Supplement

Definitions of study endpoints

The study endpoints will be adjudicated by a blinded clinical endpoint committee. In this study, only events occurred during 0-day to 1 year after coronary artery bypass grafting (CABG) or 0-day to the day conducting coronary computed tomography angiography (CCTA) will be registered as endpoints and be adjudicated by the clinical endpoint committee.

SVG occlusion

Occlusion is considered as 100% stenosis. Anastomoses of Y-grafts and jump grafts are defined as separate SVGs. Both anastomoses are defined as occluded if the proximal part of the graft is occluded but the remain graft beyond the first anastomosis is patent.

Bleeding Academic Research Consortium (BARC) classification

Type 0: no bleeding evidence

Type 1: bleeding events does not need patients to seek treatment of a healthcare professional or hospitalization.

Type 2: any clinically overt sign of haemorrhage, requiring diagnostic studies, hospitalization or treatment by a health professional, meets one of the following...
criteria and does not meet criteria for type 3, type 4 or type 5 BARC bleeding classification.

- Bleeding must require intervention, including medical practitioner-guided treatment, surgery or percutaneous intervention to stop or treat bleeding, including temporarily or permanently discontinuing or changing the dose of a medication or study drug.

- Bleeding leads to hospitalization, prolonging hospitalization or increasing level of care.

- Prompting evaluation (leading to an unscheduled visit to a healthcare professional and diagnostic testing).

Type 3: Clinically overt bleeding requiring medical therapy, as listed below

- Type 3a: any transfusion due to overt bleeding; haemoglobin drop ≥3 to <5g/dL;

- Type 3b: haemoglobin drop ≥5g/dL; cardiac tamponade; surgical intervention for controlling bleeding; bleeding requiring intravenous vasoactive medication.

- Type 3c: intracranial haemorrhage; intraocular haemorrhage compromising vision.

Type 4: coronary artery bypass grafting (CABG) related bleeding

- Perioperative intracranial bleeding within 48 hours

- Reoperation after closure of sternotomy for the purpose of controlling bleeding
● Transfusion of ≥5 U whole blood or packed red blood cells within a 48-hour period (only allogenic transfusions are registered)

● Chest tube output ≥2 L within a 24-hour period after CABG

Type 5: fetal bleeding

Fetal bleeding means bleeding that directly causes death with no other explainable cause.

**Coronary computed tomography angiography**

A high-quality cardiac CT scan is performed according to SCCT guidelines for the performance and acquisition of CCTA, specified for local practices and available technology.¹ Minimal requirements for the CT scanner consisted of a single- or dual-source 64-slice CT or higher. An axial scan mode and diastolic scans/reconstructions are preferred. A regular heart rate (preferably <60 bpm) is recommended.

**Reference**

Informed Consent Form

We invite you to participate in a trial “Timing of Platelet Inhibition after Coronary Artery Bypass Grafting (TOP-CABG Trail)” initiated by Fuwai Hospital of Chinese Academy of Medical Sciences, which has been approved by the Ethics Committee of Fuwai Hospital of Chinese Academy of Medical Sciences (Tel. +86-010-88396281). Please read the instructions carefully to understand your rights and obligations in the research and to clarify the design and risks of the trial. Participation in the trial is completely voluntary and will not affect your treatment during your stay in the hospital, whether you participate in this trial or not. When the researcher explains and discusses the informed consent form to you, you can ask questions at any time.

If you are currently participating in other clinical studies, please let the researchers know.

The leader of this multicenter trial is professor Shengshou Hu (Fuwai Hospital, Chinese Academy of Medical Science), and the sponsor of this trial is the National Clinical Research Centre of Cardiovascular Diseases.

Why is this trial carried out?

The purpose of this trial is to evaluate the effect of antiplatelet therapy strategies on SVG patency and bleeding risk through long-term follow-up of patients after coronary artery bypass grafting (CABG). The antiplatelet drugs used in this trial are aspirin and Ticagrelor.
Why are you invited to participate in this trial?

Because you have coronary atherosclerotic heart disease and you need to undergo CABG surgery and antiplatelet drugs, we invite you to participate in this trial. Researchers decide whether or not to be selected according to your actual situation.

You meet the inclusion criteria of the subjects in this trial: 1. Patients more than 18 years and less than 80 years old. 2. Patients undergo planned CABG for the first time with ≥1 SVGs. 3. Patients with written informed consent.

You do not violate the exclusion criteria for subjects in this trial: 1. Concomitant valve (excluding aortic bioprosthesis), aorta, or rhythm surgery during the index operation. 2. Patients undergo emergent/urgent CABG. 3. Patients with single vessel coronary artery disease. 4. Patients with cardiogenic shock and hemodynamic instability. 5. Patients with sick sinus syndrome, or 2nd or 3rd atrioventricular block. 6. Patients with contraindications for coronary computed tomography angiography or coronary angiography (e.g., contrast agents allergy). 7. Use of other antiplatelet drugs than aspirin (clopidogrel, prasugrel, etc) and unable to discontinue this medication after CABG. 8. Patients who take oral anticoagulants before CABG and have to use anticoagulants after surgery. 9. Contraindication for the use of ticagrelor or aspirin (e.g., history of bleeding diathesis within three months prior presentation, severe gastrointestinal bleeding within one year prior presentation, peptic ulcer without gastrointestinal bleeding in past three years or history of intracranial haemorrhage, allergy, severe gastrointestinal reaction caused by aspirin). 10. Placement of a drug-
eluting stent in a coronary or cerebral artery within six months of CABG or placement of a bare-metal stent in a coronary or cerebral artery within one month of CABG. 11. Thrombocytopenia before CABG (< 100 x 10^9/L). 12. patients with severe renal function impairment requiring dialysis or active liver disease, including patients with unexplained persistent elevated transaminase or any transaminase more than three times of the upper limit. 13. Use of strong inhibitors of CYP3A4. 14. Patients who must use methotrexate and ibuprofen. 15. Patients with active malignant tumours with increase in bleeding risk. 16. Pregnant patients, patients who have given birth within the past 90 days, or who are breastfeeding. 17. Premenopausal women who do not take adequate contraception. Adequate contraception refers to the adoption of at least two reliable methods of contraception, one of which must be a barrier method of contraception. 18. CABG performed by surgeons with a total volume of less than 50 cases.

**How many patients will the trial recruit?**

This trial is a multicenter clinical trial and plans to recruit 2300 subjects across the country.

**What do you need to do?**

Researchers will explain to you the background, purpose, steps, benefits and risks of the research, and ask you to sign the informed consent form. The first screening for in- and exclusion criteria is conducted before surgery. A second screening is conducted within 5 days post-surgery and only the patients who are tolerant to DAPT will be randomized. You will be randomized on postoperative day five by using by central randomization system based on interactive web response, to De-DAPT referred to as
ticagrelor (90 mg twice daily) + aspirin (100 mg once daily) during first three months after CABG, then switching to aspirin (100 mg once daily) + ticagrelor placebo (twice daily) for nine months or to DAPT group with ticagrelor (90 mg twice daily) + aspirin (100 mg once daily) for one year. Patients, treating physicians and investigators are blinded to allocation. You will be evaluated at one, three, six, nine, and twelve months after CABG. Evaluation in month one is performed by telephone or through an outpatient hospital visit (patient preference). In month three, six, nine, and twelve through an outpatient hospital visit, researchers will provide you with drugs for the next cycle and to collect the occurrence of major adverse cardiovascular events and drug compliance. In month twelve after CABG, you need to take coronary computed tomography angiography (CCTA) to evaluate SVG, which is free of charge. The project team is responsible for recruiting patients and monitoring the random grouping process, but they do not directly participate in the random process. The following medical records will be collected during hospitalization: age, sex, body mass index (BMI), aspirin resistance, surgical history, anastomosis of grafts, cardiopulmonary bypass, duration of cardiac arrest, postoperative complications, history of diabetes, history of hypertension, history of hyperlipidemia, history of chronic obstructive pulmonary disease, history of peripheral artery diseases, history of PCI, cerebrovascular accident, gastric ulcer, history of massive hemorrhage, left ventricular ejection fraction, drinking history, smoking history, creatinine clearance rate, postoperative hospital stay, total hospitalization cost.

How long will this trial last?
This trial is expected to last for 3 years. You will participate in this trial for one year.

**What are the risks and adverse reactions of the participants in this trial?**

Participating in this trial will not have any impact on your outpatient or hospitalization. In the follow-up, you can avoid any questions you do not want to answer. Your information will be transmitted in encrypted form and stored in the confidential database of the National Clinical Research Centre of Cardiovascular Diseases. Although there is a risk of contrast agent allergy in CCTA, according to the trial, the incidence is extremely low, and radiologists have enough experience in dealing with it. Therefore, there is no additional risk to you for such problems. Venous blood collection has the risk of hematoma or infection at the blood collection site, but such risk is extremely low, and the research doctor will provide you with timely medical treatment for such problems. The experimental drugs are aspirin and ticagrelor. Aspirin has the following side effects: upper and lower gastrointestinal discomfort, rare gastrointestinal inflammation, gastroduodenal ulcer, and very rare gastrointestinal bleeding and perforation; aspirin may increase the risk of surgery-related bleeding. The use of aspirin in this trial followed the guidelines for aspirin use in CABG peri-operation and conformed to aspirin indications. Patients with severe glucose-6-phosphate dehydrogenase deficiency may have hemolytic and hemolytic skin reactions; occasional skin itching, rash, urticaria, cardiovascular and respiratory discomfort; extremely rare severe anaphylactic shock; extremely rare transient liver injury with elevated transaminase. The most common side effects of ticagrelor are increased
bruising tendency, spontaneous hematoma, bleeding quality and dyspnea, which do not affect medication. If this happens, you can contact the project team doctor at any time.

The doctor will provide you with timely advice or treatment. The rare side effects of ticagrelor are hypotension, dizziness, headache, gout, and bleeding. If you have the above side effects during the trial, you can contact doctors of the trial at any time, and the doctor will provide you with timely medical treatment.

**Reproductive risk**

For female patients: if you are breastfeeding, pregnant, or preparing for pregnancy, you cannot participate in this trial. If you are pregnant or breastfeeding, there may be risks to you and your baby that are not yet clear. For women who are using antiplatelet drugs, there is no information on whether antiplatelet drugs are safe for breastfeeding or unborn babies.

In order to participate in this trial, you must have contraception. If you have sex, you should use contraceptive methods that are acceptable to you, doctors, and the research team. You must continue contraception until 60 days after the last administration of the experimental medication.

During the course of this trial, if you are pregnant or think it is possible to become pregnant, it is important to inform the researcher immediately. If you are pregnant, you will be discontinued and the researcher will discuss with you what you should do. Researchers will provide you with contact information for the project, and you may be asked questions about pregnancy and babies even at the end of the trial.

For male patients: participating in this trial may damage your sperm and harm the
child you conceived during the trial. This kind of damage is currently unpredictable.

Please inform your sexual partner of the risk to unborn babies. She should know that if she is pregnant, you need to inform your doctors immediately, and she should inform her doctor immediately.

Other risks

There may also be risks, drug interactions or adverse reactions that are currently unpredictable.

If the trial involves a questionnaire, please indicate the psychological discomfort that may be caused. For example, some questions in the questionnaire may make you feel uncomfortable, and you can refuse to answer them.

If the research involves personal privacy issues, we will explain the harm that may be caused to you, such as: if you accidentally disclose personal private information, it may adversely affect your work and life.

What are the possible benefits of participating in this trial?

You will not benefit directly from participating in this trial. In this trial, you will receive routine postoperative education, which will provide you with relevant knowledge and information about coronary heart disease. Using your medical information for research may help us understand the pathogenesis of the disease, promote the development of safer or more effective diagnosis and treatment, and expand new scientific knowledge.

If you do not participate in this trial, are there any other treatment options?

You may choose not to participate in this trial, which will not have any adverse
effect on your routine treatment. At present, according to your health situation, the conventional treatment methods include taking single antiplatelet drug, or other DAPT such as aspirin combined with clopidogrel.

**Cost and compensation for participation in the trial.**

The experimental medication including aspirin and ticagrelor and CCTA are free of charge in one year after CABG. The trial team provides you with a transportation subsidy to take CCTA, which is based on your tickets.

**What is the treatment of research-related damage?**

If you have any discomfort during the experiment, please feel free to contact the researcher and he/she will give you guidance timely. The drugs provided by the trial are approved by the State Food and Drug Administration, and the drug usage do not exceed drug indications. The trial will provide medical insurance for you, and the insurance company will give you financial compensation or compensation in the event of test-related injury or death. If a serious adverse event occurred on you as a result of this trial, the insurance company will remit the compensation by telegraphic transfer to the bank account designated by you.

**Is it necessary to participate in and complete this trial?**

If you want to participate in this trial, you need to read this informed consent form carefully, confirm that you fully understand the relevant issues, and then sign this informed consent form. You will not lose any legal rights conferred on you by law as a result of signing this document.

If you agree to sign this document, Fuwai Hospital will obtain your research data
free of charge.

You may withdraw from the trial at any time, which will not cause discrimination or retaliation, and the corresponding medical treatment and rights will not be affected.

If you want to withdraw from the trial, please inform the researchers to complete the relevant inspection before the withdrawal, complete the withdrawal procedures in writing. After withdrawal, the researchers will no longer continue to collect and use your medical data, but the data collected anonymously before you quit cannot be deleted or withdrawn. After quitting, you can communicate with your surgeon, who will provide you with appropriate antiplatelet treatment. If you quit and find new information related to your health and rights, we may contact you again.

**Who should I contact if I have any questions or difficulties?**

You can ask any questions to researchers about this trial at any time (Dr. Qing Chu, +86-18810919868), including any discomfort that may occur during the clinical trial.

Thank you for taking the time to read this informed consent form. If you agree to participate in this clinical trial after full consideration, we hope that you will complete this clinical trial in accordance with the requirements of the researchers. Please work with your researchers to complete and sign the last page of this document before participating in this trial.
Signature Page

I have carefully read, understood, and agreed to all the terms of this informed consent form.

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

I agree to participate in this trial and authorize your hospital to collect my medical data for this trial.

I promise that the information I provide is true.

I know that I can withdraw from the trial at any time without affecting the medical treatment and benefits I should receive, and that the researcher may terminate my participation in the trial at any time. I agree to participate in future research, to donate remaining samples, clinical diagnosis, research data and long-term follow-up data for future research and authorize researchers to use and process my own anonymous remaining samples and data in approved cardiovascular-related genetic and non-genetic medical research.

I agree to take part in this trial.

Signature of Patient

Date

I confirm that the information in the informed consent form has been correctly
interpreted to patient.

Signature of Researcher

Date