic atherosclerosis, atrial fibrillation, and spontaneous development of ultrasound) in the risk stratification criteria of The Chinese Expert Consensus on Cardiac stroke Diagnosis (2020); ② meets the surgical indications for cardiac diseases related to the Chinese Expert Consensus on the Treatment of Cardioembolic Stroke (2022) (including left atrial fibrillation occlusion, left atrial fibrillation ligation, and radiofrequency ablation of atrial fibrillation recommended for high-risk stroke patients with atrial fibrillation; Transcatheter PFO occlusion is recommended for cryptogenic stroke patients with high-risk P FO; Valvular repair or replacement, etc.); ③ understood and voluntarily signed the informed consent form.

Exclusion criteria: ① with severe mental disorder and unable to express intention; ② with other abnormal signs, laboratory tests and clinical diseases, not suitable to attend investigator; ③ and unable to complete long-term follow-up.

Project objectives and assessment indicators: (a) establish a multidisciplinary cooperative diagnosis and treatment mode of cardiovascular and brain joint treatment, and routinely carry out interdisciplinary diagnosis and treatment of cardiovascular and cerebrovascular diseases; (b) develop an optimized diagnosis and treatment process, reduce treatment links, and save medical resources and costs.

Diagnosis and Treatment process (Figure 1):

Primary prevention (mainly for patients with high embolic risk, including valvular heart disease/intracardial tumor, thrombosis/atrial fibrillation/infective endocarditis/PFO, with or without a history of stroke):

a) Patients with high risk of embolism, such as valvular heart disease/intracardiac tumors, thrombosis/atrial fibrillation/infective endocarditis/PFO, and patients with or without a history of stroke, were screened for stroke risk assessment in primary hospitals.
b) Imaging diagnosis and treatment, such as cardiac color ultrasound, cardiac CTA, foaming test (right cardiography), transesophageal ultrasound, right atrial angiography, etc., should be developed according to the research needs, and the specialized diagnosis and treatment process at the recommended level should be formulated
c) Health education and follow-up

Secondary prevention (emergency department mainly for patients with new stroke) :

a) Primary doctors should do a good job in pre-hospital treatment of suspected stroke patients and transfer the patients to superior hospitals as soon as possible, so as to quickly identify the nature of stroke; Once it is clear that it is ischemic stroke, emergency treatment should be carried out according to the diagnosis and treatment process of ischemic stroke.
b) When patients with sudden neurological deficits enter the emergency room, the stroke identification procedure and the treatment process of the stroke center should be initiated immediately, mainly using the BEFAST test /FAST test/" stroke 1-2-0 "method;
c) After the disease stabilized, the examination related to etiological diagnosis should be improved (screening for valvular heart disease/intracardiac tumor, thrombosis/atrial fibrillation/infective endocarditis/PFO);
d) Health education norms and follow-up

Multidisciplinary assisted care model group: Patients who agreed to and accepted the recommendation of multidisciplinary assisted care mode were enrolled in the multidisciplinary assisted care model group. These patients would undergo further stroke (primary/secondary) prevention intervention, as detailed in the MDT flow chart;

Any of the following treatments (including but not limited to), as recommended by the standard medical procedure, shall be deemed to have received the standard medical treatment; otherwise, they were not.

1) Surgical procedures: left atrial appendage ligation, left atrial appendage clip, valve repair or replacement, etc.

2) Medical procedures: atrial fibrillation radiofrequency ablation, valvular closure, left atrial appendage closure, PFO closure, etc.

3) Anticoagulant drug therapy: standardized anticoagulant drug therapy.

Routine treatment model group: Patients who did not agree to enter the multidisciplinary treatment mode were automatically entered into the routine treatment mode group.

Study end points:

Primary end point: Composite end point of cardiovascular and cerebrovascular events (nonfatal ischemic stroke, Nonfatal hemorrhagic stroke, Nonfatal myocardial infarction, Nonfatal heart failure, and cardiovascular and cerebrovascular death)

Secondary end points: cardiovascular and cerebrovascular death; All-cause death; Cardiac insufficiency; Cognitive dysfunction

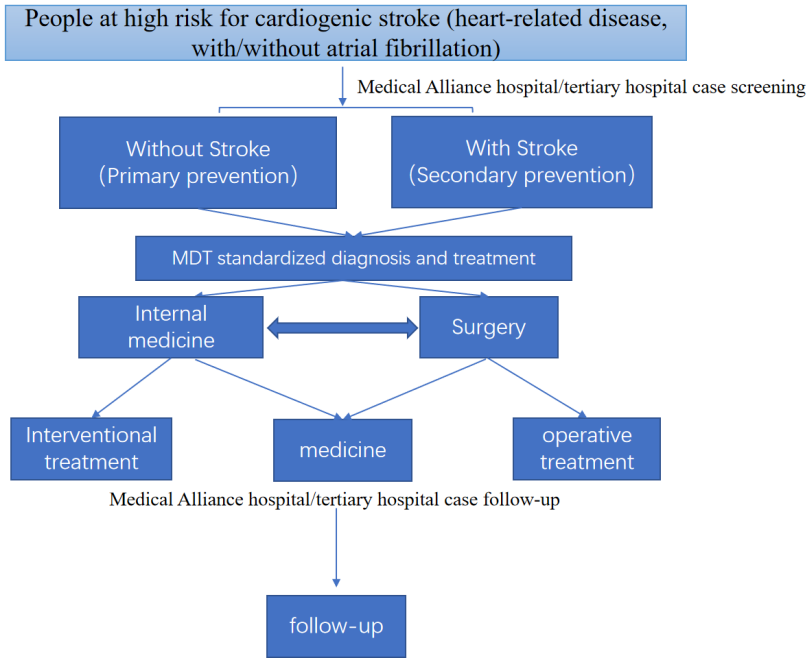

Figure 1 Flowchart of the project

3. Research background data

1. Project approval basis

Stroke, as the first cause of death in China, has the "three high" characteristics of high morbidity, high disability rate and high mortality rate. Data show that in the next 20 years, the number of stroke patients in China will increase by nearly four times, and the prevention and treatment of stroke has a long way to go. In the subtyping of ischemic stroke, the proportion of cardiac stroke is approximately 14 – 30%[1, 2]. cardioembolic stroke (CES), hereinafter referred to as cardioembolic stroke, refers to the clinical syndrome of emboli from the heart and aortic arch through the circulation leading to cerebral artery embolism causing the corresponding cerebral dysfunction. The mechanism of cardioembolic stroke is usually summarized into three types: slow blood flow (especially cardiac cavity enlargement, atrial loss of contraction function, left ventricular wall tumor, etc.) thrombosis and shedding; abnormal valve surface attachments (degenerative valve surface calcification, infectious endocarditis, artificial valve surface thrombus, etc.); systemic circulation venous system thrombosis through abnormal ventricular channel (atrial septal defect or closed orifice) causing embolism (namely "contradictory embolism").CES has more related cardiac diseases or risk factors, among which about 70% are caused by atrial fibrillation (atrial fibrillation, AF). In recent years, the prevention and treatment of CES (such as stroke high-risk AF) has improved[1]. However, there are still some problems, such as insufficient understanding and large differences in treatment strategies. Compared with stroke from other causes, the cardiac stroke course is rapidly progressive, with more extensive involvement, associated with more severe complications, and a higher incidence of adverse outcomes[3]. How to effectively prevent cardioembolic stroke and improve patient prognosis is a major dilemma in clinical practice.

The formulation and effective implementation of accurate treatment plan to improve the prognosis of cardioembolic stroke patients and stroke recurrence is an important means to prevent the onset of patients. Compared with other causes of stroke, the cause of cardiac stroke is clear and mostly preventable and treatable (e. g., an observational study of elderly patients with heart disease history (with AF history) assessing the risk of postoperative thromboembolic complications of LAA occlusion combined with cardiac surgery. The results showed significant reductions in uncorrected thromboembolism readmission rates (4.2% versus 6.2%), all-cause mortality (17.3% versus 23.9%), and the composite endpoint (20.5% versus 28.7%) when compared with those without LAA occlusion[4]. The same study in Asians showed that for high-risk PFO (atrial septal aneurysm, ASA), high activity, primary and secondary spacing 2 mm], PFO occlusion significantly reduced

the main endpoint (stroke, vascular death, thrombolysis defined primary hemorrhage) and stroke recurrence (n=120)[5]. But currently for the prevention and control of cardiac stroke heart brain barriers, diagnosis and treatment process specification, related surgical instruments clinical application is still in the primary stage, such as severe problems, precision treatment need to optimize the current diagnosis and treatment process and professional technology, and an urgent need to "brain", this project plans to explore the above scientific problems, in order to guide the clinical prevention and treatment of cardiac stroke. To explore the multidisciplinary cooperative diagnosis and treatment mode of cardioembolic stroke, and to explore the prevention and treatment mode of "screening, prevention, diagnosis and treatment" of provincial, municipal and county hospitals with the help of medical association and network. This study combined with existing consensus guidelines to develop treatment options based on CES risk stratification and specific pathogenesis[6,7]. Corresponding therapeutic measures are taken to address the different causes of CES to prevent the occurrence of stroke and to actively conduct neurorehabilitation treatment. Many cardioembolic strokes occur every year in China, and most of the cardiology department treat patients with atrial fibrillation without stroke. Many patients with high-risk CES usually improve anticoagulation and other symptomatic treatment in the neurology department, but have no further systematic investigation of whether it is "cardiac". Many neurologists do not routinely consider cardiac treatment in patients with cardioembolic stroke. Therefore, there is an urgent need for "heart and brain joint governance". For patients with previous stroke, the risk of recurrent stroke is very high if the cause of cardiac thrombosis is not addressed. There are problems in the domestic diagnosis and treatment mode, and the heart, surgery, surgery and nerve surgery are not effectively integrated. In the past two years, relevant domestic societies have issued the guidelines for the prevention and treatment of cardiac stroke (2019) and the Chinese expert consensus on the diagnosis of cardiac stroke (2020)[8,9]. According to the clinical and imaging characteristics of cardioembolic stroke, apply the preliminary assessment and risk assessment process of cardioembolic stroke (Figure 1): improve cerebral cerebrovascular imaging; 12-lead ECG and dynamic electrocardiogram; transthoracic echocardiography; laboratory examination and other related examinations, and find possible abnormalities. For example: After admission to the neurology department, the patient is routinely screened for atrial fibrillation by completing a general ECG and an ambulatory ECG. If atrial fibrillation is present, there is a high risk of cardioembolic stroke and referral to the cardiology department is required. Further investigation by the cardiology department confirms the presence of thrombus in the atria, and treatment plans are developed and evaluated accordingly. The risk factors are addressed through standardized

treatment. Regular follow-up after treatment, the incidence of stroke at the primary endpoint, neurological function, cardiac function and cardiac electrophysiological assessment, etc.

Cardiac stroke is characterized by high incidence, difficult treatment and poor prognosis. The best treatment is the early screening of people at high risk of such diseases to treat related underlying cardiac diseases and high-risk factors. Therefore, relying on the discipline construction, we start the multi-disciplinary cooperation and integrate the heart-brain advantage resources team to jointly create a new era of "heart-brain joint governance".

Reference

1. Lin SP, Long Y, Chen XH, et al. STAF score is a new simple approach for diagnosing cardioembolic stroke.Int J Neurosci.2017 Mar;127(3):261–266.

2. Marnane M, Duggan CA, Sheehan OC, et al.Stroke subtype classification to mechanism-specific and undetermined categories by TOAST, A-S-C-O, and causative classification system: direct comparison in the North Dublin population stroke study.Stroke.2010 Aug;41(8):1579–1586.

3. Vahanian A, Alfieri O, Andreotti F, et al.Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS).Eur J Cardio thorac Surg.2012 Oct;42(4):S1–44.

4. Friedman DJ, Piccini JP, Wang T, et al.Association between left atrial appendage occlusion and readmission for thromboembolism among patients with atrial fibrillation undergoing concomitant cardiac surgery[J].JAMA, 2018, 319(4):365374.-

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8. Geriatric Neurology Group of Geriatric Medicine Branch of Chinese Medical Association, Chinese Expert Consensus writing group of cardioembolic stroke diagnosis. The Chinese Expert Consensus on the Diagnosis of Cardiac Stroke (2020) [J]. The Chinese Journal of Geriatric Medicine.2020,39 (12):1369-1378.

9. Heart Rhythology professional Committee of Chinese Medical Association, Heart Electrophysiology and Pacing Branch of Chinese Medical Association. Guidelines for the Prevention and Treatment of Cardioembolic Stroke in China (2019). The Chinese Journal of Arrhythmia.2019,(06):463-484.

4. Research purpose

1. Research purpose:

Establish multidisciplinary collaboration diagnosis and treatment mode, standardize the diagnosis and treatment process: through the integration of neurosurgery, cardiac vascular surgery, neurology, cardiovascular medicine and other related disciplines, build "heart and brain treatment" multidisciplinary close cooperation system, standardize integration process and diagnosis and treatment, at the same time actively innovation relying on the relevant academic society construction, earnestly implement the multidisciplinary collaboration diagnosis and treatment mode. Based on the Internet + 5G medical model technology system and information platform, research to establish coverage relying on the remote medical service platform, the provincial, city and county center of information classification management system, by perfecting the regional collaborative emergency medical platform, improve the province cardiovascular disease acute critical patients overall treatment level, contribute to the standardization of cardiovascular stroke high-risk patients diagnosis and treatment and management. Patients with difficult and acute and critical cardiovascular and cerebrovascular diseases in the stable rehabilitation period after emergency treatment were transferred back to the primary hospital for rehabilitation, follow-up and chronic disease management and treatment.

2. Study observation endpoint

(1) Main observation endpoint: composite end point of cardiovascular and cerebrovascular events (non-fatal ischemic stroke, non-fatal hemorrhagic stroke, non-fatal myocardial infarction, non-fatal heart failure, cardiovascular and cerebrovascular death)

(2) secondary observation endpoint: cardiovascular and cerebrovascular death; all-cause death; cardiac insufficiency; cognitive dysfunction

5. Study design

1. Study site and study population

Collect high-risk patients from the Second Affiliated Hospital of Nanchang University and various hospitals of Jiangxi Province from September 2022 to September 2023.

Selection criteria: ① met the high embolic risk (including Valvular heart disease/intracardiac neoplasms, thrombosis/atrial fibrillation/infective endocarditis/PFO) in the risk stratification criteria of The Chinese Expert Consensus on Cardiac stroke Diagnosis (2020); ② meets the surgical indications for cardiac diseases related to the Chinese Expert Consensus on the Treatment of Cardioembolic Stroke (2022) (including left atrial appendicular occlusion, left atrial appendicular ligation, and atrial fibrillation radiofrequency ablation recommended for high-risk stroke patients with atrial fibrillation; Transcatheter PFO occlusion is recommended for cryptogenic stroke patients with high-risk PFO; Valve repair or replacement is recommended for patients with valvular disease. Left atrial appendage ligation or left atrial appendage clip is recommended for patients with atrial fibrillation.); ③ understood and voluntarily signed the informed consent form.

Exclusion criteria: ① with severe mental disorder and unable to express intention; ② with other abnormal signs, laboratory tests and clinical diseases, not suitable to attend investigator; ③ and unable to complete long-term follow-up.

2. Study and design flow chart:

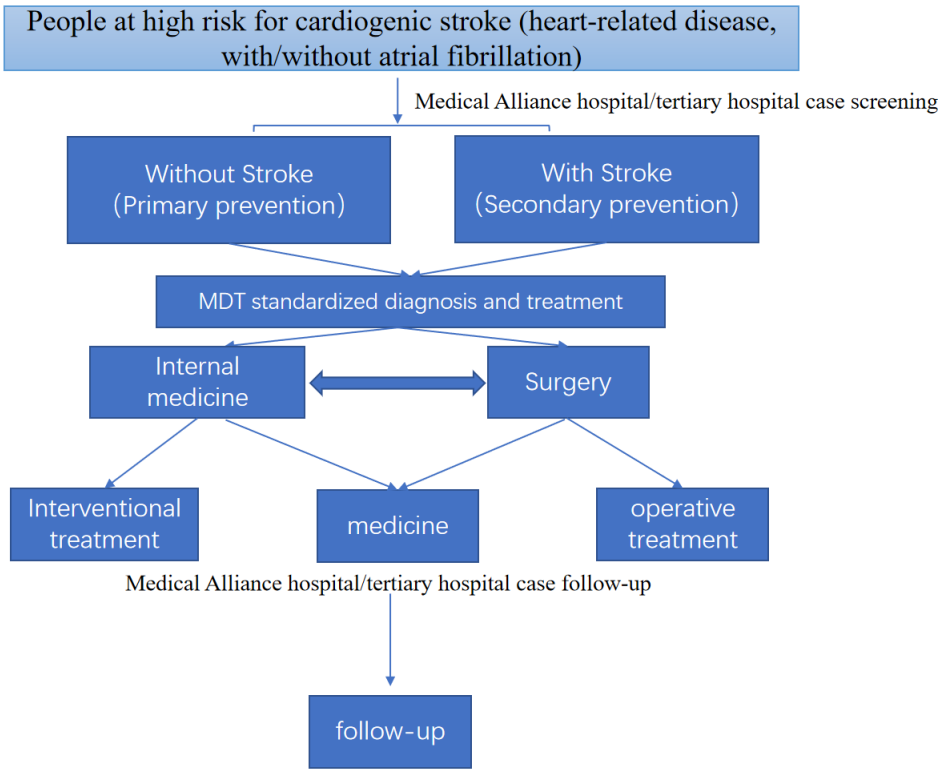

Figure 1 Flowchart of the project

3. Sample size determination method required for the study:

This study through the real world cohort research, to cross professional association as a breakthrough point, with standardization, standardization for innovation, establish interdisciplinary diagnosis and treatment team, establish "screening-prevention-diagnosis and treatment" standardized process, for cardiac stroke high-risk patients to choose standard diagnosis and treatment basis, optimize the current diagnosis and treatment process and professional technology. It is expected that 1,200 patients at high risk of cardioembolic stroke will be included in a time period of 1-1.5 years. It should be pointed out that if compared with conventional diagnosis and treatment methods, patients matched with multiple factors in the same period are selected as the control group.

6. Safety evaluation (including the definition and evaluation of adverse events and serious adverse events)

1. Definition of adverse events: adverse medical events that occur in the course of this standard treatment of the subject, whether they are drug-related or not.

2. Abnormal laboratory and instrument examination results.

3. Serious adverse events: Major adverse events may be drug-related, including but not limited to the following:

(a) Abnormal laboratory indicators (including liver and kidney function, etc.);

(b) Allergic reaction to antiplatelet drugs / anticoagulants;

(c) Stroke / transient ischemic attack or neurological deficit;

(d) Spontaneous bleeding: such as petechia, ecchymosis, digestive system and urinary system bleeding;

(e) Central nervous system damage.

4. Assessment of the severity level

Light: do not affect the daily activities;

In: affect daily activities;

Heavy: loss of daily activity ability.

7. Data collection and management

1. Survey content (CRF table)
variable:

a) Basic information of patients: name, gender, age, education level, combined diseases, past medical history, etc.;

b) Admission status: chief complaints of symptoms, general condition, vital signs, CHA2DS2-VASc score, nutrition questionnaire and epidemiological data etc.;

c) Pre-treatment laboratory and instrument examination: biochemical indicators, nutrient index (one carbon unit substance), electrocardiogram, dynamic electrocardiogram, cardiac color doppler ultrasound, foaming test, cardiac CTA, craniocerebral CT and MRI, internal and external intracranial artery evaluation, etc.;

d) Treatment medication; surgical conditions

e) The occurrence of adverse events during the hospitalization period;

f) Situation at follow-up: chief complaint of symptoms, general condition, vital signs, Quality of Life , HAS-BLED score, etc.;

g) Laboratory and instrumental examination at follow-up: biochemical indicators, electrocardiogram, cardiac color ultrasound, cardiac CTA, craniocerebral CT and MRI, internal and external intracranial artery evaluation, etc.;

h) occurrence of adverse events during follow-up.

2. Data management and statistical analysis

For All the subjects who have signed the informed consent form and are qualified to be selected, all the items in the electronic medical record report form should be carefully recorded in detail, without no empty or missing items.

The investigator records the data into the electronic medical record report according to the original records and inpatient records, and the investigator ensures that the data is true and accurate.

Data that are significantly high or outside the clinical acceptance range should be verified with necessary explanation by the investigator.

The researcher will modify the data due to filling reasons, and the dialog box will pop up in the electronic medical record report form, and the researcher should indicate the reason for the modification. Any modification by the researcher leaves a mark to ensure the authenticity of the data.

After the investigator fills in the data and the supervisor monitors, the investigator solves all the data questions and ensures that the accuracy of the data is determined, the data administrator locks the database. The data management personnel, principal researchers, statistical analysts, implementers and monitoring management personnel will jointly review the data, and complete the final definition and judgment of the analysis population, and then the data manager will finally lock the database.

The locked database or files should generally not be changed again.

8. Quality Management Plan (please introduce relevant measures to ensure project quality and progress)

Surveillance of the observational cohort studies

During the study, the inspectors will regularly visit the research center to ensure that all the content of the research protocol is strictly followed, and the original data is checked to ensure that the data filling content is true, complete and correct.

1. Method of determination

(1) Brain CT and MRI;

(2) Electrocardiogram or dynamic electrocardiogram: 12-lead routine electrocardiogram; 24-hour dynamic electrocardiogram monitoring

(3) Blood routine test, urine routine test, liver and kidney function test, blood biochemical indexes: automatic biochemical analyzer;

(4) Nutrients (one carbon unit substance) : mass spectrometry or biochemistry

(5) Cardiac ultrasonography;

(6) Cardiac CTA

(7) Surgical records

(8) Combined medication

(9) Relevant scales should be applied with international common scale or Chinese version

(10) Record of adverse events.

2. Fill in the electronic case report form

Electronic case report form (CRF) was used in this trial. For All subjects who have signed the informed consent form and are qualified to be selected, all items in the electronic medical record report form should be recorded carefully and detail, with no empty or missing items. All data in the EHR report form should be checked with the original subject medical record data to ensure correct accuracy. The investigators ensure that the data are true and accurate.

3. Preservation of the original materials

The original data of this trial includes signed informed consent, release records of test products, relevant laboratory test reports, case records and other relevant records, and should be kept in the national drug clinical trial institution of the hospital where the research center is located . Medical institutions shall keep the clinical trial data until five years after the termination of the trial. The implementer shall keep the data of the clinical trial until ten years after the last produced product is put into use.

9. Pre-assessment and risk control plan of the project risk and benefits (please describe the possible risks and benefits of the researchers, the subjects and their medical institutions when conducting the project. If there are risks, please introduce the risk control measures and feasibility.)

1. Benefit / risk assessment

(1) Benefit: through the real world cohort research, to cross-professional collaboration as a breakthrough point, to diagnosis and treatment standardization, standardization for innovation, establish interdisciplinary treatment team, establish "high-risk patients with cardioembolic stroke (acute stroke) -MDT-standardized diagnosis and treatment-rehabilitation treatment" standardized process, optimize the current diagnosis and treatment process and professional technology.

(2) Possible risks:

1) Abnormal laboratory indicators (including liver and kidney function, etc.);
2) Allergic reaction to antiplatelet drugs / anticoagulants;
3) Stroke / transient ischemic attack or neurological deficit;
4) Spontaneous bleeding: such as petechia, ecchymosis, digestive system and urinary system bleeding;
5) Central nervous system damage.

2. Ethics and ethics

(1) Ethics Committee (should describe how the plan was approved by the Research Ethics Committee / Institutional Review Board)

1) Conclusion: Cardiac stroke accounts for 14% ~ 30% of ischemic stroke, and the condition is more serious, with high mortality rate, disability rate and recurrence rate. Cardiac stroke mostly has clear underlying diseases or risk factors of the cardiovascular system, including valvular heart disease, atrial fibrillation, PFO and so on. There are disciplinary barriers to prevention and treatment of cardiac stroke, standardized diagnosis and treatment process, clinical application of related surgical instruments is still in the initial stage, such as precision treatment, and need to optimize the current treatment process and professional technology, prevention and treatment of cardiac stroke, this project explores multidisciplinary collaborative treatment mode of cardiac stroke, and develops standardized diagnosis and treatment process and related professional technology.
2) General situation of the undertaking unit (personnel, assets, business and management status):

The second Affiliated Hospital of Nanchang University is the tertiary hospital, neurosurgery is the first neurosurgery specialty in Jiangxi Province, has become a key specialty, neurosurgery medical, teaching and research center of Nanchang University, with long-term follow-up database and specimen database, laid a solid foundation for the smooth implementation of this work. Professor Xingen Zhu, the applicant of the project, was approved as the "Changjiang Scholar distinguished Professor" of the Ministry of Education, and is the "only professor" in the medical field of the province. This project sets related advantageous units and experts, covering production, learning, research, medical, inspection, use and other industries, covering research and development, production, testing, application and other links. At present, the project leader has established a scientific research team for basic BI research and stem cell intervention, whose core members have more than ten years of scientific research attainments in the fields of molecular biology, cell biology and clinical research. The personnel involved in this project all have a good training background, clinical translational research

experience, and laboratory work background, which is helpful Completed the study of this project.

3) Advantages of the participating units:

The Second Affiliated Hospital of Nanchang University of the "China Five-Star Advanced Stroke Center" won the title of "National Five-Star Advanced Stroke Center" of the Stroke Prevention and Treatment Engineering Committee of the National Health Commission in 2020. The second affiliated hospital of Nanchang university has been committed to provide efficient, high quality first aid green channel for stroke patients, formally established in 2015 stroke center, the same year approved "national senior stroke center", in 2018 in the national difficult disease (cerebrovascular disease) diagnosis and treatment promotion project (the only) in the province, the hospital established the cerebrovascular disease center, in 2018,2019,2020 consecutive "China five-star senior stroke center" title. The second Affiliated Hospital has solid technical strength and the support of the diagnosis and treatment of difficult cerebrovascular diseases. The second affiliated hospital of Nanchang university will continue to play a "China five-star senior stroke center" regional leading role, with the help of the couplet of medical, network hospital, remote consultation, nervous system difficult severe alliance platform, strengthen the training supervision, further quality medical resources sinking, at the same time to strengthen the construction of stroke prevention alliance, cultivate more stroke professional doctors, make greater contribution to stroke prevention and control, benefit more people;

In 2016, the Second Affiliated Hospital of Nanchang University took the lead in opening the "medical imaging cloud service platform", realizing the image "cloud storage" and remote film reading consultation. In 2019, with the help of cloud platform and professional operation team, the hospital established medical consortium cooperation with 111 secondary and above hospitals in the province. The telemedicine business effectively radiated to the whole province, realizing more than 100 cases of difficult diseases in a single month, and solved the problem of remote people running to see a doctor with practical measures. The remote consultation system breaks the restrictions of time, space and region, and enables high-quality medical resources to sink, so that residents in remote areas can enjoy the diagnosis and treatment of provincial medical experts without traveling hard and win valuable medical treatment time. At the same time, grassroots hospitals can also invite experts from provincial hospitals to conduct remote consultation, so as to help grassroots doctors to diagnose difficult diseases and receive support from medical technology. Each consultation process is an opportunity to receive telemedicine education and training. In the future, the construction of a comprehensive and interconnected remote platform will bring more convenient and accurate medical services to the diagnosis and treatment of difficult diseases of cardioembolic stroke.

(2) Patient information and informed consent:

This cohort study was conducted in accordance with the requirements of the current Declaration of Helsinki, medical device clinical trial regulations, GCP, and relevant national regulations.

Before the start of the study, the investigator should submit the study protocol, informed consent form and other relevant documents to the medical ethics committee of the hospital responsible for the clinical trial. Clinical trials can not be started until after obtaining ethics committee approval. Any modification to the study protocol must be approved by the ethics

committee before being implemented. Serious adverse events during the clinical trial should be promptly presented in writing to the ethics committee.

Prior to inclusion in this study, the investigator must provide the subject and his relatives with the details of the clinical trial, including the purpose of the trial, expected efficacy, possible adverse events, and countermeasures. They will be selected after the subjects fully understood the trial, accepted the informed process, and signed the informed consent.

The Informed consent was jointly signed by the study physician and the subject himself or his legal representative in duplicate, with one copy kept for each party.