

INFORMED CONSENT FORM

Project Title: Traditional Approach versus Flow Diverter for Unruptured Intracranial Wide-Neck Bifurcation Aneurysms: A Prospective International Multicenter Randomized Controlled Study (FD-BWA Study)

Protocol Version and Date: v1.0 2025.12.16

Informed Consent Form Version and Date: v1.0 2025.12.16

Sponsor: Nanfang Hospital, Southern Medical University

Dear Subject:

We invite you to participate in a study that has been reviewed and approved by the Medical Ethics Committee of Nanfang Hospital, Southern Medical University. Before you decide, we want you to understand why this study is being conducted and what it will require of you. Your participation in this study is entirely voluntary, meaning you may choose to participate or not. The research team will explain this information sheet to you and answer any questions you may have.

If there is anything you do not understand, please ask us. You are welcome to discuss this study and the information contained in this document with your partner, family, friends, and physician, or other people close to you.

After you have considered all the information related to this study and all your questions have been answered, if you agree to participate, the research team will ask you to sign and date the informed consent form (at the end of this document) before any study-related procedures are performed.

I. STUDY BACKGROUND

The background of this study is: The population prevalence of intracranial aneurysms is 3.2%. Rupture leading to subarachnoid hemorrhage is highly harmful, with a total mortality rate of 28%–67%. Vascular bifurcations are prone to forming intracranial aneurysms, accounting for 26.0%–64.7% of all intracranial aneurysms, and are highly prone to rupture, representing approximately 60% of all ruptured intracranial aneurysms. Currently, treatment for bifurcation intracranial aneurysms mainly includes surgical clipping and endovascular therapy. Although surgical clipping has a relatively definite effect, it is associated with greater trauma and longer postoperative recovery. With the development and application of new endovascular devices in recent years, endovascular therapy has gradually become the mainstream treatment choice for bifurcation intracranial aneurysms. The main endovascular treatment modalities are stent-assisted coil embolization and flow diverter implantation. Coil embolization often requires multiple stents, and because the use of multiple devices occupies more space in the parent artery, it may easily cause ischemic complications and has a higher recurrence rate. Compared with traditional endovascular approaches, placing a flow diverter at a bifurcation may be technically easier and has an extremely

low recurrence rate. However, the basic design of flow diverters makes their use at bifurcation sites controversial, because flow diverter stents covering the bifurcation vessels may lead to hypoperfusion in the corresponding vascular territories and symptomatic ischemia. Currently, which of these two treatments is better remains unclear and is debated. Therefore, this study aims to comprehensively investigate the efficacy of traditional stent-assisted coiling versus flow diverter implantation in intracranial wide-neck saccular bifurcation aneurysms in terms of complications and recurrence rates.

II. STUDY OBJECTIVE

The objective of this study is to verify whether the traditional approach (stent-assisted coiling) for unruptured intracranial wide-neck bifurcation aneurysms is superior to treatment with the Pipeline™ flow diverter (a flow-diverting device), and to investigate whether flow diverters increase postoperative complications in wide-neck saccular bifurcation aneurysms.

III. INTRODUCTION TO THE STUDY PRODUCT (OR DIAGNOSTIC/TREATMENT TECHNOLOGY)

Surgical procedure:

Traditional approach (stent-assisted coiling): The patient is placed in a supine position. After satisfactory general anesthesia, the right groin area is routinely disinfected and draped. The right femoral artery sheath is replaced. Systemic heparinization is administered, followed by continuous pressurized infusion. A Terumo guidewire is used with a long sheath and a multifunction catheter, and the long sheath is advanced to the left vertebral artery. A micro-guidewire and microcatheter are used to selectively catheterize the left posterior cerebral artery segment, and then the microcatheter is advanced into the aneurysm. Through the microcatheter, one coil is semi-deployed to form a framing coil, then one stent is deployed through the stent catheter to cover the aneurysm neck. After the first framing coil is detached, several additional coils are sequentially deployed to embolize the aneurysm. Follow-up angiography shows no opacification of the aneurysm, parent artery patency, and no intracranial hemorrhage. The microcatheter and stent catheter are withdrawn. At the end of the procedure, the right femoral artery sheath is removed, the right femoral artery puncture site is closed with a vascular closure device, and a compression device is applied for hemostasis.

Flow diverter approach: The patient is placed in a supine position. The right groin area is routinely disinfected and draped. Local infiltration anesthesia is applied at the puncture site, and the right femoral artery is punctured. A vascular sheath is inserted, systemic heparinization is administered, and continuous pressurized infusion is started. With the assistance of a Terumo guidewire and a multifunction catheter, a long sheath is advanced to the origin of the right internal carotid artery, and an intermediate catheter is advanced inside it to the petrous segment of the right internal carotid artery. Cerebral angiography is performed, and after a suitable working angle is obtained, a stent catheter is advanced to the right middle cerebral artery segment with micro-guidewire assistance. Manual injection shows no hemorrhage, confirming

the true lumen. After calibration and measurement, one flow diverter stent is deployed to cover the aneurysm neck. Follow-up angiography shows good stent position, good wall apposition, parent artery stenosis unchanged from pre-operatively, and CT shows no intracranial hemorrhage. The microcatheter and guide catheter are withdrawn, and the femoral artery puncture site is sutured with a closure device and a compression device is applied.

IV. STUDY PROCEDURES

1. How many people will participate in this study?

Approximately 266 people will participate in this study conducted at 12 different domestic and international research institutions/medical institutions. Approximately 50 people will participate at this institution.

Study Steps

- Before the study begins:

To determine if you are suitable to participate, the following procedures will be performed during screening:

- Collection of your demographic characteristics and vital signs
- Physical examination
- Inquiry about your medical history and concomitant medications
- Collection of blood and urine samples for laboratory tests
- If you are a woman of childbearing potential, a pregnancy test will be performed. You must have a negative pregnancy test result to participate in this study.

The results of the screening examinations and related questions will help the researchers decide whether you can continue with this study. If these tests indicate that you are suitable to participate, the researchers will notify you to schedule a visit as soon as possible. If you do not meet the relevant criteria, you cannot continue in this study, and the researchers will inform you of the result promptly.

Baseline Period

If the researchers confirm that you meet the criteria to join this trial, you will be enrolled and will receive interventional treatment for the aneurysm in a randomized (similar to drawing lots) manner. The following procedures will be performed during this visit:

- Reconfirmation of your eligibility to participate in this study
- Obtaining randomized study treatment assignment (stent-assisted coiling / flow diverter implantation)
- Assignment of a unique identification number for your participation in this study
- Assignment to either the experimental group (flow diverter implantation) or the control group (stent-assisted coiling) based on the randomization result

- Physical examination and collection of vital signs
- Preoperative relevant examinations: including DSA, perfusion CT/MR, moyamoya ultrasound, etc.

Treatment Period

You will be randomly assigned to the experimental group or the control group. During this period, the researchers will observe the actual effect of your receiving flow diverter implantation or control stent-assisted coiling. To ensure that your clinical manifestations are accurately recorded and assessed, you will need to cooperate in completing the following procedures:

- During the flow diverter implantation surgery, a flow diverter stent will be implanted, covering the branching vessels.
- Physical examination and collection of vital signs
- Routine imaging examinations, including DSA, cranial CT/MR, etc.

Follow-up Period

After you complete this phase of visits, you will generally be considered to have completed the entire study. The researchers will perform the following procedures during this period:

Follow-up time points follow routine clinical practice. Cerebral angiography (DSA) follow-up will be performed at 1, 2, and 5 years after surgery. This will be completed during hospitalization.

What examinations and assessments will be performed in this study?

After providing written informed consent, you will undergo certain tests, examinations, and procedures during this study. If you have any concerns about any of these tests, please discuss them with the study physician.

Regarding the tests and procedures of this study, we would like to explain the following to you:

- **Medical history:** The study physician will ask you questions to understand any current or past diseases, as well as surgical history.
- **Demographic data:** The study physician will collect personal information about you, such as date of birth, ethnic background, work information, etc.
- **Physical examination:** The study physician will perform a medical examination of your body to evaluate all or part of the following body systems: head, eyes, ears/nose/throat, chest, lungs, heart, abdomen, bones, skin, neck, and nervous system.
- **Height and weight:** Your height and weight will be measured.
- **Vital signs:** The study physician will measure your blood pressure, heart rate, body temperature, and respiratory rate.
- **Blood draws:** During this study, you will undergo two blood draws (preoperative and postoperative), each of approximately 5 ml. Blood samples

will be collected for the following items: complete blood count, lipid panel (4 items), liver function, and coagulation function.

- **Imaging:** Cerebral angiography (DSA), cranial CT/MR, etc.

How long will this study last?

This clinical study will last approximately 5 years (approximately 6 visits in total), divided into preoperative examination, surgical treatment, and follow-up visits at 6 months, 1 year, 2 years, and 5 years. During participation in this study, you must return for visits at 6 months, 1 year, 2 years, and 5 years to complete the 3rd to 6th visits.

You may withdraw from the study at any time without any penalty or loss of benefits to which you are otherwise entitled. However, if you decide to withdraw from this study during the course, we encourage you to discuss it with your physician first. For safety reasons, a related examination may be performed after withdrawal.

V. RISKS AND DISCOMFORTS

The primary goal of the research team is always to ensure your safety. However, intraoperative flow diverter implantation may cause complications, including ischemic events: clinical symptoms resulting from embolism of important vessels due to various causes, or cerebral tissue hypoperfusion; hemorrhagic events: aneurysm rupture caused by various factors; as well as rare or currently unknown side effects. During this study, we will use blood tests, urine tests, physical examinations, and imaging examinations to closely monitor your heart, kidney, and liver function, as well as other body systems.

If you feel that your health status has worsened in any way, or if you experience unexpected or unusual symptoms, you should contact the research team immediately, even if you think these issues are not caused by the study procedures.

1. Risks and discomforts associated with study procedures, such as:
 - **Blood collection:** Blood samples will be collected through a small needle inserted into a vein in your arm or hand. You may experience discomfort and/or soreness during insertion and withdrawal of the needle, and minor bruising may occur. In rare cases, the vein may become blocked, or minor nerve damage may occur, causing numbness and pain. If this occurs, it will subside over time.
 - **Cerebral angiography (DSA) :** DSA involves inserting a catheter into an artery, then injecting 3000–5000 units of heparin through the catheter to achieve systemic low-dose heparinization to prevent catheter clotting. The catheter tip is inserted into the ostium of the artery to be examined, and the catheter hub is connected to a pressure injector for rapid contrast injection. Before contrast injection, the flat-panel detector is aligned with the area to be examined. Images are captured at a rate of 1–3 frames per second or more for 7–10 seconds before and during the entire contrast injection. The subtracted vascular

images are processed at the console. During local anesthesia, pain and discomfort may occur at the anesthesia site.

VI. WHAT ARE THE BENEFITS OF PARTICIPATING IN THE STUDY?

Your participation in this study may reduce the risk of rupture of your intracranial aneurysm and ultimately achieve cure. We hope that the information obtained from your participation in this study will help in the development of new therapies for patients with this disease in the future.

VII. ALTERNATIVE TREATMENT OPTIONS

In addition to participating in this study, you have the following options:

- Receiving routine clinical care, i.e., undergoing stent-assisted coil embolization using internationally accepted surgical techniques;
- Conservative treatment to control clinical symptoms and reduce possible bleeding risk.

You may discuss your disease and its possible outcomes with the study physician at any time and decide which option is best for you.

VIII. USE OF STUDY RESULTS AND CONFIDENTIALITY OF PERSONAL INFORMATION

At the conclusion of the study, we will prepare a report and send it to the government regulatory agency: the Guangdong Provincial Health Commission. The results of this study may also be published in journals or presented at meetings, but they will not contain any information that could identify you.

To ensure privacy, records or samples released for research purposes will not be accompanied by your name or other identifiers. Instead, your information will be identified only by a code. Only the study physician and authorized personnel will be able to link this code to your name through a list that will be securely stored at the study site.

If necessary to verify that the study is being conducted correctly, the sponsor, ethics committee, and government regulatory authorities may access your records as required. They are bound by confidentiality obligations and will not infringe upon your privacy.

You have the right to control the use and disclosure of your personal information. To the extent permitted by national law, you may request to view your medical information at any time. You have the right to access all information collected about you through the study physician and request corrections if applicable.

IX. NEW INFORMATION RELATED TO THE STUDY

During the study, if changes occur in the study procedures, new side effects are discovered, or significant circumstances arise that may affect your health or willingness to participate, the research team will notify you. The study physician will inform you immediately and discuss with you whether you wish to continue participating. If you decide not to continue, the study physician will make arrangements for your continued medical care. If you decide to remain in the study, the study physician may ask you to sign a new informed consent form.

X. STUDY COSTS, COMPENSATION, AND DAMAGES

1. Costs related to study procedures and examinations

The study device and the treatments and procedures required by the protocol are implemented in accordance with guidelines. The costs for the procedures, device, examinations, and nursing care are all covered according to local medical insurance policies, including surgical fees, complete blood count, urinalysis, liver and kidney function, cranial CT/MR, DSA, etc. These costs are borne by you.

Compensation for participation

In recognition of your contribution to this study: We will provide you with a travel subsidy of RMB 500 (for both the experimental group and the control group). All other protocol-specified treatments and procedures are borne by you.

XI. RIGHTS AND RESPONSIBILITIES OF THE SUBJECT

1. Your rights

Your participation is voluntary throughout the entire study. If you decide not to participate, it will not affect the other treatments you are entitled to receive. If you decide to participate, you will be asked to sign this written informed consent form. You have the right to withdraw from the trial at any stage without discrimination or unfair treatment, and your medical treatment and rights will not be affected.

Your responsibilities

You need to provide truthful information about your medical history and current health status; inform the study physician of any discomfort you experience during this study; any experimental treatment may pose risks to you or your fetus, so you and your partner should avoid any activities that could lead to pregnancy during the study. If you become pregnant during the study, please notify your study physician immediately.

XII. CONTACT INFORMATION

If you have any questions related to this study, please contact the investigator/physician.

If you have any questions regarding your rights/interests, or if you wish to report difficulties, dissatisfaction, or concerns encountered during participation, or if you

have suggestions or opinions about the study, please contact the hospital's Medical Ethics Committee.

SUBJECT SIGNATURE PAGE

Informed Consent Declaration

I have been informed of the purpose, background, procedures, risks, and benefits of this study. I have had sufficient time and opportunity to ask questions, and I am satisfied with the answers.

I have also been informed of whom to contact if I have questions, wish to report difficulties, concerns, suggestions about the study, or need further information, or if I wish to provide assistance for the study.

I understand that I may choose not to participate in this study or may withdraw at any time during the study for any reason without penalty. Furthermore, the investigator has not used deception, enticement, coercion, or other means to force my consent to participate.

I understand that if my condition worsens, if I experience a serious adverse reaction, or if my study physician believes that continuing participation is not in my best interest, he/she may decide to withdraw me from the study. The sponsor or regulatory authorities may also terminate the study without my consent. If this occurs, the physician will notify me promptly and discuss other options with me.

I have read this informed consent form and agree to participate in this study.

I will receive a copy of this informed consent form, which includes my signature and the investigator's signature.

Subject's signature: _____ Date: _____ Contact
phone: _____

Legal representative's signature: _____ Date: _____
Contact phone: _____

(Note: If the subject lacks capacity or has limited capacity, such as when enrolling vulnerable populations like mentally impaired or unconscious individuals, a legal representative must sign below.)

Impartial witness signature: _____ Date: _____
Contact phone: _____

(Note: An impartial witness signature is required only when the subject is capable of giving informed consent but is unable to read the document (e.g., illiterate, visually impaired). When the witness is informed, it is recommended that the investigator keep video footage as evidence of the informed consent process.)

I have accurately explained this document to the subject. He/she has accurately read this informed consent form, and I confirm that the subject had the opportunity to ask questions and has given voluntary consent.

Investigator's signature: _____ Date: _____

Contact phone: _____