Research scheme

CPVI Alone Versus CPVI Plus Low-Voltage Areas Ablation During SR Versus CPVI Plus Low-Voltage Areas Ablation During AF for the Treatment of CAF

The affiliated Yantai Yuhuangding Hospital of Qingdao University

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Study summary

Brief Title	CPVI Alone Versus CPVI Plus Low-Voltage Areas Ablation During SR Versus CPVI Plus Low-Voltage Areas Ablation During AF for the Treatment of CAF
Objectives of Study	The primary objective of this investigation is to compare the efficacy of Three different AF ablation strategies in patients with Persistent atrial fibrillation: CPVI plus Low-Voltage Areas ablation during sinus rhythm Versus. CPVI Plus Low-Voltage Areas Ablation During AFand CPVI alone. The primary endpoint is freedom from AF and/or ATs with or without antiarrhythmic drugs (AADs) at 12months after a single-ablation procedure. AF and/or AT occurring in the first 3 months after the ablation (blanking period) was censored. Each episode lasts > 30 seconds. The secondary endpoint are incidence of peri-procedural complications, including stroke, PV stenosis, cardiac perforation, esophageal injury and death; procedure time; fluoroscopy time (including the total fluoroscopy time, during CPVI and after CPVI); the occurrence of the conversion from AF to AT, and its relationship with long-term outcome; the relationship between acute termination of AF and long term outcome.
Study design	This is a randomized, prospective, parallel, single-blind multicenter design. The enrollment target for this investigation is 150 patients. Patients are randomized in a 1:1:1fashion into one of the investigation arms: CPVI plus electrophysiologic substrate ablation in the left atrium during sinus rhythm (STABLE-SR) and CPVI plus electrophysiologic substrate ablation in the left atrium during atrial fibrillation rhythm (STABLE-AF) and CPVI alone. Follow-up for these patients includes visits at 3 m, 6 m, 9 m, 12 m.
Research population	Atrial Fibrillation
Total sample size	150
Description	**Inclusion Criteria** 1.Patients age is 18-80 years; 2.Patients with non-paroxysmal AF; non-paroxysmal AF will be defined as a sustained episode lasting > 7 days; 3.Patients can sign the written informed consent for the study; 4.Patients can endure the required follow-up.
	Exclusion Criteria 1.Patients who had previously undergone atrial fibrillation, atrial tachycardia, or atypical atrial flutter ablation； 2.Preoperative combined atrial tachycardia (≥30S) and atypical atrial flutter; 3.Left atrial diameter >55mm; 4.Left ventricular ejection fraction <35%; 5.Left atrial thrombus; 6.Postoperative cardiac surgery; 7.After valve replacement; 8.After permanent pacemaker implantation; 9.hypertrophic cardiomyopathy； 10.Patients with moderate-to-severe aortic valve disease, moderate-to-severe mitral stenosis, and severe other valvular disease； 11.Hemorrhagic stroke within 6 months； 12.Transient ischemic attack or ischemic stroke within 1 month； 13.Mental disorder or history of mental illness and inability to cooperate voluntarily； 14.Breastfeeding, pregnancy and women planning or likely to become pregnant；

	15.Life expectancy <12 months； 16.Participating in other interventional clinical trials； 17.The researchers judged that it was not suitable for inclusion in this study.
Design Details	PVI vs.PVI plus electrophysiologic substrate ablation in the left atrium during sinus rhythm (STABLE-SR) vs. PVI plus electrophysiologic substrate ablation in the left atrium during atrial fibrillation rhythm (STABLE-AF).
Outcome Measure	**Primary Outcome Measures** The incidence of no atrial arrhythmias greater than 30 seconds
	Secondary Outcome Measures 1.No use of antiarrhythmic drugs and no occurrence of atrial fibrillation/atrial tachycardia/flutter exceeding 30 seconds. 2.Atrial fibrillation load:Atrial fibrillation load reduction rate of a single case = 100%-atrial fibrillation load of 12m dynamic electrocardiogram after operation (%).
Statistical method	Analysis of the occurrence time of the first event
Research period	24Month

BACKGROUND: Success rates of catheter ablation for persistent atrial fibrillation (PeAF) are significantly lower than those for paroxysmal atrial fibrillation (AF). Therefore, various substrate modification strategies in addition to circumferential pulmonary vein isolation (CPVI) were adopted for PeAF.

However, in randomized controlled trials, most of these adjunctive ablation strategies did not improve long-term maintenance of sinus rhythm (SR).The correlation between atrial fibrosis and AF has been well established using multiple modalities including cardiac magnetic resonance, histopathology and high-density electroanatomic mapping. Fibrosis separates myocardial bundles, diminishes cell coupling, and causes slow, anisotropic conduction. These microscopic proarrhythmic changes manifest as alterations in the voltage and complexity of local electrograms.1previous study and other similar studies demonstrated that CPVI plus ablation targeting these abnormal areas could be an effective personalized ablation strategy and avoid excessive ablation.But most current studies on substrate modification of persistent atrial fibrillation (AF) have been conducted using pulmonary vein isolation plus Low-Voltage Areas ablation during SR. However, the area of Low-Voltage Areas during AF is different from that during SR.Some studies have found that Low-Voltage Areas during AF is a better reproducible marker reflecting the functional response to the underlying persistent AF substrate.Therefore, we aimed to compare the long-term outcome of Three different AF ablation strategies in patients with Persistent atrial fibrillation: CPVI plus Low-Voltage Areas ablation during sinus rhythm Versus CPVI Plus Low-Voltage Areas Ablation During AF and CPVI alone.

AIM OF THE STUDY: The primary objective of this investigation is to compare the efficacy of Three different AF ablation strategies in patients with Persistent atrial fibrillation: CPVI plus Low-Voltage Areas ablation during sinus rhythm Versus CPVI Plus Low-Voltage Areas Ablation During AFand CPVI alone. The primary endpoint is freedom from AF and/or ATs with or without antiarrhythmic drugs (AADs) at 12months after a single-ablation procedure. AF and/or AT occurring in the first 3 months after the ablation (blanking period) was censored. Each episode lasts > 30 seconds. The secondary endpoint are incidence of peri-procedural complications, including stroke, PV stenosis, cardiac perforation, esophageal injury and death; procedure time; fluoroscopy time (including the total fluoroscopy time, during CPVI and after CPVI); the occurrence of the conversion from AF to AT, and its relationship with long-term outcome; the relationship between acute termination of AF and long term outcome.

RESEARCH METHODS

1. Study design :This is a randomized, prospective, parallel, single-blind multicenter design. The enrollment target for this investigation is 150 patients. Patients are randomized in a 1:1:1fashion into one of the investigation arms: CPVI plus electrophysiologic substrate ablation in the left atrium during sinus rhythm (STABLE-SR) and CPVI plus electrophysiologic substrate ablation in the left atrium during atrial fibrillation rhythm (STABLE-AF) and CPVI alone. Follow-up for these patients includes visits at 3 m, 6 m, 9 m, 12 m.

2. Research population

2.1 Inclusion Criteria

a.Patients age is 18-80 years;
b.Patients with non-paroxysmal AF; non-paroxysmal AF will be defined as a sustained episode lasting > 7 days;
c.Patients can sign the written informed consent for the study;
d.Patients can endure the required follow-up.

2.2 Exclusion Criteria

a.Patients who had previously undergone atrial fibrillation, atrial tachycardia, or atypical atrial flutter ablation；
b.Preoperative combined atrial tachycardia (≥30S) and atypical atrial flutter;
c.Left atrial diameter >55mm;
d.Left ventricular ejection fraction <35%;
e.Left atrial thrombus;
f.Postoperative cardiac surgery;
g.After valve replacement;
h.After permanent pacemaker implantation;
i.hypertrophic cardiomyopathy；
j.Patients with moderate-to-severe aortic valve disease, moderate-to-severe mitral stenosis, and severe other valvular disease；
k.Hemorrhagic stroke within 6 months；
l.Transient ischemic attack or ischemic stroke within 1 month；
m.Mental disorder or history of mental illness and inability to cooperate voluntarily；
n.Breastfeeding, pregnancy and women planning or likely to become pregnant；
o.Life expectancy <12 months；
p.Participating in other interventional clinical trials；
q.The researchers judged that it was not suitable for inclusion in this study.

2.3 Exit Criteria

a.The subjects withdrew voluntarily: if the curative effect was poor, they could not tolerate adverse reactions, they wanted to take other treatment methods, or they withdrew from the trial voluntarily without any reason.

b.The researchers determined that the subjects should withdraw from the trial, such as abnormal function of important organs, allergic reactions to drugs, poor compliance, aggravation or serious adverse reactions that required stopping experimental drug treatment or using other treatments. The researchers asked the subjects to withdraw from the trial.

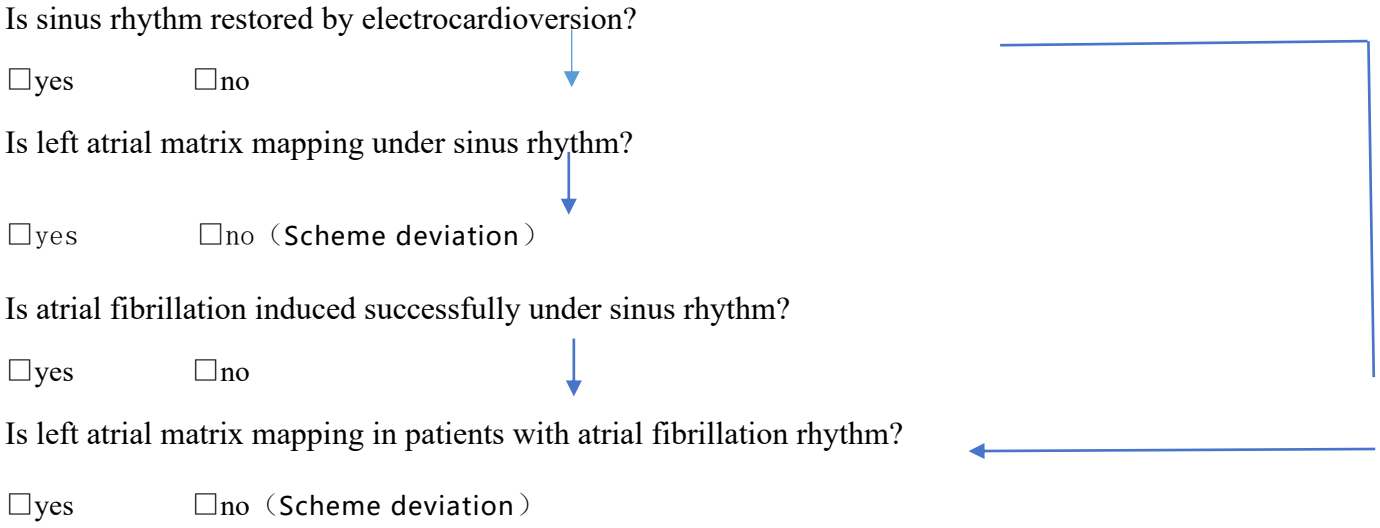
2.4 Pause / abort criteria:If the test is temporarily suspended for reasons such as unexpected events, high test risk, funds, administrative changes, etc., the test can be continued after the relevant factors affecting the test are removed.

2.5 Abort criteria:The research is terminated due to the requirements of laws and regulations or by researchers and administrative departments, such as serious safety problems are found, the efficacy can not meet expectations, there is no need to continue clinical research, and so on.

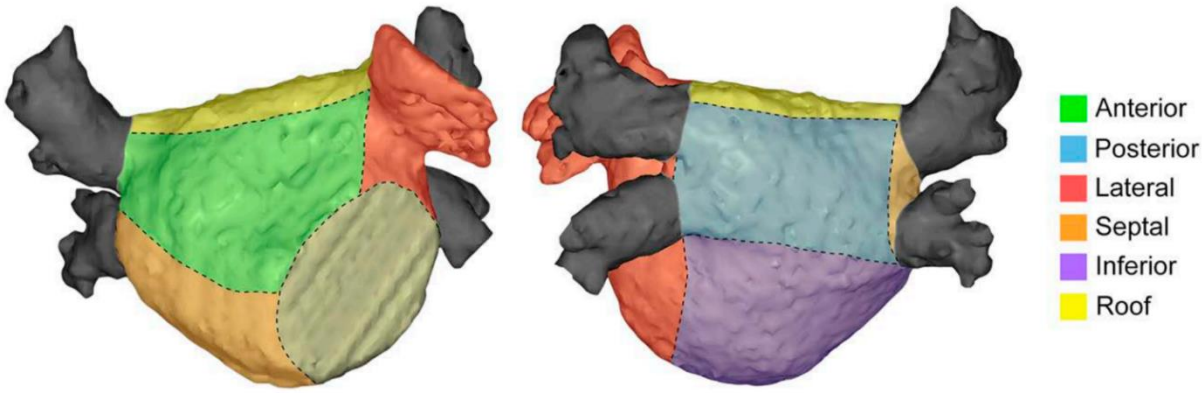
3.1 Study intervention measures

Radiofrequency ablation was used in this study, excluding cryoablation and surgical ablationAll operations were performed under local anesthesia. Antiarrhythmic drugs were not stopped before operation, and patients continued to receive anticoagulant therapy, that is, warfarin maintained an international standardized ratio (international normalized ratio,INR) of 2-3, or direct oral administration of anticoagulants rivasaban or dabigazun, which was taken for the last time the night before operation. During the operation, patients were given local anesthesia with lidocaine. Ten-grade coronary sinus electrodes were implanted into the subclavian or right femoral vein, and the right femur was punctured for atrial septal puncture. During the operation, heparin was injected intravenously to maintain the activated clotting time (activated coagulation time,ACT) of 300 to 350 seconds. Johnson's PentaRay mapping electrode catheter (PentaRay,2-6-2, Webster, USA) was placed along the sheath to the left atrium, and the CARTO three-dimensional mapping system (7th edition) was connected to establish a three-dimensional anatomical model of the left atrium and bilateral pulmonary veins.Electrocardioversion was performed in all patients before ablation, and then left atrium was modeled in sinus rhythm before Pentaray catheterization and matrix mapping of atrial low voltage area (low voltage areas,LVAs) LVAs was performed. Atrial fibrillation was induced by Burst high frequency stimulation or isoproterenal auxiliary stimulation, and endocardial voltage mapping was performed again under atrial fibrillation rhythm. If patients with failed cardioversion underwent PVI, matrix mapping in sinus rhythm was performed again, and the above mapping was completed under bipolar signal (filter set to 30~300Hz).

The mapping process is as follows:



All patients underwent PVI first. Johnson ST or STSF pressure catheter was used to ablate the right anterior wall, bottom, posterior wall and top of the right lung, and the left pulmonary vein was isolated in the same order. The discharge mode was 40-50W, the flow rate of saline was 15mL/min, and the ablation index was 450,500,380,400 in the anterior wall and posterior wall respectively.
Electrophysiological examination was performed to determine whether the bilateral pulmonary veins were completely isolated and, if necessary, to ablation until the bilateral pulmonary veins were completely isolated.After PVI, 40-50W power mode was used for ablation randomly according to sinus rhythm or low voltage area (0.1-0.5mV) under atrial fibrillation. For patients with unterminated atrial fibrillation, 200J synchronous electrocardioversion was given to restore sinus rhythm.
The electrocardiographic mapping of the left atrium established by the PentaRay catheter (excluding the left atrial appendage and bilateral pulmonary veins) was divided into 6 regions, as shown in figure 1.



Using the area measurement tool in the CAROT system, according to the color codes corresponding to the selected thresholds 0.1-0.5mV and 0.1-0.3mV, the areas of six LVAs are hand-drawn and measured.
The use of antiarrhythmic drugs is carried out according to the latest guidelines, and rhythm control is preferred. If there are taboos, patient intolerance or patients do not return to the hospital, heart rate control drugs can be selected according to the actual situation.

3.2 Combined use of drugs

None

3.3Evaluation indicators / research endpoints

Primary Outcome Measures:12-month late success rate

The 12-month late success rate will be obtained by survival analysis. The failure events of survival analysis include the following three categories, which are defined as:

1)Relapse:During the evaluation period, atrial fibrillation, atrial flutter or atrial tachycardia with a duration of ⩾ 30 seconds were recorded by dynamic electrocardiogram, or atrial fibrillation, atrial flutter or atrial tachycardia were recorded by body surface electrocardiogram.Judging by ECG records.

2)Ablation 2 or more times during the blank period:During the blank period, the frequency of catheter ablation in the treatment of atrial flutter or atrial tachycardia or atrial fibrillation was ⩾ 2. Judging by the surgical records.

Secondary Outcome Measures: immediate success rate

1)Observe the acute effect of ablation.

2)Definition: termination of atrial fibrillation caused by ablation

3)Atrial fibrillation is converted to sinus rhythm or measurable atrial tachycardia / atrial flutter, which refers to atrial tachycardia / atrial flutter with consistent activation sequence and stable rhythm interval.

Note: for patients with ablation under sinus rhythm, because it is impossible to evaluate this index, it is not included in the calculation of immediate success rate, that is, both the numerator and denominator do not include the patient.

Other effectiveness indicators:

Atrial fibrillation load reduction rate: atrial fibrillation load reduction rate of a single case = 100%-12m dynamic electrocardiogram atrial fibrillation load (%) after operation.

12-month clinical success rate: 12-month clinical success rate will be obtained through survival analysis. The failure event of survival analysis was to evaluate the recurrence of symptomatic atrial fibrillation during the period.Symptoms: palpitation, fatigue, decreased activity tolerance, shortness of breath, chest tightness, chest pain, syncope precursor (dizziness, dizziness, etc.), syncope.

Recurrence of atrial fibrillation: atrial fibrillation with duration ⩾ 30 seconds was recorded by dynamic electrocardiogram, or atrial fibrillation was recorded by body surface electrocardiogram.

Other cases are defined as censorship. Record the time when the failure event or deletion occurred. The survival time of patients with deletion (no failure event) is based on the time of the last ECG recording.

4.Visit arrangement and data collection during the study

4.1All patients were followed up regularly at 3 months, 6 months, 12 months and 24 months after operation. the follow-up window of 3 months and 6 months was ±14 days, and then the follow-up window was ±30 days. Postoperative anticoagulants are recommended for life (new oral anticoagulants or warfarin) unless there is a taboo. If warfarin is used, it is necessary to meet the international standard ratio (INR) of 2.0 to 3.0. Follow-up included symptoms, signs, electrocardiogram, echocardiography (including diastolic function assessment) and 7-day ambulatory electrocardiogram.

Project	Screening / baseline period	Treatment period	Routine follow-up				Non-periodic follow-up
	(-15d~0d)	(The day of the operation)	After operation 3M(+14 d)	After operation 6M(+14d)	After operation 12M(+30d)	After operation24M（±30d)	3M to 24M after operation
Admission diagnosis	×						
Vital signs		X (before operation	×	×	×		×
12-lead ECGⅢ	×	× (before operation、After operation)	×	×			×
24-hour dynamic electrocardiogram	×		×	×	×		×
Transthoracic echocardiography	X				×		
Combined use of drugsV	×			×	×		
Transesophageal ultrasound	×						
Approved input and discharge standard	X						
Registration number		×					
Adverse events	×	×	×	×	×		×

4.2.collecting data

Note:

I. In order to protect the rights and interests of the subjects and avoid repeated examination, the data of transthoracic echocardiography within 15 days before the signing of the informed consent form were used as baseline evaluation.

II. Vital signs: 3 months, 6 months, 12 months after operation, irregular follow-up: heart rate and blood pressure were collected only during follow-up in our hospital.

III. ECG recording:

A) Before operation: can come from any form of ECG monitoring (routine ECG, dynamic ECG, monitoring equipment, etc. Printed paper records), time, lead is not limited. The patient's medical history recorded the duration of atrial fibrillation ≥ 7 days or the history of persistent atrial fibrillation, 1 dynamic electrocardiogram within 90 days (full atrial fibrillation) or 2 atrial fibrillation electrocardiograms with intervals of at least 7 days within one year.

B) Before the day of operation: 1 electrocardiogram with body surface leads (not limited to specific leads).

C) 3 months after operation: 12-lead ECG or 24-hour dynamic ECG.

D) 6 months after operation: 24-hour dynamic ECG was the first choice, followed by 12-lead ECG.

E) Irregular on-demand follow-up: 24-hour dynamic ECG or 12-lead ECG (if applicable)

IV. Combined drugs: class I and class III AAD. In order to avoid the interference of AAD in the evaluation of the curative effect of radiofrequency ablation, caution should be taken during the evaluation period when increasing the dose of new AAD or original AAD (compared with that before operation), especially amiodarone.

V. The intraoperative effect is immediate, and the long-term effect is 3-12 months after operation.

STATISTICAL PROCESSING

Using the analysis of the occurrence time of the first event, the log-rank test will be used to compare the significance of the difference between the two groups of main end events, and the Kaplan-Meier estimator will be used to show the estimated survival function, and the Cox proportional hazard model will be used to obtain the risk ratio and 95% confidence interval.

Reporting and handling of adverse events and emergency plans

1. Definition of adverse events

Adverse event (AE) refers to any adverse medical event that occurs after a patient or clinical trial subject receives a drug, but it does not necessarily have a causal relationship with the treatment. It can be any unexpected or uncomfortable symptom, sign, disease or event that may cause bodily injury and is temporarily associated with a drug or medical device, but not necessarily a causal relationship with the drug or surgery.

Important adverse events in the course of drug use, adverse events and hematology or other laboratory tests are obviously abnormal, these adverse events and examination obvious abnormalities must take targeted medical measures to return to normal.

Serious adverse events (SAE) refer to the following adverse events that occur during the observation period with any dose of experimental drugs, usually including death, life-threatening, hospitalization, or extended hospitalization.

2.Handling of adverse events

(1) hospitalized patients

If adverse events occur during hospitalization, the following procedures shall be followed:

After finding that there are adverse events in the subjects, the bed-attendant doctor or the doctor on duty should promptly inform the researcher that if necessary, they can deal with the symptoms first, and the research physicians will initially evaluate the degree and classification of the adverse events and their correlation with the experimental drugs. and give further advice:

a. General adverse events: the outcome of the event can be closely followed or the corresponding symptomatic treatment can be carried out according to the trial scheme.

b. Important adverse events: research physicians should promptly notify key researchers, suspend treatment and deal with them according to the requirements of the program.

c. Handling of serious adverse events

When considering SAE, the first doctor shall notify the lead researcher or other responsible doctor to be present. If the condition is serious, he should notify the project leader while rescuing. If necessary, stop the trial immediately. If it is judged to be SAE, the corresponding treatment or rescue measures should be taken immediately according to the clinical manifestations to maintain the stability of the patient's vital signs as far as possible, and ECG monitoring should be carried out when necessary. if necessary, the relevant departments can be consulted and assisted in handling, and the "pre-plan for preventing and dealing with subjects' damage and emergencies in medical treatment" can be initiated.

When the project leader determines that a serious adverse event occurs, he must report to the key researcher in writing within 24 hours. The part of the sponsor's report shall ensure compliance with the reporting procedures required by all laws and regulations.

(2) Outpatients

After learning that the subjects had adverse events, the research physician should ask the subjects in detail about the symptoms, signs and location at that time, give the necessary explanations and initial guidance to the subjects, and give a preliminary assessment of the degree and correlation of the adverse events; if the subjects are in a local medical institution, contact the receiving doctor by telephone to verify the degree of the adverse events and give advice on how to deal with them:

a. General adverse events: you can go to the local hospital for preliminary treatment and inform you to closely follow up on the outcome of the incident.

b. Important adverse events: it is recommended to return to hospital or go to the local hospital for treatment, and promptly inform the major researchers. If the local hospital conditions are limited, doctors should be sent to treatment. Suspension of treatment and symptomatic treatment were adopted according to the requirements of the program. The Office of Clinical Trials assists the research team in tracking adverse events until the patient is properly resolved or the condition is stable.

c. When the treatment of serious adverse events (SAE) is considered as SAE, the first doctor shall notify the principal researcher or other responsible doctor to be present. If the condition is serious, he should notify the project leader while rescuing. If necessary, stop the trial immediately. If it is judged to be SAE, the corresponding treatment or rescue measures should be taken immediately according to the clinical manifestations to maintain the stability of the patient's vital signs as far as possible, and ECG monitoring should be carried out when necessary. if necessary, the relevant departments can be consulted and assisted in handling, and the "pre-plan for preventing and

dealing with subjects' damage and emergencies in medical treatment" can be initiated.

(3) when the out-of-hospital subjects are judged to be SAE and are unable to come to see a doctor, they are advised to return to the hospital or go to the local hospital in time, and immediately notify the project leader to get further advice; for example, when seeing a doctor in the local hospital, contact the receiving doctor to understand the specific situation and give suggestions for treatment. If necessary, go to the local area for treatment or take it back to our hospital for treatment.When the project leader determines that a serious adverse event occurs, he must report to the key researcher in writing within 24 hours. The part of the sponsor's report shall ensure compliance with the reporting procedures required by all laws and regulations.

3. Record

(1) the research physician should record the adverse events, including at least the description of the adverse events, the time of occurrence, the time of termination, the degree and frequency of attacks, whether treatment is needed, and if so, record the treatment given.

(2) record the occurrence, development and treatment of SAE in as much detail as possible in the original case, and record it in the CRF table, follow up the SAE until it is properly resolved or the condition is stable or the cause is clear, it is necessary to provide the final report to the ethics committee of the clinical research institution of the researcher of the project (if necessary, some departments should report in writing).

4. Emergency plan

(1) Emergency plan for acute pericardial tamponade

Identification of acute pericardial tamponade.

Clinical manifestations: sweating, shortness of breath, lack of consciousness, should not be called, etc.

Physical examination: blood pressure dropped significantly;

Fluoroscopy: the heart shadow was enlarged, the heart shadow beat disappeared or the heart beat inside the heart shadow.

Catheter room management of acute pericardial tamponade:

Pericardial puncture and drainage: once acute pericardial tamponade is established, pericardial puncture and drainage should be performed immediately under X-ray fluoroscopy. The symptoms were relieved quickly after emergency pericardiocentesis and drainage. In general, bleeding is drawn out by puncture needle, and no new packing is observed to terminate the drainage. Patients with perforated left atrial appendage had more pericardial hemorrhage. Considering the lack of contractility of left atrial appendage, a pigtail catheter was inserted into the pericardial cavity for drainage, and no new bleeding was observed to terminate the drainage. After the drainage was completed and stabilized, the pigtail catheter was retained in the pericardial cavity in case of rebleeding. In addition to puncture and drainage, protamine can be considered for patients with continuous bleeding. Although pericardiocentesis and drainage can avoid thoracotomy in most cases, emergency thoracotomy is still necessary.

Keep vital signs stable: if the patient's bleeding continues to increase, active fluid replacement is needed, while emergency blood transfusion is required. Unstable blood pressure requires the use of pressor drugs such as dopamine. If the patient's spontaneous breathing weakens or disappears, endotracheal intubation and ventilator assistance should be given immediately.

Emergency surgical thoracotomy heart repair: if the patient has continuous pericardial drainage, increased bleeding, unstable vital signs, etc., it is necessary to contact cardiac surgeons and anesthesiologists to prepare emergency thoracotomy repair surgery. The operator and his family members shall explain the disease and sign the informed consent forms such as operation and blood transfusion.

Research related processing.

Patients with complications and life-threatening are adverse events, which need to be reported by the ethics committee and complete the relevant documents.

(2) Emergency plan of arteriovenous fistula

Identification of arteriovenous fistula.

Clinical manifestations: pain at the puncture site of the femoral vein, aggravation after activity, etc.

Physical examination: stethoscope femoral vein murmur.

Ultrasound examination: vascular ultrasound color Doppler revealed arteriovenous fistula.

Management of arteriovenous fistula.

Diagnosis and evaluation: patients with symptoms of pain in the femoral vein puncture site, especially after exercise, and bedside auscultation indicating continuous murmur, should immediately improve vascular ultrasound examination to evaluate the existence of arteriovenous fistula. and the size of fistula and the degree of shunt. After evaluation, patients with smaller fistula and less shunt were given general symptomatic treatment, such as observation, analgesia, activity restriction and so on.

Covered stent implantation: for patients with large fistula and large shunt, after ultrasound evaluation, covered stent implantation was performed under the guidance of DSA to close the fistula.

Research related processing.

The occurrence of vascular complications in patients is an adverse event, which needs to be reported by the ethics committee and complete the relevant documents.

(3) Emergency plan for severe arrhythmia.

Clinical manifestations: palpitation, chest tightness, loss of consciousness of dim syncope, etc.

Physical examination: in severe cases, heart rate increases and blood pressure drops.

Electrocardiogram examination: severe tachyarrhythmia, such as ventricular tachycardia, ventricular fibrillation, or severe bradycardia, sinus bradycardia, high or third-degree conduction block.

Management of severe arrhythmia

After the appearance of related symptoms, 12-lead ECG examination was performed immediately, and ECG monitoring and oxygen inhalation were given. Severe tachyarrhythmia: if the patient has rapid arrhythmia and blood pressure drop, immediately give electric cardioversion or defibrillation treatment, at the same time improve the serum electrolyte examination, supplement electrolyte, sedation, antiarrhythmic drugs and other treatment.

Severe bradycardia:

Stop using antiarrhythmic drugs and be monitored by ECG, such as patients with repeated black syncope, emergency implantation of temporary pacemakers. If the patient still has severe bradycardia or related clinical symptoms after 5 half-lives of drug withdrawal, permanent pacemaker implantation should be considered.

Research related processing.

Patients with arrhythmia complications are adverse events, which need to be reported by the ethics committee and complete the relevant documents.

Quality control and quality assurance of research

Researchers' meetings were held before the start of the study and every 6 months to train the content of the research program, strengthen the program implementation rate and follow-up rate. Patients included in the study group can take special outpatient consultation (atrial fibrillation clinic) consultation and condition guidance to strengthen their compliance. The Research steering Committee will meet before the start of the study and every six months thereafter. The main responsibilities include overall supervision of trials, measures to reduce deviations from programmes, and review of safety data. The role of the data Security Monitoring Committee (DSMB) is to safeguard the interests of trial participants and to monitor the data collected during the trial. All adverse reactions will be reported to the DSNB,DSMB with the right to terminate the trial for effective safety reasons. The trial will be reviewed by the steering Committee and DSMB every 6 months. The case report form will be verified together with the source file.

Data security monitoring

The clinical research will make the corresponding data security monitoring plan according to the risk. All adverse events should be recorded, handled and tracked to proper resolution or stable condition, and serious adverse events and unexpected events should be reported to ethics committees, competent authorities, sponsors and drug regulatory departments in accordance with the regulations and time. Key researchers conduct a cumulative review of all adverse events on a regular basis and, if necessary, convene a researcher meeting to assess the risks and benefits of the study. Double-blind trials can be carried out urgently if necessary to ensure the safety and rights and interests of the subjects; low-risk studies will arrange independent data monitors to monitor the research data. the high-risk study will establish an independent data security monitoring committee to monitor the accumulated security data and validity data to make recommendations on whether to continue the research.

The form of reporting of the research results

After statistical analysis and summary of the research results, it will be reported in the form of journal papers, conference abstracts, conference speeches and so on.

Ethics of clinical research

Clinical research will follow the relevant provisions such as the Helsinki Declaration of the World Medical Congress. Before the start of the study, the clinical study will not be carried out until the program is approved by the Ethics Committee. Before each subject enters this study, the researcher has the responsibility to fully and comprehensively introduce the purpose, procedure and possible risks of this study to the subject or his legal guardian, and to sign a written informed consent form. Subjects should be informed that they have the right to withdraw from this study at any time, and informed consent should be kept as clinical research documents for reference. In the course of the study, the subjects' personal privacy and data confidentiality will be protected.

Research progress

July 2024-November 2025: completion of screening and enrollment.

December 2025-November 2027: completion of follow-up.

December 2027-November 2028: exposure, article writing and contribution