Compare IVUS with angiography ographic Guidance PCI Long-term clinical efficacy of acute STEMI

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Version Number:	**Version 1.0**
Version Date:	**April 15th, 2020**

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Scheme Summary

Clinical ison of Intravascular Ultrasound (IVUS) Guided and Angiography (angiographe) for PCI Acute ST Section Elevated Myocardial infarction (STEMI)

Research Objective	Comparing the long-term clinical efficacy of IVUS-guided and angiography-guided PCI in patients with acute STEMI
Test device	IVUS (Opticross™ catheter)
Control device	NA
Research and Design	Prospective, randomized, and multi-center observational trials
Number of planned subjects	200 Cases
Planned number of locations	Ten clinical sites
Main endpoint	The primary endpoint was major cardiac adverse events (MACE), defined as cardiac death, recurrent myocardial infarction (MI, q and non-q waves), and target vasascularization (TVR) at 12 months.
Secondary endpoint	The following indicators will be evaluated annually for 3 years. • MACE(2-3 assessed annually) • Target lesion blood revascularization (TLR) • Target lesion failure (TLF) • Target vascular revascularization (TVR) • Target blood vessel failure (TVF) • Myocardial infarction (Q waves and non-Q waves) • Cardidiac death • Noncardiac death • All-cause of death (cardiac and noncardiac)

	• In-stent thrombosis (ARC classification: determining / possible intrastent thrombosis)
Subsequent arrangements	Clinical follow-up for 30 days, 6 months, 12 months, 24 months, 36 months
Study duration	At 36 months, the
Antiplatelet therapy	Guidance according to current guide
Clinical inclusion criteria	• C1. Age> 18 • C2. STEMI Attack> 30 min, but <12 h • ST segment elevation of at least 2 consecutive guided ≥ 1 mm or new LBBB on the C3. ECG • C4. is willing and able to provide informed consent form
Angiographic inclusion criteria	The AI1. has at least one coronary artery associated with the infarction, in which the ● Criminal lesion and suitable for stent placement ● The reference diameter of criminal vessels is ≥ 2.5 mm but ≤ 4 mm ● TIMI blood flow score ≤ 1 in the criminal lesion segment before guiding the lead to pass AI2. does not have excessive twists and calcification in criminal lesion segments that allow stents
Clinical Exclusion Standards	Patients with CE1. have contraindications to the drugs to be used during the study CE2. cardiogenic shock associated with hemodynamic instability CE3. has bleeding or known coagulation disease CE4. has a history of cerebrovascular accident (CVA) or transient ischemic attack (TIA) in the past 6 months, or intracranial tumor, aneurysm or arteriovenous malformation; or active peptic ulcer or active gastrointestinal (GI) bleeding in the past 2 months; or

	scheduled major surgery within 6 weeks; or known platelet count <100,000 / mm^3Or Hb <10g/dL Planned CE5. surgery that cause deactivation of ADP receptor antagonist Other serious CE6. diseases such as cancer may reduce life expectancy to below 1 year CE7. recurrent myocardial infarction within 7 days after acute myocardial infarction
Contrast exclusion criteria	The AE1. bifurcation lesion does not identify it as a criminal lesion The AE2. criminal lesion is located in the left aorta AE3. diffuse lesions associated with unidentifiable criminal lesions AE4. or stent implantation due to stent thrombosis AE5. may plan CABG bypass surgery within 30 days AE6. patients develop renal failure during dialysis
Statistical Methods	
Major statistical assumptions	The IVUS guidance group may have better results than the angiography guidance, especially in TVR or TLR.
Statistical analysis	Descriptive statistics (e. g., mean, standard deviation, n, minimum, maximum), or median (95% CI) (continuous variable), or frequency tables (classification variables), are used to summarize their demographic characteristics, clinical history, laboratory examination, and risk factors. We will use Logistic regression to analyze the correlation of plaque morphology with clinical results both 12 and 36 months after STEMI.
Sample parameter size	To support the objectives, the sample size of this test will be at least 200 subjects.
Core Laboratory	Core Laboratory data Analysis

1. Research Background

Intravascular ultrasound (IVUS) has been increasingly used for selective and emergency percutaneous coronary intervention. Recent randomized controlled studies, large-scale registration studies, and meta-analysis have demonstrated significant advantages in reducing mortality, myocardial infarction, and target revascularization compared with separate angiographic-guided angiography.

As shown in previous studies [1-5), fewer clinical results on clinical studies of IVUS guided PCI in acute myocardial infarction (AMI) exist and the results remain controversial. This study will explore the effects of IVUS-guided PCI on clinical outcomes in patients with acute ST-segment elevation myocardial infarction (STEMI).

2. Research Objective

Comparing the long-term clinical efficacy of IVUS and angiography-guided PCI in dealing with acute STEMI.

3. study endpoint

.13. Main endpoint

The primary endpoint was major cardiac adverse events (MACE), defined as cardiac death at 12 months, recurrent myocardial infarction (MI, Q and non-Q waves), and target vascular revascularization (TVR).

.23. Secondary endpoint

The following indicators will be evaluated annually for 3 years.

- MACE(2-3 assessed annually)

- Target lesion blood revascularization (TLR)
- Target lesion failure (TLF)
- Target vascular revascularization (TVR)
- Target blood vessel failure (TVF)
- Myocardial infarction (Q waves and non-Q waves)
- Cardidiac death
- Noncardiac death
- All-cause of death (cardiac and noncardiac)
- In-stent thrombosis (ARC classification: determining / possible intrastent thrombosis)

4. Research and Design

This study is a prospective, single-center, randomized controlled trial to be conducted at the Second Affiliated Hospital of Zhejiang University School of Medicine, with plans to recruit 200 STEMI subjects.

Subjects were randomly assigned to 2 treatment groups in a 1: 1 ratio.

5. Subject Selection

Ten centers plan to include 200 male and female patients over 18 to treat subjects according to the Intervention Guidelines of the American Heart Association and the American College of Heart Disease.

The number of subjects recruited each center does not exceed 40% of the total planned enrollment.

5.1 Inclusion criteria

The 200 subjects who met the inclusion / exclusion criteria will undergo emergency angiography and the following

Clinical inclusion criteria

- C1. Age> 18
- C2. STEMI Attack> 30 min, but <12 h
- ST segment elevation of at least 2 consecutive guided ≥ 1 mm or new LBBB on the C3. ECG

- C4. is willing and able to provide informed consent form

Angiographic inclusion criteria

The AI1. has at least one coronary artery associated with the infarction, in which the

- Criminal lesion and suitable for stent placement
- The reference diameter of criminal vessels is ≥ 2.5 mm but ≤ 4 mm
- TIMI blood flow score ≤ 1 in the criminal lesion segment before guiding the lead through

AI2. does not have excessive twists and calcification in criminal lesion segments that allow stents

5.2 Elimination criteria

Clinical Exclusion Standards

Patients with CE1. have contraindications to the drugs to be used during the study

CE2. cardiogenic shock associated with hemodynamic instability

CE3. has bleeding or known coagulation disease

CE4. has a history of cerebrovascular accident (CVA) or transient ischemic attack (TIA) over the past 6 months, or intracranial tumor, aneurysm or arteriovenous malformation; or active peptic ulcer or active gastrointestinal (GI) bleeding in the past 2 months; or scheduled major surgery within 6 weeks; or known platelet count <100,000 / mm^3Or Hb <10g/dL

Planned CE5. surgery that cause deactivation of ADP receptor antagonist

Other serious CE6. diseases such as cancer may reduce life expectancy to below 1 year

CE7. recurrent myocardial infarction within 7 days after acute myocardial infarction

Contrast exclusion criteria

The AE1. bifurcation lesion does not identify it as a criminal lesion

The AE2. criminal lesion is located in the left aorta

AE3. diffuse lesions associated with unidentifiable criminal lesions

AE4. or stent implantation due to stent thrombosis

AE5. may plan CABG bypass surgery within 30 days

AE6. patients develop renal failure during dialysis

6. Research Methods

6.1 Treatment allocation method of subjects

Once the subject has signed a research informed Consent (ICF) approved by the Ethics Committee (EC), meets all clinical and contrast inclusion criteria and does not meet the clinical or contrast exclusion criteria, the subject is considered qualified and may participate in this test. Qualified subjects were randomized to 1 of the two treatment groups at 1: 1: test groups (IVUS guidance group) or control groups (contrast guidance group).

6.2 Visit Plan

The study visits included subject visits during hospitalization (Visit 1), during which the subjects were enrolled and randomized for subsequent treatment. All subjects randomized to trial treatment will be part of the safety set and will receive clinical evaluation on days 30,6,12,2 and 3 years after the surgery. Follow-up requires the collection of data required by the protocol, including accompanying medication, recording any adverse events and collecting original documents.

The number of visits and duration of the subject may be treated depending on:

(a) When patients are included in the study;

(b) When a clear or possible injury occurs, a decision needs to terminate the study early;

(C) End the study.

Subject follow-up Program:

- Visit 1 inpatient visit;
- Follow-up for 30 days after Visit 2 surgery;

- Follow-up for 6 months after Visit 3 surgery;
- Follow-up for 12 months after Visit 4 surgery;
- Follow-up for 2 years after Visit 5 surgery;
- Follow-up for 3 years after Visit 6 surgery;

6.3 The Data Collection Plan

The following page is the observation and evaluation time during the study (Table 1)

Note:

1. The vital signs include: body temperature, pulse, breathing, and blood pressure.
2. Blood routine and biochemical activities include: white blood cells, red blood cells, platelet count, hemoglobin, liver function (ALT, AST), renal function (urea nitrogen, creatinine), blood lipid (total cholesterol, LDL cholesterol, high density lipoprotein cholesterol, triglyceride), blood sugar, etc.
3. Myocardial injury markers include: CK, CK-MB, TnT/TnI.

Table 1. Observation and Evaluation Schedule during the Study

Visit:	Visit: # 1			Visit 2:	Visit 3: 3	Visit 4: 4	Visit: 5	Visit 6: 6
Evaluation	Entering the Group	Random:	Discharge:	30 Days ± 7 Days	6 months ± 30 Days	12 months ± 30 Days	2 Year ± 30 Days	3 years ± 30 Days
Sign an informed consent form	√							
Inclusion and exclusion criteria	√							
Demographic Data	√							
Related medical history and surgical history, coronary heart disease risk factors	√							
vital signs, physical examination, weight, height	√							
Myocardial injury markers	√		√					
12-Guided ECG	√		√					
Blood biochemistry and blood routine	√		√					

Aditant medication	√		√	√	√	√	√	√
Coronary angiography	√					√		
Ststent implantation		√						
Adverse events, serious Aevent end point related events	√	√	√	√	√	√	√	√
Postoperative antiplatelet therapy			√	√	√	√	√	√

Visit 1: entry (in hospital)

Written informed consent must be obtained only to determine the eligibility of the patient's participation in the study. The researchers should inform the subject that even if the subject agreed to attend the study and signed the informed consent form, cardiac catheterization may not warrant the study. The screening records are used to record information about candidates who do not meet the test selection criteria, including, but not limited to, the screening failure.

The subject was hospitalized for a planned coronary surgery (CAG or PCI). The selected CAG shall register and randomly as soon as possible to determine meeting the entry criteria and before any planned or emergency PCI.

Prior to stenting, the following assessment must be completed to confirm the clinical qualification criteria: demographic (date of birth, gender), relevant medical / surgical history, history of smoking, history of family history of coronary heart disease, targeted physical examination, weight, height, medication, vital signs (heart rate, supine blood pressure), and NYHA classification. Laboratory examination (biochemical and blood routine) and myocardial biomarkers (creponin I, creponin T and creatine kinase), ECG, etc.

All subjects were required to undergo cardiac catheterization to evaluate the angiography inclusion and exclusion criteria. Only subjects who met the clinical and angiography qualification criteria were eligible for the trial.

- Record the antiplatelet and anticoagulant agents.
- Record adverse events and endpoint-related events.

Visit 1: from random post to discharge (in the hospital)

Each subject was assigned a strict sequential registration code by a random number table, subsequently receiving a research intervention.

Random tasks must be completed before patients receive PCI and require whether all inclusion / exclusion criteria are met while evaluating patients

- Compliance and drug use.
- Take a 12-guided ECG at 4 days after surgery or before discharge.
- Record the antiplatelet and anticoagulant agents.
- Record adverse events and endpoint-related events.

Visit 1: discharge (in the hospital)

- Record the antiplatelet and anticoagulant agents.
- Record adverse events and endpoint-related events.

30 Days after Visit2 (Surgery)

All subjects in the group must be evaluated 30 days after stenting. Follow-up assessments can be conducted either by telephone or at the research center. The following assessment must be completed at 30-day follow.

- Adverse events and endpoint-related events to evaluate and collect the original documents.
- Current antiplatelet drugs. Information on dose changes, interruptions, and cessation of medication must be recorded.
- Laboratory examination that DSMB considers necessary

6 months after Visit3 ()

All subjects in the group must be evaluated within 6 months after stenting. Follow-up assessments can be conducted either by telephone or at the research center. The following assessment must be completed at 6 months of postoperative follow-up.

- Adverse events and endpoint-related events to evaluate and collect the original documents.
- Current antiplatelet drugs. Information on dose changes, interruptions, and cessation of medication must be recorded.

12 months after Visit4 ()

All subjects in the group must receive an angiography evaluation at 12 months after stenting.

• Photoast Data

• Adverse events and endpoint-related events to evaluate and collect the original documents.

• In addition, the researchers will decide which antiplatelet drugs patients should receive at the end of their research treatment as part of their ongoing clinical treatment, and this transition information will be recorded.

• NYHA cardiac function rating

• Under treatment principles, if the patient did not terminate participation in the study, the 12 months or at the end of the follow-up plan to record the end point or serious adverse events.

2 years after Visit 5()

All subjects in the group must be evaluated 2 years after stenting. Follow-up assessments can be conducted either by telephone or at the research center. The following assessment must be completed at 6 months of postoperative follow-up.

• Adverse events and endpoint-related events to evaluate and collect the original documents.

• Current antiplatelet drugs. Information on dose changes, interruptions, and cessation of medication must be recorded.

Visit 6(, 3 years after surgery)

All subjects in the group must be evaluated 3 years after stenting. Follow-up assessments can be conducted either by telephone or at the research center. The following assessment must be completed at 6 months of postoperative follow-up.

• Adverse events and endpoint-related events to evaluate and collect the original documents.

• Current antiplatelet drugs. Information on dose changes, interruptions, and cessation of medication must be recorded.

Unanticipated follow-up

Additional visits for subject safety, drug dose adjustment and need to be recorded in the case report table.

Lost visit

Patients who do not follow-up by protocol and revoke informed consent will repeatedly attempt to contact and determine their life status, the occurrence of any type of myocardial infarction or stroke. If the subject misses any 2 consecutive follow-up and fails to contact (i. e. 2 phone calls, later approved letters), the subject will be deemed missed.

6.4 Drug Treatment

According to concurrent guidelines and local routine treatment of subjects. All subjects recommended aspirin load dose (300 mg), clopidogrel load dose (300 mg) or teago load dose (180 mg) before stent implantation, and recommended load dose for at least 6 hours prior to surgery. Perioperative anticoagulant therapy in all subjects included: general heparin or alternative anticoagulant (low molecular heparin, bialudine, enoxaparin) and ACT> for 250 seconds during interventional surgery. After stenting, the subject lifelong aspirin for 75-150 mg per day. Biplex antiplatelet therapy should last for at least 12 months, with the physician's determination that individual subjects may require clopidogrel / teagrelo treatment for life.

6.5 Intravascular ultrasound examination

It is recommended that intraoperative intravascular ultrasound is recommended with a 40 MHz mechanical rotating probe for intravascular ultrasound.

Inoperative IVUS Guidelines

Standardized use of intravascular ultrasound is recommended:

It is recommended to use endovascular ultrasound preoperative, during and after surgery to guide PCI, with preoperative use of nitroglycerin to prevent spasm. After full exhaust, fully pass the lesion, automatically retract with

0.5mm/s speed and record the image to the vessel opening.

Refer to the ULTIMATE study results to optimize the PCI effect under IVUS guidance:

The IVUS standard standards shall meet the following 3 requirements:

The lumen area of the distal reference vessel with the stent segment MLA greater than 5.0 mm^2, or 90% after 1,;

The patch load within the edge of 2, bracket is less than 50%;

3, has no edge mezzanine deep to mid level more than 3 mm

7. Data Management

The researchers must timely record the research data in accordance with the instructions provided in the CRF specified in the study programme.

7.1 Data Records

The investigator ensures the accuracy, completeness, and timeliness of the recorded data, and provides answers to the data queries. Trained researchers enter the data in the specified CRF data bar directory. Data will be frozen during audit, editing, and source data validation (SDV) to prevent further editing. The principal investigator signed the CRF and copies of the CRF will be archived at the Research Center.

All AE/SAEs s will be recorded in CRF and all subjects ' AEs/SAEs s occurring after the group are reported until the final visit period.

8. Ethics and Regulatory Requirements

8.1 Ethical considerations

The investigator will ensure that this study will follow the ethical principles outlined from the Helsinki Declaration of 1996; the National Ethics Review (trials) in 2007; and the 2002 international ethical guidelines for

biomedical research involving human subjects. It was conducted after obtaining the approval of the Ethics Committee of Zhongshan Hospital Affiliated to Fudan University.

8.2. Ethics Review

Copies of the test protocol, proposed informed consent, other written subjects information, and any suggested advertising materials must be submitted to IEC for written approval. A copy of the IEC written approval of the test protocol and the informed consent form must be obtained before recruiting subjects to enter the study and transport of research products.

Upon all subsequent revisions to the test protocol and all modifications to the informed consent form, the investigator must submit and obtain IEC approval if necessary. The investigator must notify local procedures of deviations or SAE, and intra-stent thrombosis, TVR, MI and death and other SAE reports obtained from the sponsor.

The investigator is responsible for obtaining annual approval and renewal of the TEC throughout the study period. Copies of the investigator report and the IEC renewal documents must be sent to the sponsor.

8.3 Informed consent form

Samples of informed consent will be provided to the investigator for use at the research center. The informed consent form used shall comply with the Good Clinical Code (GCP) guidelines of the International Coordination Conference (ICH), the ISO 14155, Helsinki Declaration, and current guidelines for applicable local regulations / laws.

Before attending the clinical trial, each subject must give written consent after the study content is fully explained to it in the easily understandable language of the subject. The subject must have the opportunity to raise

questions and to have satisfactory answers to them. Written informed consent must be properly recorded by signature and dated by the subject or his legal representative. If the subject is illiterate, an impartial witness may be required to sign on behalf of the patient. All subjects will receive a copy of the informed consent form. The consent process must be recorded in the subject's medical record.

8.4 Revision plan

This Programme must be strictly followed and can be changed only by written amendments.With appropriate approval, the revised test protocol will be distributed to all program recipients.

8.5 Scheme deviation under emergency conditions

Exit when endovascular ultrasound guided PCI due to acute complications from ultrasound.

9. Research Management

9.1 Programme Compliance

The study shall be conducted to the approved protocol and any breach or deviation shall be documented.

9.2 Scheme modification

After the protocol is approved by the Ethics Committee, if the clinical trial plan needs to be modified, the revised protocol shall be submitted to ethical approval, and if the group, the clinical trial can be continued after documents obtaining ethical approval.

10. Data management

10.1 Data collection and processing

Subject data will be collected over the Internet in a secure electronic data collection (EDC) system. The principal or associate investigator must ensure the accuracy and integrity of the recorded data and then provide electronic signatures on the corresponding eCRF.

10.2 Data quality assurance

Take the necessary control measures to ensure the accuracy and reliability of the data, including reviewing the clinical programs together with the clinical units, and making regular supervisory visits by the sponsor or other designated supervisors. During the clinical site supervision visit, review the accuracy and integrity of the case records and original data, and any errors will be preserved by the clinical unit or supervisor. Beyond this:

- Follow-up rate above 95%
- The Data Administrator challenges the data
- Important indicators for 100% verification
- Monitor 100% data of input system SDV.
- Review the data and give an audit report before the database is locked.

The case record table (Case Report Form,CRF) and the original research data are kept by the researchers, and the data management and statistical unit are responsible for the entry, cleaning, locking library and analysis report of the data.

10.3 Raw Data management

The investigator will retain all the necessary test documents and original data in the original form that support the data collected from the study subjects consistent with the ICH/GCP and SFDA GCP guidelines. Documents must be retained for at least 5 years after the completion of the clinical trial.

10.4 Deflection and system error control

All subjects who meet the inclusion / exclusion criteria and have signed an

informed consent form will be eligible for the trial. Continuous compliant subjects will be included in the study to minimize selection bias. Subjects were randomly assigned to each treatment group.

11. Statistical analysis

11.1 Statistical software

The research statistical analysis was done using SPSS (version 18.0 or later and Stata (version 12.0 or later).

11.2 Statistical Methods

Statistical description is given below:

Continuous variables: number of group description examples, number of missing cases, average, median, standard difference, quartile range, minimum, and maximum.

Classification variable: Number of missing cases, number of splitting frequencies, and percentage of the group description.

Statistical tests: All statistical tests are bilateral tests, and P values less than or equal to 0.05 will be considered to be of statistical significance. (Unless specifically specified).

Overview of s tatistical methods: different analysis methods will be adopted according to the classification of groups and data characteristics, see the statistical analysis plan for details. The main statistical analysis methods include t test, card square test, Fisher accurate probability method, ANOVA, covariance, Logistic regression, CMH card square and rank and test methods to compare the differences among different groups.

11.3 Sample size calculation

This study belongs to the pilot study and has no design sample size calculations.

12. Research results were published

The results will be published in professional academic conferences and published in the cardiovascular journal. Publication and author issues will be determined by the Steering Committee based on the overall participation in the study (drafting programs, core laboratories, responsibilities, end committee members, etc.) and the number of the patients included.

References

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