Protocol

Effect of systemic inflammatory response attenuating cardiopulmonary bypass strategy reduces new ischemic/embolic lesions after acute type A aortic dissection surgery: the sirA-CPB randomized clinical trial.

Study code: 202606087

Promoter: Lian Duan, Xiangya Hospital, Central South University

Version: 2.0 (2026-04-01)

1. SUMMARY

1.0. Identification of the promoter.

Lian Duan, Xiangya Hospital, Central South University

1.1. Title of the study.

Effect of systemic inflammatory response attenuating cardiopulmonary bypass strategy reduces new ischemic/embolic lesions after acute type A aortic dissection surgery: the sirA-CPB randomized clinical trial.

1.2. Study code.

202606087

1.3. Local principal investigator.

Lian Duan, Xiangya Hospital, Central South University

1.4. Centres where the study will be performed.

Xiangya Hospital, Central South University

1.5. Principal objective.

To reduce the incidence of new ischemic/thrombosis lesions (nITLs) after type A acute aortic dissection (TAAAD) surgery patients requiring extracorporeal circulation (cardiopulmonary bypass, CPB) by 15% (from 45% to 30%) in the first postoperative month, by using non-pharmaceutical systemic inflammatory response attenuating CPB (sirA-CPB) strategy.

1.6. Study design.

Prospective, randomized, single-blind controlled study. Patients requiring sirA-CPB strategy who require TAAAD surgery are eligible for inclusion in the study. Those who meet the inclusion criteria and sign informed consent will be randomly assigned through a block randomization program [1], to one of the two treatment arms:

sirA-CPB: Maintain mean artery pressure (MAP) 65-100 mmHg during the whole CPB period, reinfusion shed blood after adsorption, limiting air-blood contact, pulsatile mode and no ultrafiltration unless necessary.

 STANDARD-CPB: conventional CPB without intervention.

1.7. Disease or disorder under study.

Patients who require TAAAD open surgery and who require CPB with a planned duration of more than 120 minutes.

1.8. Study population and number of subjects.

Patients who require TAAAD surgery and who require CPB with a planned duration of more than 120 minutes. A total sample size of 270 patients will be required: i.e., 135 patients in each arm of the study.

1.9. Timing.

- Date of inclusion of the first patient: December 2026.

- Date of inclusion of the last patient: December 2029.

- Date for publication of results: December 2030.

1.10. Source of funding.

None.

2. ABBREVIATIONS.

AE: adverse event.

CEIC: clinical research ethics committee.

CPB: cardiopulmonary bypass.

CRP: C-reactive protein.

CRRT: continuous renal replacement therapy.

CS: cardiac surgery.

DVT: deep vein thrombosis

EBE: excessive bleeding events

IL-1β: interleukin 1β

IL-6: interleukin 6

IL-10: interleukin 10

INR: international normalized ratio

ITEs: ischemic/thromboembolic events

MAP: mean artery pressure

MI: myocardial infarction

MODS: multiple organ dysfunction syndrome

NETs: neutrophil extracellular traps

NIRS: near-infrared spectroscopy

nITL: new ischemic/embolic lesions

PE: pulmonary embolism

sirA-CPB: systemic inflammatory response attenuating cardiopulmonary bypass

SIRS: systemic inflammatory response syndrome.

TAAAD: type A acute aortic dissection

TEE: transesophageal echocardiography

TNF-α: Tumor necrosis factor-α

3. Rationale and hypothesis of the study.

Aim of the project.

The body enters an acute systemic inflammatory state after major cardiac surgeries such as acute type A aortic dissection, which can promote coagulation overactivation and thrombus formation, leading to various ischemic/thromboembolic complications. Routinely administering early postoperative anticoagulants affects the normal coagulation pathway and leads to excessive bleeding. This study aims to reduce postoperative ischemic/thromboembolic lesions through non-pharmaceutical sirA-CPB strategy with a novel anti-inflammatory approach without affecting the coagulation process.

Background.

Type A acute aortic dissection (TAAAD) is a life-threatening condition, which often requires emergency surgery to prevent major bleeding caused by rupture, while insufficient attention paid to its embolic morbidities[2]. Previous literature has defined multiple types of morbidities based on separate organs or systems, such as stroke, myocardial infarction, renal failure, pulmonary embolism, etc[3,4]. We wonder almost thrombosis of these morbidities, few studies have viewed them as a whole imbalance in coagulation state, while hemorrhage in surgical and non-surgical areas is usually classified as the same category of bleeding. Recent studies showed that TAAAD patients who survived 3 months after surgery, the 2-year and 10-year observed mortality were >25%, >40%, respectively[5]. These data are much higher than the 9.8-10.6% hospitalization mortality[6,7]. Although postoperative anticoagulation is routine in clinic, consensus emphasize the monitoring connective tissue disease progression, long-term lifestyle habits and medication[8], yet a perioperative one is difficult to find[9,10]. TAAAD as a typical disease, which is necessary to be observed the detailed situation of ischemic/thromboembolic events (ITEs) [11], in order to determining perioperative risk factors, whether they can be regulated, preparing for standardized perioperative ITEs prevention protocol in the future.

Current state of scientific/technical knowledge.

The mechanisms by which CPB causes systemic inflammatory response syndrome (SIRS) have been widely studied.

The contact of blood with non-endothelial surfaces (in the CPB circuit) activates various protein systems (contact, intrinsic and extrinsic pathways, fibrinolysis and complement) and cellular systems (endothelial cells, lymphocytes, monocytes and platelets) producing what is called a systemic inflammatory response syndrome (SIRS).

The diagnostic criteria for SIRS are meeting two or more of the following four criteria: temperature>38℃ or <36℃; heart rate >90/min; respiratory rate >20/min or $PaCO_2$<32 mmHg; white blood cell count>12000/mm^3 or <4000/mm^3 or >10% immature bands[12].

SIRS can cause hemodynamic alterations such as vasodilation and loss of effective volume due to permeability disorder and leading to organ ischemia. The elevation of cytokines [interleukins 1β, 6, 10 (IL-1β, IL-6, IL-10) and tumour necrosis factor alpha (TNF-α)] is a constant and early finding; the concentrations of these cytokines correlate with ischemia time during cardiac surgery (CS) and organ damage; and TNF-α concentrations increase after release of the aortic clamp. The coagulation cascade is activated, leading to tissue damage. The complement is activated very early (C3a is detectable two minutes after CPB initiation) and its levels are related to the duration of CPB. It should be stressed that complement plays a crucial role as the initial stimulus in the activation of the inflammatory response to contact with foreign surfaces.

With the aim of avoiding the adverse effects of CPB, surgical techniques have been developed with minimal periods of CPB or even without any CPB at all.

However, due to the complex surgical condition of many patients undergoing CS, the interventions are usually performed with CPB, and many of them with prolonged periods. In these patients with CPB, various therapeutic strategies have been tried (corticosteroids, bicarbonate,

statins, nitric oxide, ulinastatin, leukapheresis, hemofiltration, etc.) aimed at minimizing the inflammatory response and thus reducing SIRS, but none of them have managed to demonstrate a clear improvement in the patient's clinical evolution.

Previous studies on reducing inflammation in CPB were taken by two main measures: first, pharmacological anti-inflammatory agents such as hormones, heparin, serine protease inhibitors, antibiotics, vitamins, free radical scavengers, etc. Second, optimizing CPB strategy, which include shortening the CPB period, reducing gas-blood contact, reducing the suction or allogeneic blood products, ultrafiltration, hemoadsorption, washing shed blood or disposal, etc[13].

Shortening the period and closed CPB physically reducing the gas-blood contact duration and area, which state no benefits of closed CPB (or minimally invasive extracorporeal circulation MiECC) in the latest adult CPB guidelines in 2025, but there is a recommendation for "minimally invasive CPB measures" because a meta-analysis of 42 RCTs did not confirm its advantages in mortality and protection of vital organs (heart and kidney). However, it is acknowledged that the incidence of postoperative arrhythmias in the minimally invasive group is lower than that in the traditional CPB group, possibly due to improving cellular microstructural integrity by reducing inflammatory response[14].The recommended MAP in guidelines has always been 50-80 mmHg during CPB, mainly based on previous randomized controlled trials: There was no significant difference in postoperative cardiovascular, cerebrovascular, and renal complications, cognitive dysfunction between the high (80-100 mmHg) and low MAP (50-60 mmHg) groups[15,16]. However, these studies mainly were coronary artery bypass graft cases, and rarely aortic dissection with hypertension. In this study, we raised the MAP to 65-100 mmHg, mainly considering the pathophysiological characteristics of the dissection and closing to physiological blood pressure need. The inflammatory indicators of aspiration blood during surgery are higher than normal. Discarding blood can alleviate the inflammatory response, but it can increase allogeneic transfusion. Therefore, reducing the inflammatory response before reinfusion may be beneficial.

The innovation of this study lies in its antithrombotic approach from the perspective of reducing inflammation, without interfering normal coagulation pathways, so adverse reactions such as excessive bleeding caused by previous antithrombotic drugs or embolism caused by inadequate antithrombotic standards are eliminated. The sirA-CPB strategy of in this study may reduce contact activation, complement activation, cytokine secretion, etc., which belongs to the intervention of pre coagulation mechanisms or pathways. So far, our research group has not found any relevant clinical studies published.

4. Study design.

4.1. Type of study.

Prospective, randomized, single-blind and controlled study. Patients who require TAAAD open surgery with CPB with a planned duration of more than 120 minutes will be candidates to participate in the study. Those who meet the inclusion criteria, after providing signed informed consent, will be randomized using a sequential randomization program[1] to one of the two treatment arms:

• sir-A CPB: Maintain mean artery pressure (MAP) 65-100 mmHg during the whole CPB period, reinfusion shed blood after adsorption, limiting air-blood contact, pulsatile mode and no ultrafiltration unless necessary.

• STANDARD-CPB: conventional CPB without intervention.

4.2. Study population

4.2.1. Inclusion criteria.

 Patients of both sexes over 18 years of age.

 Patients who diagnosed of TAAAD and undergone open surgery requiring CPB lasting more than 120 minutes.

 Provision of written informed consent from the participant, oral in exceptional cases and in the presence of a witness.

4.2.2. Exclusion criteria.

 Patients over 80 years old, pregnant women, individuals with tumors;

Those in a critical preoperative status (with IABP or ECMO or high-dose inotropics in the operating room, latrogenic dissection);

Those who are allergic to resin, plastic materials, or heparin; or have history of heparin induced thrombocytopenia, severe hepatic or renal dysfunction, have fever (body temperature>38℃), systemic infection or sepsis;

Those unable to sign informed consent or transfusion consent;

Those who have participated in other blood related clinical trials.

4.2.3. Criteria for withdrawal among patients included in the trial.

If a patient decides to withdraw from the study, no new data will be added to the database and, at the patient's request, all identifiable samples previously stored will be destroyed.

A patient may be removed from the study when the promoter or investigators of the study consider it appropriate, either for safety reasons or due to any adverse event that occurs associated with the device under study, or because promoter or investigators consider that she/he is not complying with the procedures established.

Cases where CPB duration is less than 60 minutes, or allergies occur during intraoperative infusion of allogeneic blood products, protamine, and other coagulation related drugs, or the procedure is cancelled after inclusion should be eliminated.

4.3. Description of the study.

Patients who meet the eligibility criteria described in previous sections will be invited to participate in the study upon admission to the cardiac surgery ward. After providing signed informed consent, patients will be randomly allocated to one of the two treatment arms.

In patients randomized to the sirA-CPB arm (Figure 1B):

During the preparation and priming of the CPB, a venous filter and hemoadsorption device will be primed and connected to the CPB circuits. All the venous drainage will pass through the venous filter to remove gas and emboli and avoiding air-blood contact to the reservoir. A bypass was set between the blood reservoir and the centrifugal pump head. The hemoadsorption device was installed in the left and right cardiac suction tubes, and the shed blood was returned to the blood reservoir. During the bypass period, venous blood is drawn directly from the bypass to the centrifugal pump head, reducing the area and time of gas-blood foreign body contact between the blood and the blood reservoir. The shed blood was sucked back through the hemoadsorption device to the reservoir and reinfusion into the circuits. Closely cooperate with the surgical department to minimize the duration of circulatory arrest and CPB. Other measures such as organ protection, medication, and blood product transfusion are the same as those in the standard CPB group. The flow, pressures and alarms of the venous filter and hemoadsorption device will be controlled by the Stockert S5 system.

The ultrafiltration is closed. If the patient's clinical situation requires hemoconcentration (the Hematocrit<20% or hypoxia evidence), ultrafiltration can be performed to remove fluid.

Maintaining MAP 65-100 mmHg by flow increase, pulsatile mode, hemoconcentration, RBC transfusion, and cooling.

In patients in the standard CPB group (Figure 1A):

Blood samples and all CPB circuits variables will be collected and recorded without modifying standard CPB practice.

The standard CPB group underwent TAAAD surgery using traditional CPB strategy, including centrifugal pump head, membrane lung (with blood reservoir and oxygenator), ultrafiltration, hemoadsorption device, filter, and priming of circuits. During the bypass period, MAP was maintained at 50-80mmHg according to adult CPB guidelines, with a flow rate of 2.2-2.4L/min. Low temperature flow reduction or circulatory arrest was performed in conjunction with surgery. Selective perfusion of the brain or other important organs during circulatory arrest was performed, and myocardial protection measures such as cardiac arrest decompression were implemented. Uniform cooling and rewarming were performed, pH acid-base electrolyte balance was maintained, and hemodynamic stability was maintained intermittently with fluid replacement or inotropics. Ultrafiltration was used to concentrate circulating blood, and cell saver was used for intraoperative autologous blood. The infusion criteria of allogeneic blood products (red blood cells, plasma, platelets, cryoprecipitate) is based on bleeding status, oxygenation metabolism indicators, and the results of thromboelastography.

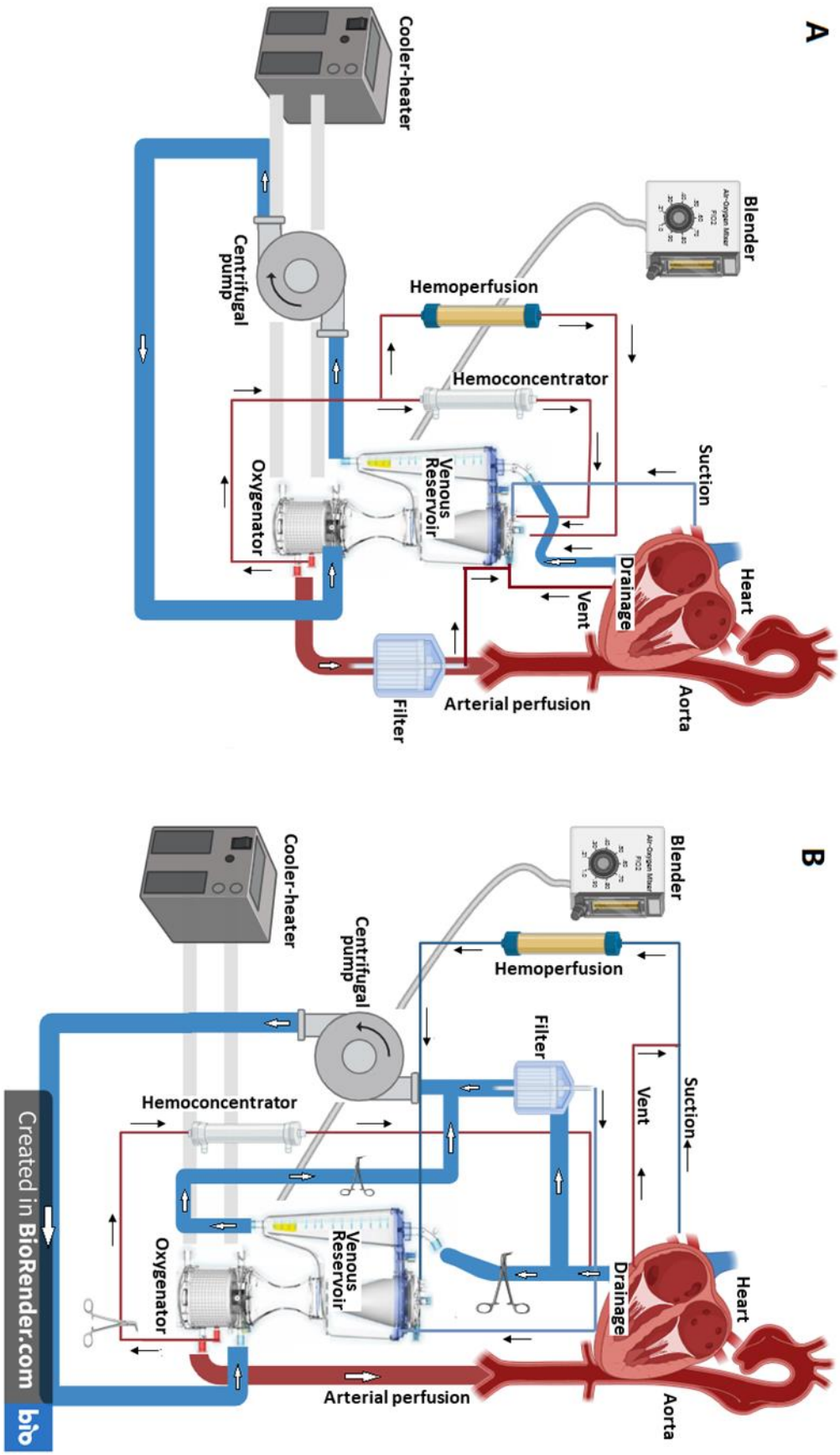


Figure 1 Diagram of circuits installation for the standard CPB group and the sirA-CPB group

4.3.1. Concomitant treatments.

During this trial, all concomitant and supportive pharmacological treatments that the medical team considers necessary may be used in accordance with standard clinical practice.

4.4. Selection of the control group.

The study is randomized, with a total sample size of 270 patients. The control group will comprise 135 patients.

4.5. Sample size.

Using superiority test for the ratio of two proportions, the incidence of acute type A aortic dissection postoperative ischemic/thromboembolic events in the two largest cardiac centers in China ranged from 26.4% to 32.68%[3,4]. Based on our previous research[17], we estimated the incidence of new ischemic/thromboembolic lesions (nITI) to be 45%. The intervention group was considered to be a 15% absolute reduction, which was considered clinically and statistically significant difference with 90% power ($\alpha = 5\%$). The sample size was calculated to be 121 cases per group, and considering 10% dropout cases, each group required 135 cases.

4.6. Statistical analysis.

A database will be created for all the variables collected to aid patient analysis and monitoring. The statistical analysis will be carried out by a statistician who is not a member of the research team. Categorical variables are summarized as frequencies and percentages, while continuous variables are expressed as the mean ± SD when the data were normally distributed, and as the interquartile range [P50 (P25, P75)] when the data were nonnormally distributed. The Mann–Whitney U-test, the Student's t test will be used for continuous variables and Chi-squared test for categorical variables. To assess whether there are differences between groups in the variables that are recorded repeatedly, an ANOVA for repeated measures will be used. A *P* value <0.05 was considered significant. Data analysis was performed using IBM SPSS 26.0 (SPSS Software, IBM Corp., Armonk, NY, USA).

5. Variables.

Inflammatory response parameters (blood):

neutrophil extracellular traps (NETs), IL-1β, IL-6, IL-10, TNF-α,

Conventional analytical parameters (blood):

blood count, fHb, pH value, FiO_2, PaO_2, Glucose, lactate, sodium, potassium, albumin, bilirubin, transaminases, creatinine, CRP, procalcitonin and coagulation (fibrinogen, D-dimer, INR and prothrombin time) will be measured following the usual monitoring protocol.

Hemodynamic parameters:

Temperature, heart rate, respiratory or oxygenation parameters, near-infrared spectroscopy (NIRS), blood pressure, and central venous pressure were continuous monitored during surgery. The need for vasopressor and inotropic drugs and the doses required will also be recorded.

TEE related hemodynamic parameters will be measured to observe the dissection involvement, pericardial tamponade, aortic valve regurgitation, missed diagnosis of malformations, true lumen catheterization guidance, preoperative and postoperative cardiac function, and the patency of artificial grafts.

Safety and effectiveness of hemoadsorption

Randomly select 5 cases from each group, three-way connections in the front and back pipelines of the hemoadsorption will be installed. Samples 5 minutes after pump on and 5 minutes before pump off, before and after passing through the hemoadsorption will be collected: ①The difference in platelets count, albumin concentration, and fibrinogen concentration before and after hemoadsorption device is less than 10% as the qualified indicators for the safety evaluation, as

well as any equipment failure; ②The difference in concentrations of IL-1β, IL-6, IL-10, and TNF-α in the samples before and after the hemoadsorption as the effectiveness indicator.

Clinical-demographic data:

Age, sex, BMI, relevant clinical history, type of surgery, surgical times, CPB times, surgical complications, consumption of blood products, Excessive bleeding events (EBE): the occurrence of one or more of the following five components during the procedure through hospital discharge: fatal bleeding; perioperative intracranial bleeding within 48 h; surgical re-exploration for the purpose of controlling bleeding; 12-h chest tube output of more than 1 L; or packed red blood cell (RBC) transfusion of more than 6 units. Collect mechanical ventilation time, hypoxia events (prone position ventilation, non-invasive ventilator ventilation, mechanical ventilation again, hydrothorax, hemothorax, pneumothorax and pneumothorax), incidence of pneumothorax and atelectasis, 24-hour drainage volume, types and volumes of allogeneic transfusions, postoperative hospitalization days with body temperature above 38 ℃ or below 35 ℃, infections, morbidities, mortalities, and total hospitalization costs.

ICU and hospital stay, clinical status at discharge and at 30 days, including survival, and ITEs [the occurrence of one or more of the following six components during the procedure through postoperative 3 years diagnosed by image positive accompanied or not accompanied by clinical symptoms: myocardial infarction (MI), ischemic stroke, ischemic spinal cord injury, deep vein thrombosis (DVT), pulmonary embolism (PE), and local arterial embolism]. Follow-up data inquiry will be conducted at 3 months, 6 months, 12 months, 2 years, and 3 years after surgery to evaluate the recovery of patient complications and long-term prognosis.

Evaluation of systemic inflammatory response

We will analyze the incidence of SIRS, pulmonary infection, and sepsis during hospitalization.

6. Outcomes.

Primary outcome:

new ischemic/thrombosis lesions (nITL)

within 30 days postoperatively

Imaging examination revealed new ischemic or embolic lesions in the non-surgical area, regardless of clinical symptoms. The non-surgical area includes one or more of the following six: brain, spinal cord, deep vein thrombosis, pulmonary embolism, heart, and peripheral arteries. Any positive findings, or more, are recorded as follows: 1. New findings: discovery time(day after surgery)+organ (heart, brain, spinal cord) name/vessel name (deep vein, pulmonary artery, peripheral artery)+range (length * width, or scattered distribution within a certain area)+symptoms (none/present)+signs (none/present).

Secondary outcomes

1.new ischemic/thrombosis events，nITE

Within 3 years postoperatively

The composite incidence of myocardial infarction (MI), ischemic stroke, ischemic spinal cord injury, deep vein thrombosis (DVT), pulmonary embolism (PE), and local arterial embolism.

2. the incidence of myocardial infarction (MI)

3. the incidence of ischemic stroke

4. the incidence of ischemic spinal cord injury

5. the incidence of deep vein thrombosis (DVT)

6. the incidence of pulmonary embolism (PE)

7. the incidence of local arterial embolism

7. Adverse events.

The following safety variables will be recorded: treatment-related adverse events (AEs), AEs resulting in withdrawal of the intervention, serious treatment-related AEs, and death. They will be recorded on the corresponding case report form, specifying their date of appearance, duration, intensity, outcome and the assessment of causality.

The promoter will keep a record of adverse events that occur during the clinical trial, beginning at the moment the patient signs the informed consent.

7.1. Definition of terms.

Adverse event (AEs):

Any harmful incident to health in a patient or subject of a clinical trial administered medication, even if there is no causal relationship with the said medication. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or illness temporally associated with the use of a medicinal product in the research setting, whether or not it is related to the product.

AEs can be characterized based on a series of attributes:

- Causation: if a causal relationship with a medication is suspected, it will be considered an adverse reaction.

- Severity: depending on the presence of corresponding criteria.

- Intensity: due to the magnitude of the event.

- Probability: whether it is expected or not.

Adverse reaction (AR):

Any harmful and unintended reaction to a medication administered in a research setting, regardless of the dose administered. Unlike an AE, in the case of an AR a relationship is assumed to exist between the drug and the event.

Serious adverse event (SAE) and serious adverse reaction (SAR).

Any adverse event or adverse reaction that, at any dose:

- May cause death.

- Is potentially life threatening (i.e., in the opinion of the investigator, the patient at the time of the AE is at real risk of death).

- May require hospitalization or prolong an existing hospitalization.

- May cause a persistent or significant disability/incapacity.

- Is a congenital anomaly/birth defect.

Suspected adverse events or adverse reactions that are considered important from a medical point of view, even if they do not meet the above criteria, will be treated as serious, including important medical events that require intervention to prevent one of the consequences described above.

Similarly, all suspicions of transmission of an infectious agent through a medication will be reported as serious.

For each SAE and SAR, the investigator must provide information on the intensity, start and end dates, relationship to the study drug, action taken in relation to the study drug, and outcome.

Serious adverse events must be urgently reported to the promoter of the study, within a maximum period of 24 hours.

The following will not be reported as SAE:

- Hospitalizations or extensions of hospitalization required for protocol procedures.

- Hospitalizations or extensions of hospitalization that are part of the center's routine.

- Hospitalizations planned before the start of the study, due to pre-existing pathologies, which do not represent a worsening of the previous condition.

Unexpected serious adverse reaction (USAR).

Any SAR whose nature, severity or consequences do not correspond to the information on the medicine in the investigator's manual in the case of an investigational medicine not authorized for marketing, or on the technical information sheet in the case of an authorized medication.

7.2. Evaluation of adverse events and reactions.

Evaluation of intensity.

When the assessment of the intensity of the AE/AR is based on medical judgment, it will involve the participation of a medically qualified investigator.

The intensity of AEs will be qualified using the following definitions:

a) Mild: the sign, symptom or event is discernible but is well tolerated.

b) Moderate: the discomfort is enough to interfere with usual activity and may require intervention.

c) Intense: incapacitates the patient and curtails normal daily activities or significantly affects clinical status and requires intervention.

d) Potentially fatal: Immediate risk of death.

Evaluation of causality.

A medically trained investigator should assess the relationship of any AE/AR (including SAEs/SARs) to the use of the study drug as unlikely, possible or a probable, based on the available information and following these guidelines:

a) Unlikely: there is no temporal association; the cause of the event has not been identified, or the drug, biological product or medical device cannot be implicated based on the available information;

b) Possible: temporal association, although the cause is likely to be different; however, the involvement of the drug, biological product or medical device cannot be ruled out based on the available information;

c) Probable: temporal association; It is possible that the cause is different, but the information available suggest that this is unlikely.

7.3. Notification of severe adverse events.

Any SAR, regardless of the presence or absence of a causal relationship, must be reported immediately to the promoter within one working day, by Tel to +8689753004.

8. Terminal point.

The patient completed follow-up or died before completing follow-up;

SAE occur, or the supervising physician requests to stop the study;

During the experiment, the patient or their family members requested to terminate the experiment.

9. Ethical aspects.

The study has been evaluated by the CEIC of Xiangya Hospital (number 202606087). In all cases, informed consent will be requested from participating patients (in written form, or provided by the legal representative).

10. Test records and data storage.

During the trial and after its completion (even if premature), the investigator will keep copies of all documents and records related to the trial. This documentation will consist of protocols, case report forms and other instruments, reports of AEs, original data from the participants, correspondence with health authorities and with the CEICs, and consent documents.

11. Publications.

After the completion of the trial and analysis of the results, the promoter undertakes to publish the results, whether they are positive or negative.

The principal investigator has the right to publish the results of the trial or to present them publicly.

The publications or originals will not contain confidential information, and will be limited to new discoveries and interpretations of scientific evidence.

12. Confidentiality.

The principal investigator of the trial and the collaborating team will ensure that the confidential nature of the personal data of the subjects participating in the clinical trial is upheld in accordance with Chinese Personal Information Protection Law/2021.

Subjects included in the clinical trial will be identified by a numerical code that will be allocated once the informed consent document is signed. The principal investigator will be responsible for keeping an updated list of subjects that will include the link between the numerical code and the patient's personal identifying data (name and surname, medical record number, affiliation/contact data, date of inclusion. and date of signing the informed consent document).

Only members of the research team, the monitor, the corresponding Health Authorities and the center's CEIC will have access to this information.

This numerical code given to each subject participating in the clinical trial will be used to identify all those documents in paper or electronic format related to the clinical trial (i.e., data collection form, the trial management database for and descriptive analysis, etc.)

In accordance with the regulations, the right of participating subjects to access, rectify, cancel or oppose the recording of their data collected on the occasion of this clinical trial will be guaranteed.

13. Summary table

Table 1 Evaluation Content Schedule

Items	**Selection& treatments**		**Follow up**									
Time points	**Selection S pre**	**S in**	**S po24h**	**S po2d**	**S po3d**	**S po7d**	**S po28d**	**S po3m**	**S po6m**	**S po12m**	**S po2y**	**S po3y**
windows	**-14d~0d**	**0d**	**0-24h**	**1-2d**	**2-3d**	**7d±3d**	**28±7d**	**3m±1m**	**6m±1m**	**12m±1m**	**2y±3m**	**3y±3m**
Informed consent	**X**											
Inclusion and exclusion	**X**											
history	**X**											
Demographic data	**X**											
Signs	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**				
EuroScore	**X**											
CTA	**X**					**X**	**X**	**X**	**X**	**X**	**X**	**X**
TTE	**X**					**X**	**X**	**X**	**X**	**X**	**X**	**X**
TEE		**X**										
ECG	**X**					**X**	**X**	**X**	**X**	**X**	**X**	**X**
Blood data: regular	**X**		**X**	**X**	**X**	**X**						
Blood data: inflammatory	**X**		**X**	**X**	**X**	**X**						
Blood data: coagulation	**X**		**X**	**X**	**X**	**X**						
NIRS		**X**										
Hemodynamic data		**X**										
Bleeding & Transfusions	**X**	**X**	**X**	**X**	**X**	**X**						
Special drugs	**X**	**X**	**X**	**X**	**X**	**X**						
AEs or SAEs		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**

morbidities			**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Device defects		**X**										
Health Quality of Life Survey Questionnaire	**X**						**X**	**X**	**X**	**X**		

S pre: preoperative; S in: intraoperative; S po: postoperative; CTA, computed tomography angiography; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; ECG, electrocardiogram; NIRS, near-infrared spectroscopy; AEs, adverse events; SAEs, severe adverse events

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