Informed consent

We invite you to participate in a randomized controlled clinical trial of "PARIS coronary thrombosis risk score combined with D-dimer to guide antithrombotic therapy of novel oral anticoagulants in participants after acute coronary syndrome intervention" funded by the Fuwai Hospital of the Chinese Academy of Medical Sciences and the National Clinical Research Center for Cardiovascular Diseases . This study has been approved by the Ethics Committee of the Fuwai Hospital of the Chinese Academy of Medical Sciences (Tel. 010-88396281, 010-88396282). Please read the instructions carefully to understand your rights and obligations in the study and clarify the nature and risks of the study. Participation in this study is completely voluntary. Whether or not you participate in this study will not affect your treatment in the hospital and other legal rights . When the researchers explain and discuss the informed consent form with you, you can ask questions at any time and ask the researchers to explain to you what you don't understand. You have enough time to discuss with your family, friends and your doctor before making a decision.

If you are currently participating in other clinical research studies, please inform the researchers.

The project leader of this study is Yuan Jinqing , chief physician , Coronary Heart Disease Ward 1, Fuwai Hospital, Chinese Academy of Medical Sciences . The lead unit is Fuwai Hospital, Chinese Academy of Medical Sciences, and the project leader of the lead unit is Yuan Jinqing . The sponsors of this study are Fuwai Hospital, Chinese Academy of Medical Sciences, and the National Clinical Research Center for Cardiovascular Diseases .

1. Why was this study conducted?

The residual risk of thrombosis is an important factor affecting ischemic events in participants after acute coronary syndrome (ACS) intervention, and thrombin is closely related to it. Currently, domestic and international guidelines recommend anticoagulation therapy for participants with high ischemic risk. (IIb) . How to accurately identify participants at high risk of ischemia, inhibit thrombin and reduce its activity, and thus reduce ischemic events has always been a major challenge in clinical anticoagulation therapy. Identifying high-risk groups through coronary thrombosis scores and thrombosis markers, and guiding precise treatment with new oral

anticoagulants to reduce ischemic events is an important research topic at present.

This study is a multicenter, prospective, open-label, randomized controlled clinical trial. Among the ACS study participants who underwent PCI, the medium- and high-risk study participants with a PARIS coronary thrombosis score ⩾ 3 or a D-dimer ⩾ 0.28 μg/ml are planned to be included: (1) low-dose rivaroxaban is given on the basis of dual antiplatelet therapy to reduce the risk of ischemia; (2) a short course of triple antithrombotic therapy for 3 months is given to reduce the risk of bleeding caused by long-term use. The follow-up period of this study is 12 months, the primary endpoint is major adverse cardiovascular events, and the safety endpoint is BARC type 3, 5 bleeding events.

2. Why were you invited to participate in this study?

You are diagnosed with acute coronary syndrome this time, and according to risk stratification (PARIS score), laboratory tests (D- dimer), etc., you belong to the high-risk group for ischemia recurrence. Ischemic events will harm your health, and anticoagulation therapy is an important treatment for this group of people. In view of this, we invite you to participate in this study, screen you through our risk score and laboratory tests, and accurately guide short-term anticoagulation therapy, hoping to reduce the risk of ischemic recurrence.

After preliminary evaluation, you meet the inclusion criteria, including: ① confirmed ACS, 1-7 days after initial symptoms stabilize; ② age range of 18-75 years old; ③ increased D-dimer level on admission (⩾0.28 μg/ml); ④ PARIS coronary thrombosis risk score ⩾3 points; ⑤ currently receiving PCI treatment and has stopped taking non-oral anticoagulants; ⑥ There is an indication for taking dual antiplatelet drugs.

And you do not meet the exclusion criteria, including: (1) platelet level below 90 x10 ^{6}; (2) hemoglobin level below 11g/dL; (3) creatinine clearance <30mL/min during enrollment screening; (4) Clinically significant gastrointestinal bleeding occurred 12 months before randomization; (5) Previous intracranial hemorrhage, or intracranial aneurysm, cerebrovascular malformation, etc.; (6) Previous ischemic, hemorrhagic stroke or TIA; (7)) Severe hepatic insufficiency; (8) There are indications for anticoagulation, such as combined with atrial fibrillation, mechanical valve replacement, deep vein thrombosis and other diseases

We invite you to participate in this study. Whether you are ultimately selected or not will be judged by the researchers based on your actual situation.

3. The process and methods of this research

The aspirin, clopidogrel and rivaroxaban used in this study are all commonly used clinical drugs approved by the State Food and Drug Administration. This study does not involve drugs and devices that have not been approved by the National Medical Products Administration and are still in the research stage.

This is a randomized controlled clinical study. You may be assigned to the experimental group or the control group with a probability of 1 : 1 through a central randomization system .

① The treatment method of the experimental group was a short-term triple antithrombotic therapy of 3 months (aspirin + clopidogrel + low-dose rivaroxaban for 3 months), followed by conventional dual antiplatelet therapy.

②The control group was treated with conventional dual platelet therapy (aspirin + clopidogrel).

4. **Duration and number of participants in this study**

This is a multicenter clinical study, which plans to recruit a total of 3,944 research participants in 40 research centers , of which this center plans to recruit approximately 800-1,000 research participants from January 2023 to December 2026. You are expected to participate in the medication intervention for 3 months and the follow-up period will be 12 months (until 12 months after you complete percutaneous coronary intervention) .

5. What do you need to do to participate in this study?

Before you are selected for the study, you will undergo a routine coronary heart disease examination to determine whether you meet the conditions for participating in the study . No additional blood tests are involved . We will determine whether you can participate in this clinical study based on the examination results .

Things to note when participating in this study:

① You are required to take the medicine in accordance with the doctor's instructions during the study. You cannot stop or change the medicine without authorization, or take the medicine in violation of the prescribed usage and dosage. If you feel uncomfortable or have adverse events during the medication, please go to the outpatient or emergency department for medical treatment and report it in time. We will assist in guiding the treatment.

② You need to attend follow-up regularly. We will follow up with you regularly by phone. Since you are a high-risk group for acute coronary syndrome, you should have regular office visits (3 months, 6 months) and review abnormal indicators according to your condition. According to

your situation, we will assist you in arranging outpatient follow-up in our hospital. The researchers will notify you in advance before each follow-up, so please be ready to answer our phone calls.

6. Any risk and adverse events for study participants taking part in this study ?

(1) The treatment options in this study are all existing treatment options in the current guidelines. They will not bring you any risks beyond routine diagnosis and treatment . All the examinations you will undergo are routine clinical examinations. No blood specimens will be collected specifically for this study. No additional examination items or times will be added, and no additional harm will be caused.

The following are risks that study participants may face during routine care:

Risk of bleeding

Anyone who takes antiplatelet and anticoagulant drugs to treat coronary heart disease may be at potential risk of bleeding. Bleeding is one of the adverse reactions to taking rivaroxaban. However, this study used the small dose recommended by the guidelines, and the incidence of severe bleeding was low, including a risk of major bleeding of 1-1.8%, and a risk of intracranial hemorrhage within two years of 0.4%. You are at high risk of ischemia and do not have high-risk factors for bleeding. The probability of severe bleeding caused by taking a short course of low-dose rivaroxaban is very low. We have developed a complete plan for bleeding events and situations where anticoagulant therapy needs to be adjusted. If you experience severe bleeding during the study, please go to the emergency department immediately and contact us, and we will help with the treatment.

Reproductive risks

For female study participants: If you are breastfeeding, pregnant, or think you may be pregnant or trying to get pregnant, you cannot participate in this study. Pregnancy status of women of childbearing age will be checked during the study.

It is very important that you tell the researchers right away if you become pregnant or think you may be pregnant while you are taking part in this study. If you become pregnant, you will be taken off the study and the researchers will talk to you about what you should do. The researchers will give you ways to contact people on the project, and you may be asked questions about your pregnancy and baby even after the study is over.

Other risks

There may also be some currently unforeseen risks, discomforts, drug interactions or adverse reactions.

7. Will I benefit from participating in this study ?

You are at high risk of ischemia. Participating in this study may bring you indirect benefits and may further reduce the risk of ischemic events.

Your participation will help us understand the pathogenesis of diseases, promote the improvement of medical standards, promote the development of safer or more effective diagnosis and treatment methods, and expand new scientific knowledge.

During the follow-up of this study, you may receive relevant medical services, and the follow-up staff will provide you with treatment-related suggestions based on your condition.

8. If I do not take part in this study, are there any other treatment options?

You can choose not to participate in this study, which will not have any adverse effects on your access to conventional treatment. Currently, for your health condition, the conventional treatment is to take dual antiplatelet drugs within 1 year after discharge.

9. **Any cost or compensation for participating in this study?**

You do not have to pay any research-related costs to participate in the study.

Your anonymous information will not bring any commercial products or benefits to anyone, nor will it cause any losses to you or your family.

If you are willing to receive outpatient follow-up, we will arrange for you to come for outpatient follow-up in the 3rd and 6th months.

You will not be paid or compensated for this research .

If any participant in the trial group experiences serious adverse bleeding events related to the trial drugs during the study (events that meet the relevant terms of the insurance company, such as intracranial hemorrhage, severe gastrointestinal bleeding, need for blood transfusion, etc.), the insurance company will pay the relevant expenses for you.

The cost of trial drugs will be borne by the project team, and other routine medical expenses will be borne by the research participants.

10. Dealing with research-related harm

We have purchased clinical research liability insurance for this study. If you experience

severe adverse bleeding events related to the trial medication during the study , please inform the investigator . We will take necessary medical measures in a timely manner , and the investigator will bear the treatment costs and financial compensation stipulated in the insurance terms through the insurance company , except for those caused by medical errors .

11. Will my information be kept confidential ?

If you decide to participate in this study, your participation in the study and your personal information in the study will be kept confidential. When your research data is used in this study, your personal information will be kept confidential, and all your information will be properly stored and used only for this study.

Information in research databases and samples will be strictly anonymized to remove personal identifying features, and information that could identify you will not be disclosed to anyone other than the researchers without your permission.

To ensure that the research is conducted in accordance with regulations, without violating the principles of confidentiality and relevant laws and regulations, the researcher team, ethics committee, and inspectors from the drug supervision and administration department and the health and health authority may review the original medical records of the research participants to verify the process and data of the clinical research.

If the research results are published publicly, your personal information will not appear in any public medical records or publications, and we will not disclose this information to anyone or any organization.

12. What rights do research participants have during the research process?

During your participation in this study, you can keep informed of clinical information related to your diagnosis and treatment at any time.

Participation in this study is voluntary and you are free to decide whether to participate or refuse to participate in this study. Whether you agree to participate in this study or not, it will not affect the routine clinical diagnosis and treatment measures you should have during your visit to our hospital.

You may refuse to participate at any time or have the right to withdraw from the study at any stage during the study without any reason, and will not be discriminated against or retaliated against, and the corresponding medical treatment and rights will not be affected.

If you want to withdraw from the research project during the participation, please inform the researcher, complete the relevant pre-withdrawal examinations as required by the researcher, and complete the relevant withdrawal procedures in writing as required. After withdrawal, you can choose conventional dual antiplatelet therapy. If we find new information related to your health and rights after withdrawal, we may contact you again.

You have the right to be informed of the potential benefits and risks of participating in this study. You have the right to agree or disagree to participate in the study. If you want to participate in this study, you need to read this informed consent carefully and sign it after confirming that you fully understand the relevant issues. You will not lose any legal rights granted to you by law by signing this document.

During the research process, you have the right to obtain new information about this research, as well as the right to obtain the informed consent form and to sign the new version of the informed consent form again.

If you agree to sign this document, the Fuwai Hospital of the Chinese Academy of Medical Sciences will obtain your research data free of charge, and researchers may use your research data.

13. Situations where a research participant may be terminated from the research

If you experience any of the following during the study, the researcher will ask you to withdraw from the study:

(1) After randomization, serious violations of the inclusion or exclusion criteria are found, affecting the efficacy evaluation;

(2) Severe complications, diseases or special physiological changes occur, making it unsuitable to continue the trial;

(3) If allergic reactions or serious adverse events occur, the trial should be stopped according to the doctor's judgment;

The study sponsor or regulatory agency may also terminate the study during the study. If the study is terminated early, we will notify you in a timely manner, and your researcher will provide you with advice on the next treatment plan based on your health condition. For study participants who withdraw midway, we have a final follow-up plan for safety reasons, and you have the right to refuse. If you withdraw and find new information related to your health and rights, we may contact you again.

After your withdrawal, new data related to you will not be collected. The researchers will strictly keep the relevant information before you withdraw from the study until it is finally destroyed, and will not continue to use or disclose it. However, in rare cases, such as when the government supervisory department conducts supervision, inspection, and statistics, it will be required to view all research information, which will include relevant information about your participation in the study at that time.

14. Will the study medication continue to be provided after the study ends?

After the study is over, the investigators will no longer provide you with the study drug. Your doctor will discuss your future treatment options with you.

15. Are you willing to participate in future research?

If you agree, we also hope to follow up with you for a long time after the study is completed to understand your health status and medication information. Your anonymous research data, clinical diagnosis and treatment data (including but not limited to medical records, imaging data, clinical test and monitoring data, including external hospital examination data, etc.) and follow-up data will continue to be used for subsequent approved non-genetic medical research on cardiovascular diseases, in order to explore the causes, mechanisms and influencing factors of the occurrence and development of diseases, and to develop and evaluate disease prevention and treatment measures. If you do not agree, after the completion of this study, your research data and clinical diagnosis and treatment data will be kept for a specified period of time in accordance with national regulations and will be kept strictly confidential.

Participating in future research will not add any additional risks or financial burdens to you. All samples and data from future research will be properly stored in the Fuwai Hospital of the Chinese Academy of Medical Sciences and kept strictly confidential. You can voluntarily choose whether to participate in future research and can contact the researchers at any time to withdraw from the research in writing.

16. Who should I contact if I have questions or problems?

You can ask any questions about this study at any time and get the corresponding answers, including any discomfort that may occur during the study . Please contact researcher Xu Jingjing at 010-88322457

If you have any questions about your rights, please contact the Ethics Committee of Fuwai

Hospital at 010-88396281 , 010-88396282.

Thank you for taking the time to read this informed consent form. If you and your family agree to participate in this study after careful consideration , we hope that you and your family will complete this study in accordance with the researcher's requirements . Before participating in this study , please complete and sign the last page of this document (signature page) with your researcher in duplicate. You and the hospital will each keep one signed copy.

Study participant contact information

Study Participant Name:_____

In accordance with the requirements of the study you are participating in, a follow-up group will conduct long-term follow-up to track the medication and health status of the study participants.

Since the follow-up covers a long period of time, please leave **2-3** phone numbers (mobile or landline) to ensure that the follow-up team staff can understand your health status in a timely manner.

When conducting follow-up, the follow-up team staff will call the contact numbers in order. Please write the phone number that can directly reach the research participant first.

Please remember to leave the area code for landline calls.

Contact information 1 :_____ Relationship with research participants_____

Contact 2 :_____ Relationship with research participants_____

Contact information 3 :_____ Relationship with research participants_____

address:

Signature Page

Research Participant Statement

I have carefully read, understood and agreed to all the terms of this Informed Consent Form.

I have been informed of the purpose, content, procedures, possible risks , research compensation, and my rights of this clinical trial ; I have had sufficient time and opportunity to ask questions and received satisfactory answers.

I agree to participate in this study and authorize your hospital to collect my biological samples and research data for this study.

I promise that the information I provide is true; if I provide false information, I promise to be responsible for the consequences.

I was also told who to contact if I had questions or wanted further information.

I confirm that the contact information I signed is my valid contact information. If the contact information changes, I will inform your hospital in time. Otherwise, I am willing to bear the corresponding consequences of being unable to be contacted and not being able to receive notifications.

I understand that I can withdraw from this study at any time without affecting the medical treatment and rights I deserve. I also understand that the researcher may suspend/terminate my participation in this study at any time.

I will receive an original copy of this informed consent form, which contains my and the researcher's signatures.

I agree to participate in this research.

Do you agree to participate in future research? ☐ Agree ☐ Disagree (Please select) Clinical diagnosis and treatment, research data and long-term follow-up data will be used for future research. I authorize researchers and joint research units of related medical research projects to use and process my anonymous data in approved cardiovascular-related medical research.

Study Participant’s Name and Signature:

date:

Guardian's name and signature:

Relationship to research participant: date:

I confirm that the information in the Informed Consent Form has been correctly interpreted and understood by the research participant and / or the research participant's legal representative. The research participant voluntarily agrees to participate in this study.

Signature of Notarized Witness [if applicable]: date:

Investigator Statement

I confirm that the details of this study have been explained to the research participant, including his/her rights as well as the benefits and risks, that his/her questions have been answered, and that he/she has been given a copy of the signed informed consent form, and that the research participant voluntarily participates in this study.

Researcher : Signature:

date: