INFORMED CONSENT FORM

Study title: Prophylactic Intra-Aortic Balloon Counterpulsation for Delayed-Presentation Anterior ST-Segment Elevation Myocardial Infarction: A Prospective, Multicentre, Randomised Controlled Trial (PROACTIVE-AMI)

Study site name: _____

Participant name: _____ **Sex:** ☐ Male ☐ Female **Age:** _____ years

Identity-card number: □□□□□□□□□□□□□□□□□□

Participant telephone: □□□□□□□□□□□ **Contact-person telephone:** □□□□□□□□□□□

Mailing address: _____

We invite you to take part in a medical research study. This study is led by Professor Yuguo Chen and Professor Chuanbao Li of Qilu Hospital of Shandong University. This informed consent form provides you with information to help you decide whether to take part. Please read it carefully, and raise any questions you may have with the study lead/study physician.

Your participation in this study is entirely voluntary, and the study has been reviewed and approved by the ethics review committee. Signing this informed consent form does not necessarily mean that you will take part in the study; you must also meet certain requirements. If you do not meet the study requirements, the physician will inform you.

1. Background

1.1 About your (or your family member's) condition

Acute ST-segment elevation myocardial infarction (STEMI) is one of the most critical cardiovascular emergencies. It usually means that a coronary artery supplying the heart has become completely blocked, causing the heart muscle to die. If the vessel is not opened and blood flow restored in time, the area of dead muscle continues to enlarge, posing a direct threat to life. Although early reperfusion therapy substantially improves outcomes, in real-world practice—constrained by factors such as transport and delayed recognition of the illness—many patients are still unable to reach hospital promptly after onset; this situation is termed "delayed presentation."

1.2 Why is anterior myocardial infarction more dangerous?

The anterior wall of the heart is the most important region for the heart's pumping function. For an infarction occurring in the anterior wall, as in your (or your family member's) case, together with delayed presentation, a larger area of heart muscle is affected and cardiac function is more severely impaired. In such patients, the risk of fatal complications during or after the procedure—such as cardiogenic shock (the heart being unable to pump blood out), malignant arrhythmia, or cardiac rupture—is markedly

increased. This study is aimed precisely at these high-risk patients with large anterior myocardial infarction and delayed presentation.

1.3 Limitations of current treatments

Under current medical conditions, once the serious complications described above occur, although physicians will attempt rescue with medication or conventional invasive support measures, existing evidence unfortunately shows that these "after-the-event rescue" measures are often unable to fundamentally reverse the situation, and the risk of death remains high.

1.4 What is intra-aortic balloon counterpulsation, and what are its indications?

Intra-aortic balloon counterpulsation (IABP) is a mechanical cardiac-assist device. By placing a balloon within the aorta that inflates and deflates in time with the heartbeat, it can increase the blood supply to the heart while reducing the heart's pumping workload. IABP is currently approved for the treatment of acute coronary syndrome (ACS) and its serious complications; acute anterior STEMI is the highest-risk and most critical type of ACS.

2. Why is this study being conducted?

In past clinical practice, IABP has usually been used as a "last resort," started only after a patient has developed a critical condition such as shock. However, research suggests that this "after-the-event" approach does not effectively reduce mortality. Recent studies indicate that, for high-risk patients such as you (or your family member), placing an IABP "prophylactically" to support the heart before serious complications occur may be more effective than using it only after a crisis. However, high-quality randomised controlled trials confirming whether this approach is indeed superior to conventional treatment are currently lacking worldwide. We have therefore undertaken this prospective, multicentre, randomised controlled study to evaluate scientifically whether "prophylactic IABP insertion" can genuinely improve the survival and quality of life of patients with delayed-presentation anterior myocardial infarction.

3. Who will take part, and how long will the study last?

This study will enrol 504 participants across multiple study sites. It is aimed at a high-risk population with large anterior myocardial infarction. The specific screening criteria are as follows.

Inclusion criteria:

1) Age ≥18 years;
2) First electrocardiogram on arrival at the emergency department showing ST-segment elevation ≥2 mm in at least two contiguous anterior leads, or a summed ST-segment elevation ≥4 mm across the anterior leads;
3) Symptom-onset-to-presentation ≥4 hours and ≤12 hours, with primary percutaneous coronary intervention (PPCI) planned;

4) Coronary angiography confirming the infarct-related artery to be the left anterior descending artery, with complete occlusion (TIMI grade 0 flow) in a proximal segment (before the origin of the first septal or first diagonal branch);
5) Written informed consent provided by the patient or his/her legal representative.

Exclusion criteria:

1) Established cardiogenic shock (defined as systolic blood pressure <90 mmHg without pressor support, or a requirement for vasoactive agents to maintain blood pressure, together with blood lactate >2.0 mmol/L);
2) Established severe heart failure: Killip class III or higher before enrolment, or a requirement for non-invasive or invasive positive-pressure ventilation;
3) Established malignant arrhythmia, including cardiac arrest, ventricular fibrillation, ventricular flutter, pulseless ventricular tachycardia, or high-degree atrioventricular block;
4) Established serious mechanical complication (e.g., free-wall rupture, ventricular septal rupture, or acute severe mitral regurgitation);
5) Contraindication to IABP insertion (e.g., severe peripheral arterial disease precluding cannulation, aortic dissection, known aortic aneurysm, or known moderate-to-severe aortic regurgitation);
6) Prior myocardial infarction or known chronic heart failure (LVEF <50%);
7) Prior coronary artery bypass grafting (CABG);
8) Stroke within the preceding month, or known haemorrhagic stroke at any time;
9) Active gastrointestinal bleeding within the preceding 3 months, or any gastrointestinal condition associated with increased bleeding risk (e.g., severe oesophageal varices, active peptic ulcer);
10) Thrombolytic therapy already administered for the index event;
11) Any mechanical circulatory support device (IABP, Impella, extracorporeal membrane oxygenation [ECMO]) already initiated before coronary angiography;
12) Severe hepatic impairment (Child-Pugh class C, or ALT >5×ULN with total bilirubin >3×ULN), renal impairment (eGFR <15 mL/min/1.73 m² or long-term dialysis), or any end-stage condition with a life expectancy of less than 1 year;
13) Pregnancy or lactation;
14) Current participation in another interventional clinical trial.

You will complete 180 days of follow-up visits in this study.

4. What will the study involve?

4.1 Study description

This study is a prospective, multicentre, randomised controlled trial in patients with delayed-presentation acute anterior STEMI, evaluating the effect of prophylactic IABP insertion before PPCI, compared with standard PPCI, on patients' clinical outcomes. Your time in the study comprises mainly a treatment period and a follow-up period. If you agree to take part, the study physician will first assess you to confirm whether you meet

the eligibility criteria, and will ask you to provide basic information, past medical history and other details that need to be recorded.

4.2 Study groups

Patients meeting the eligibility criteria—delayed-presentation (4–12 hours after onset) acute anterior STEMI—will be allocated to groups generated randomly by a computer program. You have a 50% chance of being assigned to the intervention group and a 50% chance of being assigned to the control group; no one can influence this allocation.

- **Intervention group:** the IABP will be inserted and activated before opening of the infarct-related artery, at a 1:1 augmentation ratio. Peri- and post-procedural anticoagulation will follow guideline-directed standard pharmacotherapy at the investigator's discretion. IABP support is recommended to be maintained for at least 24 hours and no longer than 72 hours. In patients with haemodynamic instability, the investigator may appropriately extend the duration of counterpulsation as clinically judged. Weaning requires satisfaction of the predefined criterion of haemodynamic stability for ≥6 hours and will employ a stepwise reduction in the augmentation ratio.
- **Control group:** patients will receive guideline-recommended standard primary PCI.

All enrolled patients will receive standardised pharmacotherapy in accordance with current guidelines.

4.3 Collection and handling of biological samples

Peripheral venous blood will be collected at enrolment, before discharge, at 90 days after randomisation and at 180 days after randomisation, approximately 5–10 mL each time, with an anticipated cumulative volume of about 20–40 mL over the study. The samples at enrolment and before discharge may be drawn together with routine blood sampling required for clinical care; if additional sampling is needed, the study physician will explain this to you. The samples at 90 and 180 days after randomisation are research samples added by this study, used chiefly to measure NT-proBNP and to assess recovery of cardiac function. The costs of study-related additional sampling and testing will be borne by the project team. After processing, the blood samples will yield plasma or serum. Once testing is complete, any remaining plasma or serum will be coded with the study number and stored in the biobank of Qilu Hospital of Shandong University for 5 years from the date of study completion or from the 180-day follow-up of the last randomised participant. The stored samples will be used only for verification and quality control of this study's test results, and for follow-up research related to this study that has been approved by the ethics committee and appropriately authorised; no genetic testing will be performed, and the samples will not be provided to unrelated third parties. After the storage period expires, the samples will be destroyed in accordance with the hospital's biological-sample management regulations.

4.4 Outcome measures

The primary outcome of this study is the first occurrence of a major adverse cardiovascular event (MACE) within 180 days after randomisation. MACE comprises all-cause death, cardiogenic shock, and new or worsening heart failure. The study physician will record whether and when these events occur. Suspected endpoint events will be reviewed and adjudicated by an independent clinical events committee blinded to treatment allocation. Where a single participant experiences multiple events within 180 days, the primary composite endpoint records the first event to occur, in accordance with a pre-specified statistical analysis plan. The study will also observe the individual component events (all-cause death, cardiogenic shock, new or worsening heart failure), length of hospital stay, NT-proBNP, left ventricular ejection fraction and left ventricular end-diastolic volume at 90 and 180 days after randomisation, and safety events such as major bleeding, major vascular complications, thrombocytopenia and stroke.

4.5 Participant responsibilities

You should attend the study procedures as agreed and report to the study physician any abnormalities in your health.

4.6 Participant withdrawal procedure

If you decide not to continue in the study, you may withdraw at any time; please contact the study physician or the study site.

5. Potential risks and discomforts

This study adds prophylactic intra-aortic balloon counterpulsation (IABP) insertion to standard treatment. The associated risks include:

- **Puncture-related:** access-site bleeding, haematoma, infection;
- **Vascular:** vascular injury (e.g., dissection, pseudoaneurysm), ischaemia of the cannulated lower limb;
- **Device-related:** balloon rupture, thrombosis or embolism, thrombocytopenia;
- **Counterpulsation-related:** improper counterpulsation timing may induce or worsen arrhythmia or affect cardiac ejection function.

These are the known possible adverse effects of IABP insertion. The study physician will monitor your condition closely and, should any of the above occur, will immediately take appropriate medical measures. If any harm related to this study occurs, the study site will actively provide treatment. Clinical-trial liability insurance has been purchased for this study, and the insurer will provide reasonable compensation in accordance with the relevant laws and regulations.

6. Pregnancy/contraception

If you are pregnant, planning to become pregnant, or breastfeeding, you cannot take part in this study. If at any time during the study you believe you are or may be pregnant, you must inform your study physician immediately; he/she may discuss with you whether

treatment needs to be stopped. Your physician will promptly report this information, including the outcome of your pregnancy, to the study sponsor.

7. Potential benefits

Patients with delayed-presentation (4–12 hours after onset) acute anterior STEMI have prolonged ischaemic time and extensive myocardial involvement, and remain at substantial risk of cardiogenic shock, recurrent myocardial infarction and death after PPCI; they represent a population that may benefit from haemodynamic support. Taking part in this study may confer a prognostic benefit in the treatment of your condition, although this cannot be guaranteed. In addition, you will not receive any form of direct financial benefit from this study.

8. Costs and compensation

This study follows the principle that "study-related additional costs are borne by the project team, and routine care costs are borne by the participant."

8.1 Routine care costs (borne by you)

Regardless of whether you take part in this study, the standard medical costs arising from the diagnosis and standard treatment of your condition must be borne by you personally (or by your medical insurance) through the normal care process. These include, but are not limited to:

1. Emergency-department registration fees, and nursing and bed fees during hospitalisation;
2. Routine laboratory tests, medications and routine treatment during the emergency and inpatient periods;
3. Procedure fees for emergency coronary angiography and percutaneous coronary intervention (PCI), and the cost of stents and related consumables;
4. Routine post-procedural medications (e.g., antiplatelet agents, statins, ACE inhibitors/ARBs).

8.2 Study-related costs (borne by the project team)

If you are randomly assigned to the IABP group (intervention group), the project team will bear the following additional costs arising specifically from this study protocol:

1. **IABP-specific consumables:** the cost of the IABP balloon catheter;
2. **IABP procedure:** costs related to intra-procedural IABP insertion and to IABP monitoring and treatment during hospitalisation;
3. **Protocol-specified follow-up tests:** the protocol-specified blood tests at 90 and 180 days after the procedure (approximately CNY 150–300 per test, 2 tests in total).

Note: if you are in the standard-treatment group and urgently require IABP insertion because of clinical deterioration, this constitutes clinical care, and the resulting costs will be borne by you personally through the routine care process.

8.3 Travel subsidy

To compensate for the travel and time you incur in returning to the hospital to complete the 30-day, 90-day and 180-day follow-up visits, the project team will provide a travel subsidy of CNY 200 per visit after you complete each in-person follow-up. Once the follow-up is complete and the data verified, a research assistant will assist you in receiving the subsidy in cash or by transfer.

8.4 Compensation for study-related harm

During the study, the physician will make every effort to prevent and treat any harm that may arise from this study. If an independent expert panel, or a qualified third-party medical-assessment body jointly commissioned by both parties, determines that the harm you have suffered is indeed directly related to the study intervention, the project team will bear the resulting treatment costs and provide corresponding financial compensation in accordance with the relevant national laws and regulations. This study has purchased "clinical-trial liability insurance" as a supplementary source of protection for participants' rights.

9. Data handling/confidentiality

Privacy protection and the relevant laws and regulations confer on you the right to control the use of your medical data. By signing this informed consent form, you expressly authorise the collection, recording, storage, review, transmission or other processing—within the scope of the sponsor's responsibilities—of your medical data, and the processing and reporting of your medical data for scientific purposes (including use in future medical or pharmacological research). Your medical data will be handled under conditions of strict confidentiality, and your identity will not be disclosed in any publication or report arising from this study.

All study-related documents and computer-processed data (information and results) will be treated as confidential and will identify you only by the study number. However, authorised personnel of the sponsor or its agents (such as monitors and auditors), as well as members of government regulatory authorities and the independent ethics committee, will be granted direct access to your medical data so that they can verify the accuracy of the information collected in this study. Such verification will be carried out to the extent permitted by applicable laws and regulations and without prejudice to your right to privacy.

The data collected in this study (including data relating to you) may be used by the sponsor for further analysis to address other scientific questions concerning delayed-presentation STEMI. The sponsor will take appropriate measures to protect your information and will use and share only coded data for such additional research.

You expressly agree that, if you decide to withdraw from the study, the medical data (and samples) collected before your withdrawal may still be processed as part of the study

together with the other data collected. If you wish to have any previously stored samples destroyed, you must notify your study physician in writing.

Finally, you also understand and agree that the sponsor's staff (or agents working on its behalf) may have access to your coded health information, but may not always carry out this work under the direct supervision of a health professional. The sponsor nonetheless ensures that these staff access your information for technical reasons only, will make no decisions about you or your participation in this study, and are all bound by an obligation of confidentiality.

10. Termination of participation

Your participation in this study is voluntary. If you agree to take part, you may still withdraw your consent at any time without giving any reason. Your decision will be fully respected, will not affect your normal clinical care, and will not result in the loss of any medical benefits to which you are entitled. In addition, your participation may be stopped for any of the following reasons: you do not follow the study physician's instructions; a serious event occurs that may require treatment; your study physician determines that stopping the study is in the best interests of your health and welfare; there are insufficient participants in the study; or the sponsor stops or suspends the study.

11. Your rights and responsibilities

You have the following rights:

1. **Privacy protection:** if you decide to take part in this study, your participation and your personal data in the study will be kept confidential. Your information will be identified by a study number rather than by your name. Information that could identify you will not be disclosed to anyone outside the study team without your permission. All study team members are required to keep your identity confidential. Your records will be kept in a locked filing cabinet, accessible only to study personnel. Our study results will be published in open scientific journals, but your personal information will not appear. If you wish to learn of the study findings, you may contact your study physician for a brief summary report.
2. You may choose not to take part in this study, or notify the study physician at any time to withdraw; none of your medical care or rights will be affected as a result.

As a study participant, you have the following responsibilities:

- To provide truthful information about your basic circumstances, medical history and clinical care, and to provide relevant medical documentation in the event of out-of-hospital follow-up.

12. Contact information

If you have any questions about this study, please contact the study physician or a designated study staff member:

- **Study physician name: _____ Telephone: _____**

If you have any questions about your rights as a study participant, please contact the hospital ethics committee:

- **Ethics committee contact name: _____ Telephone: _____**

Declarations and Signatures

Study physician declaration

I have accurately conveyed the contents of this informed consent form to the participant/legal representative, who has accurately read this form, and I certify that the participant has had the opportunity to ask questions. I certify that his/her consent is given voluntarily.

Study physician signature: _____

Date: _____ Year _____ Month _____ Day _____ Hour _____ Minute

Participant declaration

I have read all the above information in detail; my questions concerning this clinical study have also been explained in detail by the study physician; I understand the overall nature of the study; and after full consideration, I voluntarily agree to become a participant in this clinical study.

Participant signature: _____

Date: _____ Year _____ Month _____ Day _____ Hour _____ Minute

If applicable, legal representative signature: _____ (Relationship to participant: _____)

Date: _____ Year _____ Month _____ Day _____ Hour _____ Minute