Randomized Controlled Trial of Optical Coherence Tomography Versus Angiography for Culprit Lesion Revascularization in Patients with Acute Myocardial Infarction

Optical Coherence Tomography Versus Angiography for Culprit Lesion Revascularization in Acute Myocardial Infarction PatiEnts

(FRAME-AMI3 Trial)

Version No: 1.3

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Chonnam National University Medical School

Cardiovascular Center & Clinical Research Center,
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Samsung Medical Center,
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Table of Contents

Research Summary

Study title	**Randomized Controlled Trial of Optical Coherence Tomography Versus Angiography For Culprit Lesion Revascularization in Patients with Acute Myocardial Infarction:** Optical Coherence Tomography Versus Angiography For Culprit Lesion Revascularization in Acute Myocardial Infarction Patients (**FRAME-AMI3 Trial)**
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Trial Management	Seung Hun Lee, MD, PhD (Chonnam National University) Joo Myung Lee, MD, MPH, PhD (Samsung Medical Center)
Executive Committee	Joo Myung Lee, MD, MPH, PhD (Samsung Medical Center) Young Bin Song, MD, PhD (Samsung Medical Center) Seung Hun Lee, MD, PhD (Chonnam National University) Min Chul Kim, MD, PhD (Chonnam National University)
Funding agencies	Abbott Vascular
Purpose / Objectives	The aim of the study is to compare clinical outcomes between optical coherence tomography-guided versus angiography-guided percutaneous coronary intervention (PCI) in patients with acute myocardial infarction (AMI).
Study design	Prospective, multicenter, open-label, randomized controlled trial to compare clinical outcomes between optical coherence tomography (OCT)-guided versus angiography-guided PCI in AMI patients undergoing PCI.
Subject enrollment	1500 Subjects with STEMI undergoing PCI.
Study Duration	IRB Approval dates ~ 31.DEC.2028
Eligible criteria	**1) Inclusion criteria** ① Subject must be at least 19 years of age ② Acute ST-segment elevation myocardial infarction (STEMI) *STEMI: ST-segment elevation ≥0.1 mV in ≥2 contiguous leads or documented newly developed left bundle-branch block[1] ③ Primary percutaneous coronary intervention (PCI) in < 12 h after the onset of symptoms for STEMI patients ④ Subject is able to verbally confirm understandings of risks, benefits and treatment alternatives of receiving invasive physiologic evaluation and PCI and he/she or his/her legally authorized representative provides written informed consent prior to any study related procedure. **2) Exclusion criteria** ① Target lesions not amenable for PCI by operators' decision ② Ostial lesions located in left main vessel or right coronary artery (left main body or distal bifurcation lesions can be enrolled by operator's discretion) ③ Creatinine clearance ≤30 ml/min/1.73 m^2 and not on dialysis (chronic dialysis dependent patients are eligible for enrolment regardless of creatinine clearance) ④ Cardiogenic shock (Killip class IV) at presentation ⑤ Intolerance to Aspirin, Clopidogrel, Prasugrel, Ticagrelor, Heparin, or Everolimus ⑥ Known true anaphylaxis to contrast medium (not allergic reaction but anaphylactic shock) ⑦ Pregnancy or breast feeding

	⑧ Non-cardiac co-morbid conditions are present with life expectancy <2 year or that may result in protocol non-compliance (per site investigator's medical judgment) ⑨ Unwillingness or inability to comply with the procedures described in this protocol.
Follow-up	After the index procedure, clinical follow-up will occur at 1, 6, 12, 24 months, and annually thereafter.
Primary endpoint	Target Vessel Failure (TVF, a composite of cardiac death, target-vessel myocardial infarction [MI], clinically-driven target-vessel repeat revascularization [TVR], definite or probable stent thrombosis) according to the Academic Research Consortium (ARC) II-consensus.[2]
Secondary endpoint	① All-cause death ② Cardiac death ③ Any MI, defined by Forth Universal definition of MI[1] ④ Spontaneous MI, defined by Forth Universal definition of MI[1] ⑤ Procedure-related MI, defined by ARC II definition[2] ⑥ Any revascularization (clinically-driven or ischemia-driven) ⑦ Target vessel revascularization ⑧ Definite or probable stent thrombosis ⑨ Total procedural time (primary PCI to end of the procedure including amount of staged procedure) ⑩ Total fluoroscopy time (primary PCI to end of the procedure including amount of staged procedure) ⑪ Total amount of contrast use (primary PCI to end of the procedure including amount of staged procedure) ⑫ Incidence of contrast-induced nephropathy, defined as an increase in serum creatinine of ≥0.5mg/dL or ≥25% from baseline within 48-72 hours after contrast agent exposure.

1. Title of Study

Randomized Controlled Trial of Optical Coherence Tomography Versus Angiography For Culprit Lesion Revascularization in Patients with Acute Myocardial Infarction

Abbreviation: Optical Coherence Tomography Versus Angiography For Culprit Lesion Revascularization in Acute Myocardial Infarction Patients (**FRAME-AMI3 Trial)**

2. Clinical Research Center

① Chonnam National University Hospital, Chonnam National University Medical School, Gwangju, South Korea
② Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea
③ Uijeongbu St Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea
④ Yeungnam University Medical Center, Yeungnam University College of Medicine, Daegu, South Korea
⑤ Ewha Womans University Mokdong Hospital, Seoul, South Korea
⑥ Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, South Korea
⑦ Korea University Guro Hospital, Korea University College of Medicine, Seoul, South Korea
⑧ Kosin University Gospel Hospital, Kosin University College of Medicine, Busan, South Korea
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4. Background and Hypothesis

4.1. Background

Percutaneous coronary intervention (PCI) is a standard treatment for significantly stenotic lesion of coronary arteries, especially in the setting of acute myocardial infarction (AMI) where timely reperfusion

is important.[3] Traditionally, visual assessment by coronary angiography has been the main tool to identify coronary artery disease and guide revascularization.[4] However, it is known that angiography alone is unable to adequately evaluate significance of stenotic lesion or optimization status of the stent, and that angiography suffers from high intra- and interobserver variability.[5] Thus, methods for intracoronary imaging and/or physiology have been developed to aid these limitations.[6]

During the PCI procedure, intravascular imaging devices such as intravascular ultrasound (IVUS) and optical coherence tomography (OCT) are useful tools for providing information on lesion characteristics and optimal stent implantation with regard to appropriate reference segment, stent expansion, stent apposition, and possible acute complications.[7] Therefore, intravascular imaging guidance may improve clinical outcomes after complex PCI. However, although previous randomized controlled trial and registries showed significantly lower rates of major adverse clinical events following IVUS-guided PCI compared with angiography-guided PCI,[8-13] the randomized controlled trials were limited with small sample size and dealt with very selected lesion subsets such as chronic total occlusion (CTO) or long lesions. Moreover, although some studies observed similar clinical outcomes between IVUS-guided PCI and OCT-guided PCI,[14-16] it is uncertain whether OCT-guided PCI improves clinical outcomes compared with angiography-guided PCI.

Currently, randomized controlled trial to support beneficial impact of OCT-guided PCI, especially in patients with acute myocardial infarction (AMI) is lacking. One randomized clinical trial in 2016 with 240 non-ST-elevation myocardial infarction patients have reported higher postprocedural fractional flow reserve and similar incidence of major adverse cardiac events with the use of OCT compared to angiography alone,[17] but this study mostly focused on immediate physiologic findings of OCT-guided PCI and only demonstrated clinical outcomes on short-term follow-up. Although the ILUMIEN IV trial evaluated efficacy of OCT-guided PCI among high risk patients including lesions were considered to be responsible for a recent myocardial infarction, there was no apparent difference in the target-vessel failure at 2 years.[18] There is no randomized controlled trial that can provide information on its long-term clinical impact, and current clinical guidelines puts OCT on Class 2a recommendation as an alternative for IVUS, with the exception of ostial left main disease.[19,20]

In this regard, randomized controlled trial comparing clinical outcome following PCI in patients with AMI where procedural optimization is performed under OCT-guidance or angiography alone would provide valuable evidence to enhance prognosis after treatment of AMI. Therefore, FRAME-AMI3 trial has been designed to compare clinical outcomes after PCI for infarct-related artery using either OCT-guided or angiography-guided strategy.

4.2. Primary Hypothesis

Optical coherence tomography (OCT)-guided PCI would reduce risk of a target vessel failure (TVF, a composite of cardiac death, target-vessel myocardial infarction [MI], clinically-driven target-vessel repeat revascularization [TVR], definite or probable stent thrombosis), compared with angiography-guided PCI in AMI patients undergoing PCI.

5. Study Objectives

5.1. Primary endpoint

Target Vessel Failure (TVF, a composite of cardiac death, target-vessel myocardial infarction [MI], clinically-driven target-vessel repeat revascularization [TVR], definite or probable stent thrombosis) according to the Academic Research Consortium (ARC) II-consensus.[2]

Definitions of clinical events is attached as Appendix #1.

5.2. Secondary endpoint

① All-cause death
② Cardiac death
③ Any MI, defined by Forth Universal definition of MI[1]
④ Spontaneous MI, defined by Forth Universal definition of MI[1]
⑤ Procedure-related MI, defined by ARC II definition[2]

⑥ Any revascularization (clinically-driven or ischemia-driven)
⑦ Target vessel revascularization
⑧ Definite or probable stent thrombosis
⑨ Total procedural time (primary PCI to end of the procedure including amount of staged procedure)
⑩ Total fluoroscopy time (primary PCI to end of the procedure including amount of staged procedure)
⑪ Total amount of contrast use (primary PCI to end of the procedure including amount of staged procedure)
⑫ Incidence of contrast-induced nephropathy, defined as an increase in serum creatinine of ≥0.5mg/dL or ≥25% from baseline within 48-72 hours after contrast agent exposure.

6. Research Materials and Indication for Revascularization

1) General principle of procedure for coronary artery lesions
Complete revascularization during index hospitalization will be recommended. In case of staged procedure during the same hospitalization is planned for non-infarct related artery stenosis, following the initially allocated strategy would be strongly recommended. Treatment decision regarding non-infarct related artery will be guided by angiographic stenosis (>70% diameter stenosis by visual estimation) or fractional flow reserve (≤0.80), according to operator's discretion. Use of Xience™ stents (everolimus-eluting stent) are recommended.

2) Optical coherence tomography-guided PCI group
Use of OCT will be allowed at any step of PCI (pre-PCI, during PCI and post-PCI), but OCT after stent implantation will be mandatory. In this group, the recommendations for selecting reference segment, selecting appropriate size of stent, and stent optimization are as follows. OPTIS imaging catheter (Abbott Vascular) will be used for the imaging arm according to MLD MAX algorithm.

	OCT
Reference Site	Most normal looking segment No Lipidic plaque
Stent Sizing	Operator can decide 1 of 2 methods. [1] By measuring vessel diameter at the distal reference sites (in case of ≥180° of the external elastic membrane can be identified). In this case, stent diameter will be determined using mean external elastic membrane diameter at the distal reference, rounded down to the nearest 0.25 mm (Ex> mean external elastic membrane reference diameter 3.15 mm → 3.0 mm stent diameter will be chosen). [2] By measuring lumen diameter at the distal reference sites (in case of ≥180° of the external elastic membrane cannot be identified). In this case, stent diameter will be determined using mean lumen diameter at the distal reference, rounded up to the nearest 0.25 mm (Ex> mean distal reference lumen diameter 2.55 mm, 2.75 mm stent diameter will be chosen).
Stent Length	By measuring distance from distal to proximal reference site
Stent Optimization	
● **Stent Expansion**	Visually assess residual angiographic diameter stenosis <10% "AND" ① In non-LM lesions: In-stent minimal lumen area (MSA) > 80% of the average reference lumen area "OR" >4.5 mm^2 ② In LM lesion: MSA>7 mm^2 for distal LM and >8 mm^2 for proximal LM
● **Stent Apposition**	No major malapposition (defined as a distance from stent strut to adjacent intima ≥400 um and < 1mm length) of the stent over its entire length against the vessel wall
● **Edge**	No major edge dissection in the proximal or distal reference segments,

Dissection	defined as 5 mm from the edge of the stent, extended to media layer with potential to provoke flow disturbances (defined as >60° of the circumference of the vessel at site of dissection and/or >2 mm in length of dissection flap)
Optimization technique of the stent	**If 1 of above findings are notified, additional procedure including adjunctive post-dilatation or additional stent implantation for residual reference segment disease will be mandatorily recommended.** In adjunctive post-dilatation procedure, the diameter of the non-compliant post dilatation balloon chosen should not be larger than the post-PCI OCT determined mean reference external elastic membrane diameter of one or both segments (proximal or distal), or no more than 0.5 mm larger than the mean reference segment lumen diameter of one or both segments (proximal or distal) nearest to the dilatation site (if the EEL cannot be measured).

3) Angiography-guided PCI group
The PCI procedure in this group will be performed as standard procedure. After deployment of stent, stent optimization will be done based on angiographic findings. The optimization guided by angiography should meet the criteria of angiographic residual diameter stenosis less than 10% by visual estimation and the absence of flow limiting dissection (≥Type C dissection). When angiographic under-expansion of the stent is suspected, adjunctive balloon dilatation will be strongly recommended.

4) Adjunctive treatment/procedure for both arms
Regardless of allocated arms, best available medical treatment will be the performed according to the current ACC/AHA/SCAI or ESC/EACTS guidelines.[19-22] Any adjunctive pharmacologic treatment will be left to the operator's discretion. For example, a loading dose of aspirin (300 mg) and P2Y12 inhibitor – clopidogrel (600 mg) or prasugrel (60 mg) or ticagrelor (180 mg) – or use of glycoprotein IIbIIIa inhibitor, etc**.** In case of PCI is performed, dual antiplatelet therapy is recommended according to current ACC/AHA/SCAI or ESC/EACTS guidelines and operator's discretion. In addition, in both groups, the use of invasive physiologic assessment at pre- and post-PCI will be left to operator's discretion. If the patient misses scheduled follow-up visits, other effort using telephone, e-mail to communicate with the patient will be available.

7. Study Population

1500 Subjects with STEMI undergoing primary PCI with balloon dilatation or stent implantation for revascularization will be enrolled in the present trial.

8. Study Period

IRB Approval dates ~ 31.DEC.2028
Subject enrollment: IRB approval date ~ DEC. 2026 (roughly 36 months of enrollment)
Analysis and report: ~31.DEC.2028

9. Eligible criteria, Sample size calculation

9.1. Eligible Criteria

1) Inclusion criteria

① Subject must be at least 19 years of age

② Acute ST-segment elevation myocardial infarction (STEMI)
*STEMI: ST-segment elevation ≥0.1 mV in ≥2 contiguous leads or documented newly developed left bundle-branch block[1]

③ Primary percutaneous coronary intervention (PCI) in < 12 h after the onset of symptoms for STEMI patients

④ Subject is able to verbally confirm understandings of risks, benefits and treatment alternatives of

receiving invasive physiologic evaluation and PCI and he/she or his/her legally authorized representative provides written informed consent prior to any study related procedure.

2) Exclusion criteria

① Target lesions not amenable for PCI by operators' decision
② Ostial lesions located in left main vessel or right coronary artery (left main body or distal bifurcation lesions can be enrolled by operator's discretion)
③ Creatinine clearance ≤30 ml/min/1.73 m^2 and not on dialysis (chronic dialysis dependent patients are eligible for enrolment regardless of creatinine clearance)
④ Cardiogenic shock (Killip class IV) at presentation
⑤ Intolerance to Aspirin, Clopidogrel, Prasugrel, Ticagrelor, Heparin, or Everolimus
⑥ Known true anaphylaxis to contrast medium (not allergic reaction but anaphylactic shock)
⑦ Pregnancy or breast feeding
⑧ Non-cardiac co-morbid conditions are present with life expectancy <2 year or that may result in protocol non-compliance (per site investigator's medical judgment)
⑨ Unwillingness or inability to comply with the procedures described in this protocol.

9.2. Sample Size Calculation

Hypothesis: Optical coherence tomography-guided PCI would reduce risk of a target vessel failure (TVF, a composite of cardiac death, target-vessel myocardial infarction [MI], clinically-driven target-vessel repeat revascularization [TVR], definite or probable stent thrombosis), compared with angiography-guided PCI in AMI patients undergoing PCI.

Null hypothesis: Optical coherence tomography-guided PCI would not reduce risk of a target vessel failure, compared with angiography-guided PCI in AMI patients undergoing PCI.

Based on the previous studies[23-26] which compared Intravascular OCT-guided PCI versus angiography-guided PCI in AMI patients, the following assumptions were made.

- Primary end point: Time to occurrence of TVF
- Expected annual rate of TVF
  Angiography-guidance group (6.0%) vs. OCT-guidance group (4.2%)
- Accrual time: 3 years
- Total follow-up time: 2~5 years (median 3.5 years, until 2 years after the last patient enrollment)
- 1:1 Randomization
- Drop-out rates: total 4.0% up to 2-year

Based on the above assumption, **a total of 1500 patients** (750 patients for OCT guidance group and 750 patients for angiography guidance group) will provide 80% power at a 2-sided alpha of 5%.

9.3. Recruitment

All consecutive patients with AMI will be screened for enrollment in this study. A member of each research team should review the patients' medical history for eligibility. If all eligibility criteria are met and written informed consent is provided, the patient may be enrolled in the study. Prior to collecting study data, the details of the study will be explained to the participant including: (1) that the study represents a phase IV clinical trial, (2) that participation is voluntary, and there is no penalty for withdrawal, (3) potential risks and benefits for participation, and (4) contact information for additional concerns. Vulnerable subjects are excluded according to the eligible criteria.

10. Methods

10.1. Study designs

Before primary PCI for STEMI, the patients who are eligible for enrollment without any exclusion criteria will be randomized 1:1 at the time of enrollment to undergo either OCT-guided strategy or angiography-guided strategy for PCI.

After identification of infarct-related artery and lesion, intervention will be done per operator's decision. As recommended, OCT will be allowed to be used at any step of PCI but OCT at post-stent implantation will be mandatory in OCT-guided PCI group. According to the pre-defined criteria for stent optimization, determination of stent site and length, assessment of stent expansion and apposition state as well as identification of acute complication will be done. On the other hand, stent optimization will be done based on angiographic findings in angiography-guided PCI group. Optimization criteria should include residual diameter stenosis less than 10% by visual estimation and absence of acute complication including flow limiting dissection.

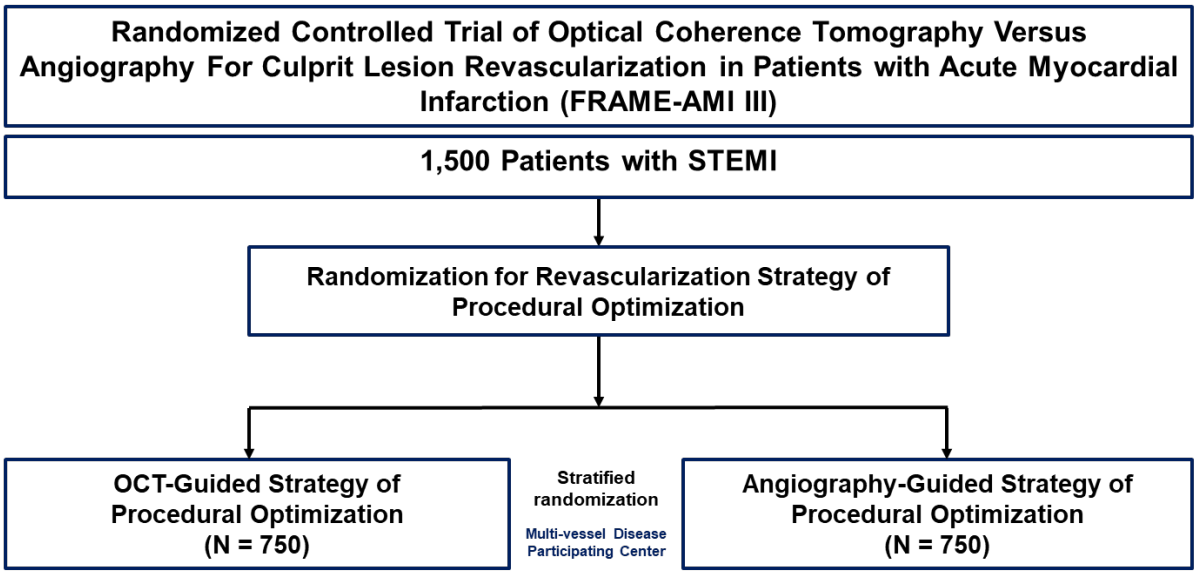
If malapposition, underexpansion or edge dissection of stent is identified in any of the group, adjunctive therapy such as post-dilation by balloon or additional stent implantation is mandatorily recommended.

If any violation of the recommendation of protocols (for example, OCT is not used in the OCT-guided PCI group, or OCT is used in the angiography-guided PCI group) occurs according to operator's discretion, the specific reasons will be mandatorily described in electronic case report form.

Regarding the extent of revascularization, complete revascularization during index hospitalization will be recommended based on the current ACC/AHA/SCAI or ESC/EACTS guidelines.[19-22].

Regardless of allocated arms, best available medical treatment will be the performed according to the current ACC/AHA/SCAI or ESC/EACTS guidelines. Any adjunctive pharmacologic treatment will be left to the operator's discretion. For example, a loading dose of aspirin (300 mg) and P2Y12 inhibitor – clopidogrel (600mg), prasugrel (60 mg bolus) or ticagrelor (180mg) – or use of GPIIbIIIa inhibitor, etc**.** Duration and dosing of dual antiplatelet therapy after initial PCI is recommended as with the current guideline. If the patient misses scheduled follow-up visits, other effort using telephone or e-mail to communicate with the patient will be available.

10.2. Flow chart



Trial Design	Superiority testing of OCT-guided strategy of procedural optimization
Time Frame	Accrual Time 3 Years, Follow-up Time 2 Years from Last Patient Enrollment (Median 3.5 Years)
Primary Endpoint	Target Vessel Failure (TVF, a composite of cardiac death, target-vessel myocardial infarction [MI], clinically-driven target-vessel repeat revascularization [TVR], definite or probable stent thrombosis)
Secondary Endpoints	All-cause death, cardiac death, any MI, spontaneous MI, procedure-related MI, target vessel revascularization, any revascularization, Academic Research Consortium (ARC)-definite or probable stent thrombosis, total procedural time, total fluoroscopy time, total amount of contrast use, or incidence of contrast-induced nephropathy

10.3. Randomization

Patients will be randomized to either the OCT guidance group or angiography guidance group at the time of enrollment with 1:1 ratio. Stratified randomization according to participating center and presence of multi-vessel disease will be performed. This process will be done by a web-based randomization program, run by an independent organization (S-software, Seoul, Korea).

11. Schedule of Assessments and Procedures

Visit	Screening & Baseline -30day	Post-Procedure	Follow Up					
			1 month ±14days	6 month ±30days	1 year ±30days	2 years ±30days	3, 4 ~ years ±90days	SCV
Medical/Clinical History (age, sex, risk factors, clinical dx, angina status, cardiac hx)	×							
Informed Consent	×							
Inclusion/Exclusion Criteria	×							
Brief Physical Examination	×							
Vital status	×		×	×	×	×		
Weight, height	×							
12 lead ECG[1)]	×	×	×			×		
Angiogram[2)]	×	×						
Randomization	×							
Quantitative coronary angiography[2)]	×	×						
Intravascular imaging[3)]	×	×						

Visit	Screening & Baseline -30day	Post-Procedure	Follow Up					
			1 month ±14days	6 month ±30days	1 year ±30days	2 years ±30days	3, 4 ~ years ±90days	SCV
CBC	×					×		
Electrolytes, LFT	×					×		
Creatinine, BUN	×	×				×		
Fasting plasma TG, HDL, LDL, total cholesterol	×		×	×	×	×		
Fasting glucose level	×					×		
HbA1C	×					×		
Medications[4)]	×	×	×	×	×	×		
CK, CK-MB, Troponin I or Troponin T[5)]	×	×						
BNP/NT-proBNP	×					×		
Clinical event[6)]		×	×	×	×	×	×	×

1) Except pre- and post-PCI cardiac biomarkers, lack of blood laboratory tests will not be regarded as protocol violation.
2) Coronary angiograms (with or without coronary physiologic test) will be systematically collected and analyzed by quantitative coronary angiography in independent core laboratory in Chonnam National University Hospital.
3) Images will be systematically collected and analyzed in independent core laboratory in Chonnam National University Hospital.
4) Medication profiles include baseline and discharge medications.
5) Baseline (pre-PCI) and post-PCI cardiac biomarkers (CK, CK-MB, and high sensitive troponin) will be mandatorily collected to adjudicate periprocedural MI.
6) Clinical events including primary and secondary endpoints will be systematically collected. Clinical follow-up will occur at 1, 6, 12, 24 months after the procedure, and annually thereafter. Angiographic follow-up is not routinely recommended to all participants. Investigator or designee may conduct follow-up as telephone contacts or office visits. Last follow-up will be finished 24 months after last patient enrollment.

12. Measurement of study outcome variables

12.1. Visit 1 Screening & Baseline(-30day)

① Informed consent

Informed consent will be acquired before diagnostic coronary angiography and randomization will be performed before or during PCI in patients without exclusion criteria. However, as this study includes patients in critical medical conditions who need primary PCI for AMI, in patients presenting with conditions that preclude their understanding of the trial process, informed consent will be obtained after stabilization by revascularization of target lesion.

Before any examination, they will be informed about the study aims, procedures, and possible risks and the Investigator will ensure that the patient or the patient's legally acceptable representative has provided written informed consent. Written consent should include signature and date of legally authorized representatives and investigator. If possible, verbal consent of patient will be obtained. When written consent is obtained from the patient after the procedure, the patient will voluntarily choose to or not to participate in this study. After coronary interventions are performed, written consent of patients should be obtained at the earliest possible time.

A copy of the signed consent form will be given to the subject or legal representative of the subject and the original will be maintained with the subject's records.

② Inclusion/Exclusion Criteria

Refer to 'Eligible Criteria'

③ Medical/Clinical History

Demographic information (age, sex, risk factors, clinical diagnosis, angina status, cardiac history, cardiovascular, and cerebral event) will be recorded at Screening & Baseline.

Relevant medical history, including history of current disease, other pertinent cardiac history, and information regarding underlying diseases will be recorded at Screening & Baseline

④ Brief Physical Examination, Height and Weight, Vital signs
Height, weight, blood pressure and pulse will be measured

⑤ 12 lead ECG, Angiogram
Angiogram will be obtained at Screening & baseline visits. [At the time of the index PCI] ECG at follow up visits will only be obtained when clinically indicated such as recurrent chest pain, ischemia, or significant arrhythmias, heart failure or other signs or symptoms of clinical instability

⑥ Randomization
Patients will be randomized to either the OCT-guided strategy or angiography-guided strategy at the time of enrollment with 1:1 ratio. Stratified randomization by participating center and presence of ST elevation in ECG will be performed. This process will be done by a web-based randomization program, run by an independent organization.

⑦ Intravascular imaging/ Quantitative coronary angiography

The raw data of intravascular imaging measurement data will be analyzed in the Core-Laboratory in Chonnam National University Hospital. The post-procedural data will be collected in case PCI is performed. Baseline and post-primary PCI for coronary angiography will be collected and undergo quantitative coronary angiographic evaluation in the Core-Laboratory in Chonnam National University Hospital.

⑧ Clinical Laboratory Measurements

CBC	WBC, RBC, Hb, Hct, Platelet count, WBC differential count
Electrolytes, LFT	AST, ALT, ALP, T. Bilirubin Na, Ca, P, K, Cl
Chemistry profile	Creatinine, BUN, Fasting glucose level, HbA1c, Fasting plasma TG, HDL, LDL, Total cholesterol
Cardiac enzymes	CK, CK-MB, Troponin I or Troponin T, BNP/NT-proBNP

⑨ Concomitant Medication
Concomitant medication will be documented at Baseline/Screening and at follow-up. Dose, route, unit frequency of administration, and indication for administration and dates of medication will be captured.

12.2. Visit 2 (Post-Procedure)

① 12 lead ECG
ECG at follow up visits will only be obtained when clinically indicated such as recurrent chest pain, ischemia, or significant arrhythmias, heart failure or other signs or symptoms of clinical instability

② Intravascular imaging/ Quantitative coronary angiography

The raw data of intravascular imaging measurement data will be analyzed in the Core-Laboratory in Chonnam National University Hospital. The post-procedural data will be collected in case PCI is performed.

Baseline and post-primary PCI for coronary angiography will be collected and undergo quantitative coronary angiographic evaluation in the Core-Laboratory in Chonnam National University Hospital.

③ Clinical Laboratory Measurements

Chemistry profile	Creatinine, BUN
Cardiac enzymes	CK, CK-MB, Troponin I or Troponin T

④ Adverse events/ Serious Adverse Event
Information regarding occurrence of adverse events (death, MI or repeat revascularization, etc) will be captured throughout the study. Duration (start and stop dates and times), severity/grade, outcome, treatment and relation to procedure will be recorded on the case report form (eCRF).

⑤ Concomitant medication

Concomitant medication will be documented at Baseline/Screening and at follow-up. Dose, route, unit frequency of administration, and indication for administration and dates of medication will be captured.

12.3. Follow-up

Follow-up will occur at 1, 6, 12 and 24months. Investigator or designee may conduct follow-up as office visits.

① Vital signs

Blood pressure and pulse will be measured.

② 12 lead ECG

ECG at follow up visits will only be obtained when clinically indicated such as recurrent chest pain, ischemia, or significant arrhythmias, heart failure or other signs or symptoms of clinical instability.

③ Clinical Laboratory Measurements

- Clinical Laboratory Measurements will be done at 24months

CBC	WBC, RBC, Hb, Hct, Platelet count, WBC Differential count
Electrolytes, LFT	AST, ALT, ALP, Total Bilirubin, Na, Ca, P, K, Cl
Chemistry profile	Creatinine, BUN, Fasting glucose level, HbA1C,
Cardiac enzyme	NT-proBNP

- Clinical Laboratory Measurements will be test at 1, 6, 12 and 24months

Chemistry profile	Fasting plasma TG, HDL, LDL, Total cholesterol

④ Concomitant Medication

⑤ Adverse events/ Serious Adverse Event

Information regarding occurrence of adverse events (death, MI or repeat revascularization, etc) will be captured throughout the study. Duration (start and stop dates and times), severity/grade, outcome, treatment and relation to procedure will be recorded on the case report form (eCRF).

13. Potential risk and adequacy of protection against risks

Complications of OCT imaging includes coronary dissection, thrombus formation, transient ST-elevation, bradycardia, ventricular arrhythmia, coronary spasm, etc. Previous studies reported little to no serious adverse events related to OCT, and almost all complications were self-limiting which resolved after catheter retrieval.[27-29] Therefore, OCT is deemed safe procedure which poses no additional hazard in conducting this study.[28,29]

Complications caused by angiography itself are commonly shown in complications from insertion of guidewire, balloon dilatation or stent insertion, which does not cause additional risks related to procedures or devices used in the study.

Patients are randomized at a 1:1 ratio to two arms, **OCT-guided strategy arm** and **Angiography-guided strategy arm. The possibility to be assigned to each arm is 50% each.**

Expected adverse events in each arm are as follows:

1) OCT-guided strategy arm – adverse events related to OCT

OCT catheter itself is 2.7F thick which can cause damage to a coronary artery when forcefully inserted, resulting in complications such as coronary spasm, coronary dissection or perforation. Also the entry of OCT catheter could disrupt thrombose or cause blockage of narrow lesion. However, previous studies demonstrated rare incidence of adverse events, most of which were self-limiting, and reported no significant difference in safety profile compared to intravascular ultrasound (IVUS) or angiography-guided PCI.[27-29]

Of note is the fact that OCT uses contrast injection to acquire imaging, and that OCT-guided PCI uses significantly higher volume of contrast compared to IVUS-guided or angiography-guided PCI.[15,16] While this could pose higher risk of contrast-induced nephropathy, studies report no significant difference in the incidence of nephropathy.[17,29]

3) Both arms – adverse events related to angiography and PCI

- Complications during procedures
If coronary angiography is only performed, its death rate is very low, but it will increase with old age, significant decrease in heart function, severe heart failure, severe heart valve diseases, serious lesion of coronary artery origin, and other critical medical conditions. Other than those, there might be complications related to arteries such as myocardial infarction, stroke, and severe bradycardia or tachycardia.
- Complications after procedures
The most common complications are hematoma in insertion area, bleeding, complications involving arteries and veins, and other local complications such as infection. Complications related contrast agents are skin rash, urticaria, nausea or vomiting, headache, hypotension, fever, and stiffness. Severe complications like anaphylactic shock caused by contrast agent are very rarely shown. Conditions like kidney dysfunction, arrhythmia, chest pain and others due to uses of contrast agents may occur, which is very unlikely to be observed.

Methods of safety monitoring will be given at the bottom of this page.

14. Subject withdrawal

Once enrolled, each Subject should remain in the study until the required follow-up period is completed. However, all Subjects have the right to withdraw at any point during the study without penalty or loss of benefit. The investigator may discontinue any Subject at any time if medically necessary.

The following events will result in terminating the patient's follow-up:

① Patient voluntary withdrawal
② Patient withdrawn by investigator as clinically indicated

If the study treatment(s) or observations are discontinued in any Subject, the reason will be recorded, and the data coordinating center must be notified promptly.

15. Violence of study protocol

Although the strategy of stent selection and optimization during PCI for AMI subjects will be decided by randomization process to either OCT-guided strategy or angiography-guided strategy, specific response to information acquired through OCT or angiography will be left to operator's discretion according to the clinical situation. However, the followings will be recorded as protocol violation and the reason will be recorded and the data coordinating center must be notified promptly.

① OCT was not used after stent implantation (OCT-guided strategy arm).
② OCT was used in the angiography-guided PCI group.

16. Event adjudication and reporting, Data safety and monitoring plan

16.1. Data safety and monitoring plan

Type of Report	Prepared by Staffs for:	Time limit of notification
Serious adverse event	IRB	According to IRB regulation of Site
	DCC/EC/Principle investigator DSMB	Within 48 hours
Annual progress report	EC/Principle investigator	Submitted per 1 year
Deviations from investigational plan	IRB	According to IRB regulation of Site
	EC/Principle investigator	Notify within 7 days.
Final summary report	EC/Principle investigator	Within 1 month

*DCC: Data Coordinating Center, EC: Executive Committee (Co-researchers)

16.2. Executive Committee

	Name	Center	Position

Chairman	Young Joon Hong	Chonnam National University Hospital, Chonnam National University	Professor
	Joo-Yong Hahn	Samsung Medical Center, Sungkyunkwan University School of Medicine	Professor
Committee members	Seung Hun Lee	Chonnam National University Hospital, Chonnam National University	Assistant Professor
	Joo Myung Lee	Samsung Medical Center, Sungkyunkwan University School of Medicine	Assistant Professor
	Young Bin Song	Chonnam National University Hospital, Chonnam National University	Professor
	Min Chul Kim	Chonnam National University Hospital, Chonnam National University	Assistant Professor

16.3. Serious Adverse Events

The definition of serious adverse events is in the following paragraph. **It must be reported to the principal investigator within 48hours after recognition of the event and to the IRB according to IRB regulation of site.**

① Results in persistent or significant disability or incapacity (significant, persistent or permanent change or disruption in subject's body function/structure, physical activity or quality of life

② Requires in-patient hospitalization or prolongs hospitalization

③ Results in a congenital anomaly/birth defect or,

④ Life-threatening events or death

Clinical events include not only TVF, all death, stent thrombosis, stroke, but also other endpoint events. Clinical events and safety data will be reported to principal investigator regularly, and examined by staffs for subject's safety throughout the study.

The coordinating center needs to report progress to Executive committee and principal investigator annually. This study will not be stopped early based on efficacy results.

16.4. Event adjudication Committee

All primary and secondary events will be independently adjudicated by Event Adjudication Committee.

	Name	Center	Position
Chairman	Hyun Kuk Kim	Chosun University Hospital, Gwangju, Korea	Professor
Committee members	Sung-Woo Cho	Inje University Paik Hospital, Ilsan, Korea	Assistant Professor
	Doyeon Hwang	Seoul National University Hospital, Seoul, Korea	Assistant Professor

16.5. Data Safety and Monitoring Board

All serious adverse events will be reviewed by independent DSMB.

	Name	Center	Position
Chairman	Joon-Hyung Doh	Inje University Paik Hospital, Ilsan, Korea	Professor
Committee members	Seon Woo Kim	Academic Research Service Headquarter, LSK Global PS, Seoul, Korea	Executive ARS Director
	Sang Yeob Lim	Korea University Ansan Hospital, Ansan, Korea	Professor

16.6. Data safety monitoring plan

The principal investigator will make the monitoring manager to visit and examine coordinating centers regularly. A designated trial monitor will review data not only for completeness, but also for accordance of the hospital data and eCRF data. Compliance with the protocol and adverse events will be also examined. This trial monitor may inspect all documents and required records that are maintained by the

Investigator/site, including medical records (office, clinic, or hospital) for the subjects in this trial. The coordinating centers will permit access to such records.

17. Statistical Consideration and Analysis

17.1. Analysis Population

All subjects are to be randomized in a 1:1 fashion to either OCT-guided strategy or Angiography-guided strategy group. All primary and secondary endpoints will be analyzed both on an intention-to-treat basis (all subjects analyzed as part of their assigned treatment group).

For intention-to-treat analysis, all subjects who signed the written informed consent form and are randomized in the study will be included in the analysis sample, regardless of whether the correct treatment was administered, or whether crossover occurred.
Per-protocol population will be defined as population who did not violate the study protocol. The definition of protocol violation is as follows;

① **OCT was not used after stent implantation (OCT-guided strategy arm).**

② **OCT was used in the angiography-guided PCI group.**

Analysis with Per-protocol population will be performed as exploratory and sensitivity analysis for that of intention-to-treat population.

17.2. Primary Endpoint Analysis

Primary endpoints (target vessel failure) will be analyzed firstly on an intention-to-treat basis (all subjects analyzed as part of their assigned treatment group), and then, per-protocol basis. The null hypothesis will be evaluated with Kaplan-Meier survival with log rank test. All primary and secondary endpoints will be analyzed on per-patient basis.

17.3. Secondary Endpoint Analysis

The individual components of primary composite outcome will be analyzed on an intention-to-treat basis and per-protocol basis.
Other secondary endpoints including all-cause and cardiac death, any myocardial infarction with or without periprocedural myocardial infarction and any revascularization, will be analyzed using χ^2-test and Kaplan-Meier survival with log rank test. Acute success of procedure (device, lesion, and procedure), incidence of contrast-induced nephropathy will be analyzed using χ^2-test.
Total amount of contrast use, total procedural time, and total fluoroscopy time will be compared between the two groups with independent sample t-test.

17.4. Treatment of Missing Values

The primary analysis of the study endpoints will not be covariate adjusted. No imputation meth ods will be used to infer missing values of baseline variables. For the study endpoints, patients lost to follow-up and subsequently lost to assessment of primary endpoint, will be considered to be censored in the estimation of Kaplan-Meier event rates. As a secondary analysis, we will also e xamine the patients who have been lost to follow-up. We will perform a comparison of baseline characteristics in patients with vs. without follow up. In addition, a sensitivity analysis will be pe rformed to assess the impact of these patients on the study outcomes. For patients lost to foll ow-up, multiple imputation techniques will be used to calculate pooled estimates of the treatme nt effect and confidence intervals which will then be compared to the primary statistical analysi s.

17.5. Multivariate Analyses

Multivariate predictors of all primary and secondary endpoints will be determined using multivariate regression models, using either binary or Cox's proportional hazard method. Forward or backward stepwise selection algorithms will be used to select predictors as needed. Baseline demographic and clinical variables that are predictive at the 0.1 level will be included in the models. The purpose of this is twofold: to do a covariate adjusted analysis of treatment for all primary and secondary endpoints and

to identify the risk factors which are associated with the study endpoints. The included covariates in univariate analysis will be as with Table 1.

Table 1.

Demographics	***Cardiac Risk Factors***	***Severity of AMI***
Age, years	Current smoker	Killip Class
Gender	Previous PCI	
Diabetes mellitus	Previous CABG	
Hypertension	Previous MI	
Dyslipidemia	Previous CHF	
Peripheral artery disease	Previous CVA	
Chronic kidney disease	Family history of CAD	
	LV ejection fraction	
	LV dysfunction (LVEF<30%)	
Complexity of CAD	***Medication at discharge***	
Angiographic disease extent	Aspirin	
1VD	Prasugrel	
2VD	Clopidogrel	
3VD	Statin	
No. of treated lesion/patients	ACE inhibitor/ Angiotensin-II	
Type B2 or C lesions†	receptor blocker	
At least 1 ISR	Beta-blocker	
At least 1 Bifurcation	Calcium-channel blocker	
At least 1 Small vessel*		
At least 1 Long lesion**		
Severe calcification		

† Type B2 or C lesions according to ACC/AHA classification.
*small vessel denotes lesion with reference diameter ≤2.75mm
**long lesion denotes lesion with length ≥20mm

17.6. Survival Analyses

All time-to-event outcomes will be summarized using Kaplan-Meier survival estimates and compared between treatment groups using log-rank tests.

17.7. Pre-specified subgroup analysis

① Pre-specified sub-analysis regarding imaging-related parameters
- Comparison of TVF according to optimized versus un-optimized procedure defined by prespecified imaging protocols
- Prognostic impact of 3 major imaging parameters (stent expansion, stent malapposition, and edge dissection)

② Pre-specified subgroup analysis will be performed in various subgroups
- Intended timing of non-infarct related artery (non-IRA) PCI (during primary PCI, staged PCI during same hospitalization)
- Complete revascularization defined by residual SYNAX of 0
- IRA involving LM or LAD vs. non-LM or non-LAD
- Sex
- Age
- Left ventricular ejection fraction
- Diabetes mellitus
- Type of P2Y12 inhibitor (Clopidogrel, Ticagrelor, Prasugrel)

18. Care for the safety of the subjects

18.1. Institutional Review Board (IRB) / Ethical Committee Approval

Institutional Review Board / Ethical Committee approval for the protocol and informed consent form will be obtained by the investigator prior to study participation. The approval letter must be signed by the

IRB Chairperson or authorized representative prior to beginning the present study. No changes will be made to the protocol or informed consent form without appropriate approval from the IRB. According to IRB requirements, the investigator will report study progress until it is completed. Further, any protocol amendments as well as associated informed consent changes will be submitted to the IRB and written approval must be obtained prior to implementation.

18.2. Elements of Informed Consent

This trial will involve patients with AMI who need primary PCI with balloon dilatation or stent implantation for revascularization. We anticipate enrolling 1500 patients with a mean age in the 60s. Pregnant women and patients under the age of 18 will be excluded from the trial for ethical and safety concerns. Prior to collecting study data, the details of the study will be explained to the participant including: (1) that the study represents a phase IV clinical trial, (2) that participation is voluntary, and there is no penalty for withdrawal, (3) potential risks and benefits for participation, and (4) contact information for additional concerns. Patients are informed of the purpose of the study, the treatment alternative, the random manner of assignment to treatment, the need to be available for telephone follow-up and return clinic visits at regular intervals for questionnaires and/or medical tests, and of their options to accept or refuse entry into the study without affecting their clinical care.

All patients or legally authorized patient representatives must sign the current IRB approved informed consent form prior to any study-related activities and the index procedure. Failure to obtain signed informed consent will render the patient ineligible for the study. However, as this study includes patients in critical medical conditions who need primary percutaneous coronary intervention (PCI) within 12 hours for STEMI after the onset of symptoms, written consent from legally authorized representatives or verbal consent from patients should be obtained in advance. After coronary interventions are performed, written consent of patients should be obtained at the earliest possible time.

The signed informed consent will be kept in the patient's medical records and a copy given to the patient or legally authorized patient representative. All sources of research materials will be in the form of medical records, coronary angiograms, electrocardiograms and routine blood work. This material will be obtained both for routine medical care as well as for research purposes.

18.3. Confidentiality

The confidentiality of protected health information shall be maintained by all parties involved at all times throughout the clinical trial. All data should be secured against unauthorized access. Study patients will be assigned a unique coded identifier on electronic case report form (eCRF). Patient data will be protected by the use of locked cabinets at the Clinical Centers and use of passwords, data encryption and secure, limited access storage of electronic data. The explicit issue of privacy and confidentiality is outlined in the Informed Consent Form.

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Appendix #1. Definitions of Clinical Events

Anticipated Adverse Event

Any undesirable experience (sign, symptom, illness, abnormal laboratory value, or other medical event) occurring to a patient, whether or not considered related to the investigational product(s) or drug regimen prescribed as part of the protocol, predefined in the protocol and/or IFU, that is identified or worsens or occurs in frequency that is not considered normal during a clinical trial. See also: Adverse Event (AE), Serious Adverse Event (SAE).

Adverse Event (AE)

An AE is any untoward medical occurrence in a patient or clinical investigation when the patient was administered a study product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product whether or not related to the study product. See also: Anticipated Adverse Event, Serious Adverse Event (SAE).

Cerebrovascular accident (CVA)

Sudden onset of vertigo, numbness, aphasia, dysarthria or central neurologic deficit secondary to vascular lesions of the brain such as hemorrhage, embolism, thrombosis, or rupturing aneurysm, that persists for > 72 hours

* CVA type

Hemorrhagic: A stroke with documentation on imaging (e.g., CT scan or MRI of hemorrhage in the cerebral parenchyma, or a subdural or subarachnoid hemorrhage). Evidence of hemorrhagic stroke obtained from lumbar puncture, neurosurgery, or autopsy can also confirm the diagnosis.

Nonhemorrhagic: A focal neurological deficit that results from a thrombus or embolus (and not due to hemorrhage) that appears and is still partially evident for more than 24 hours

Unknown/no imaging performed: if the type of stroke could not be determined by imaging or other means (from lumbar puncture, neurosurgery, or autopsy)

Contrast-induced Nephropathy

contrast-induced nephropathy is defined as an increase in serum creatinine of ≥0.5mg/dL or ≥25% from baseline within 48-72 hours after contrast agent exposure.

Death

Death defined by the Academic Research Consortium II[2] is as follows:

All death is considered to be cardiac death unless an unequivocal noncardiac cause can be established. Specifically, any unexpected death even in patients with coexisting potentially fatal noncardiac disease (eg, cancer, infection) should be classified as cardiac. The cause of death (cardiac vs. non-cardiac) will be adjudicated by an independent clinical event adjudication committee

Cardiac death: Any death due to proximate cardiac cause (eg, myocardial infarction, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, and all procedure-related deaths,

including those related to concomitant treatment, will be classified as cardiac death.

Vascular death: Death caused by noncoronary vascular causes, such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular diseases.

Non-cardiovascular death: Any death not covered by the above definitions, such as death caused by infection, malignancy, sepsis, pulmonary causes, accident, suicide, or trauma.

Myocardial Infarction (MI)

The definition of myocardial infarction used in this trial is based on the Academic Research Consortium II and Fourth Universal Definition of Myocardial Infarction with modification.[1,2]

The term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. Under these conditions any one of the following criteria meets the diagnosis for MI:

1. 1) Detection of a rise and/or fall of cardiac troponin (cTn) with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:

▪ Symptoms of ischemia.

▪ New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB).

▪ Development of pathological Q waves in the ECG.

▪ Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

▪ Identification of an intracoronary thrombus by angiography or autopsy.

2) For recurrent MI including MI originated from non-culprit lesions in patients with elevated and are stable or falling cTn values during the index hospitalization, cTn must rise by >20% and be at least 5 times the 99th percentile URL. Additionally, new ischemic symptoms of at least 20 minutes and new significant ST–T changes or new LBBB are required. These ECG changes must be distinct from the original myocardial infarction and not due to the usual ECG evolution of this event.

2. Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.

3. 1) Percutaneous coronary intervention (PCI) related MI is defined by absolute rise in cardiac troponin (from baseline) ≥35 times URL plus 1 (or more) of the following criteria: (i) new significant* Q waves or equivalent; (ii) flow-limiting angiographic complications; or (iii) new “substantial” loss of myocardium on imaging (e.g., echocardiography).

* Q-wave criteria requires the development of new Q waves ≥40 ms in duration and ≥1 mm deep in voltage in ≥ 2 contiguous leads

2) For procedure-related MI from PCI for non-culprit lesions, angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or a side branch occlusion/thrombus, disruption of collateral flow, or distal embolization need to be confirmed.

4. Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL.

5. Coronary artery bypass grafting (CABG) related MI is arbitrarily defined by elevation of cardiac biomarker values (>10 × 99th percentile URL) in patients with normal baseline cTn values (≤99th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographic documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

Revascularization

Revascularization is defined by the Academic Research Consortium II[2] as follows:

Target lesion revascularization: TLR is defined as any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion. All TLRs should be classified prospectively as clinically indicated* or not clinically indicated by the investigator prior to repeat angiography. An independent angiographic core laboratory should verify that the severity of percent diameter stenosis meets requirements for clinical indication and will overrule in cases where investigator reports are not in agreement. The target lesion is defined as the treated segment from 5 mm proximal to the stent and to 5 mm distal to the stent.

Target vessel Revascularization: TVR is defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel. The target vessel is defined as the entire major coronary vessel proximal and distal to the target lesion, which includes upstream and downstream branches and the target lesion itself.

Non-Target Lesion Revascularization (non-TLR): Any revascularization in a lesion other than the target lesion is considered a non-target lesion revascularization.

Non-Target Vessel Revascularization (non-TVR): Any revascularization in a vessel other than the target vessel is considered a non-target vessel revascularization.

[1] Clinically indicated revascularization: A revascularization is considered clinically indicated if angiography at follow-up shows a percent diameter stenosis ≥ 50% (core laboratory quantitative coronary angiography assessment) and if one of the following occurs:

(1) A positive history of recurrent angina pectoris, presumably related to the target vessel;

(2) Objective signs of ischemia at rest (ECG changes) or during exercise test (or equivalent), presumably related to the target vessel;

(3) Abnormal results of any invasive functional diagnostic test (eg, Doppler flow velocity reserve, fractional flow reserve);

(4) A TLR or TVR with a diameter stenosis ≥ 70% even in the absence of the above-mentioned ischemic signs or symptoms.

[2] Ischemia driven revascularization is defined as a revascularization procedure with one of the followings,

A positive history of recurrent angina pectoris, presumably related to the target vessel

Objective signs of ischemia at rest (EKG changes) or during exercise test (or equivalent), presumably related to the target vessel

Abnormal results of any invasive functional diagnostic test (eg, fractional flow reserve)

Stent Thrombosis

Stent thrombosis is defined and discussed by the Academic Research Consortium II[2] as follows:

Stent thrombosis should be reported as a cumulative value at the different time points and with the different separate time points. Time 0 is defined as the time point after the guiding catheter has been removed and the subject left the catheterization laboratory.

Timing

Acute stent thrombosis*	0-24 hours post stent implantation
Subacute stent thrombosis*:	> 24 hours-30 days post stent implantation
Late stent thrombosis†:	> 30 days-1-year post stent implantation
Very late stent thrombosis†:	> 1-year post stent implantation

* Acute/subacute can also be replaced by early stent thrombosis. Early stent thrombosis (0-30 days) is currently used in the community.

† Including “primary” as well as “secondary” late stent thrombosis; “secondary” late stent thrombosis is a stent thrombosis after a target segment revascularization.

Stent Thrombosis Categories: a) Definite b) Probable, and c) Possible

a) Definite stent thrombosis: Definite stent thrombosis is considered to have occurred by either angiographic or pathologic confirmation.

Angiographic confirmation of stent thrombosis [*The incidental angiographic documentation of stent occlusion in the absence of clinical signs or symptoms is not considered a confirmed stent thrombosis (silent occlusion).]: The presence of a thrombus [†Intracoronary thrombus] that originates in the stent or in the segment 5 mm proximal or distal to the stent and presence of at least 1 of the following criteria within a 48-hour time window:

. Acute onset of ischemic symptoms at rest

. New ischemic ECG changes that suggest acute ischemia

. Typical rise and fall in cardiac biomarkers (refer to definition of spontaneous MI)

. Nonocclusive thrombus: Intracoronary thrombus is defined as a (spheric, ovoid, or irregular) noncalcified filling defect or lucency surrounded by contrast material (on 3 sides or within a coronary stenosis) seen in multiple projections, or persistence of contrast material within the lumen, or a visible embolization of intraluminal material downstream.

. Occlusive thrombus: TIMI 0 or TIMI 1 intrastent or proximal to a stent up to the most adjacent proximal side branch or main branch (if originates from the side branch).

Pathological confirmation of stent thrombosis: Evidence of recent thrombus within the stent determined at autopsy or via examination of tissue retrieved following thrombectomy.

b) Probable stent thrombosis: Clinical definition of probable stent thrombosis is considered to have occurred after intracoronary stenting in the following cases:

. Any unexplained death within the first 30 days [‡ For studies with ST-elevation MI population, one may consider the exclusion of unexplained death within 30 days as evidence of probable stent thrombosis.]

. Irrespective of the time after the index procedure, any MI that is related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause

c) Possible stent thrombosis: Clinical definition of possible stent thrombosis is considered to have occurred with any unexplained death from 30 days after intracoronary stenting until end of trial follow-up.