Supplementary data

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Supplementary methods

Inclusion and exclusion criteria

Inclusion criteria

① Subject must be at least 19 years of age
② Coronary artery disease requiring percutaneous coronary intervention (PCI)
③ Patients with a complex lesion defined as:
    1) True bifurcation lesion (Medina 1,1,1/1,0,1/0,1,1) with side branch ≥ 2.5 mm
    2) Chronic total occlusion (≥ 3 months) as target lesion
    3) Unprotected left main (LM) disease PCI (LM ostium, body, distal LM bifurcation, including nontrue bifurcation)
    4) Long coronary lesions (implanted stent ≥ 38 mm in length)
    5) Multivessel PCI (≥ 2 vessels treated at 1 PCI session)
    6) Multiple stents needed (≥ 3 stents per patient)
    7) In-stent restenosis lesion as target lesion
    8) Severely calcified lesion (encircling calcium in angiography)
    9) Ostial coronary lesion (left anterior descending artery, left circumflex artery, right coronary artery)
④ Subject is able to verbally confirm understandings of risks, benefits and treatment alternatives of receiving invasive evaluation and PCI and he/she or his/her legally authorized representative provides written informed consent prior to any study-related procedure

Exclusion criteria

① Target lesions not amenable to PCI based on operators' review
② Cardiogenic shock (Killip class IV) at presentation
③ Intolerance to aspirin, clopidogrel, prasugrel, ticagrelor, heparin, or everolimus
④ Known true anaphylaxis to contrast medium (not allergic reaction but anaphylactic shock)
⑤ Pregnancy or breast feeding
⑥ Noncardiac comorbid conditions are present with life expectancy < 1 year or that may result in protocol noncompliance (per site investigator's medical judgment)
⑦ Unwillingness or inability to comply with the procedures described in this protocol

Primary and secondary endpoints

Primary endpoint	
Target vessel failure	A composite of cardiac death, target vessel MI, and clinically-driven target vessel revascularization
Secondary endpoints	
Target vessel failure without procedure-related MI	
Cardiac death or target vessel MI	
All-cause death	
Cardiac death	
Target vessel MI with procedure-related MI	
Target vessel MI without procedure-related MI	
Any MI with procedure-related MI	
Any MI without procedure-related MI	
Nontarget vessel related MI	
Target lesion revascularization	
Target vessel revascularization	
Any revascularization (clinically-driven)	
Stent thrombosis	
Incidence of contrast-induced nephropathy	
Total amount of contrast use	
Total procedural time	
Total medical cost–not reported in this publication	

MI, myocardial infarction.

Supplementary statistical analysis

Hypothesis: An intravascular imaging-guided PCI strategy for patients with complex coronary artery lesions would reduce target vessel failure (a composite of cardiac death, target vessel myocardial infarction, and target vessel revascularization) compared with an angiography-guided PCI strategy.

Null hypothesis: An intravascular imaging-guided PCI strategy for patients with complex coronary artery lesions would not reduce target vessel failure (a composite of cardiac death, target vessel myocardial infarction, and target vessel revascularization) compared with an angiography-guided PCI strategy.

Reported event rates in previous studies of complex PCI

Study	Sample size	Time point	MACE		
			Intravascular imaging-guided PCI	Angiography-guided PCI	Relative risk reduction, %
ADAPT-DES[1]	8665	1 y	3.1%	4.7%	34.0%
AVIO trial[2]	284	2 y	16.9%	23.2%	27.2%
HOME DES IVUS[3]	210	1.6 y	11.0%	12.0%	8.3%
RESET[4]	543	1 y	4.5%	7.3%	38.4%
CTO-IVUS[5]	402	1 y	2.6%	7.1%	63.4%
IVUS-XPL[6]	1400	1 y	2.9%	5.8%	50.0%

The current trial was designed as a superiority trial to follow enrolled patients until a prespecified follow-up duration of the last patient enrolled. Since the follow-up duration of the previous studies varied, we assumed that the annual incidence of target vessel failure in the angiography-guided PCI group would be 6.0%, based on the results of the CTO-IVUS, RESET, and IVUS-XPL trials. These 3 studies were selected because they were randomized trials conducted in South Korea and the follow-up duration was 1 year. As presented in the above table, the relative risk reduction of target vessel failure of the 3 studies ranged from 38.4% to 63.4%. To be conservative, we assumed that the relative risk reduction at 1 year would be 40% and, in turn, the annual incidence of target vessel failure in the intravascular imaging-guided PCI group would be 3.6%.

Sample size calculation

- Primary endpoint: Time to occurrence of target vessel failure (a composite of cardiac death, target vessel myocardial infarction, and target vessel revascularization)
- Assumed annual event rate of target vessel failure:
  - Intravascular imaging-guided PCI group (3.6%) vs angiography-guided PCI group (6%)
- Alpha = 0.05 (2-sided), β = 10%, power (1- β) = 90%
- Accrual time: 3 years
- Total follow-up time: 1 year after last patient enrollment (median 2.5 years)

- 2:1 randomization
- Primary statistical method: Kaplan-Meier survival analysis with log-rank test
- Assumed dropout: total 5.0%

Based on the above assumptions, a total of 1620 patients (1080 and 540 patients for the intravascular imaging-guided group and the angiography-guided group, respectively) would be needed to evaluate the primary hypothesis with consideration of dropouts.

Consideration of 2:1 randomization

Although previous randomized controlled trials were potentially limited by enrolling a small number of patients, limited follow-up duration, or enrolling patients with highly selected coronary artery lesion subsets, they consistently showed the potential benefit of intravascular imaging-guided PCI compared with angiography-guided PCI.[2,3,5,7,8] In this regard, the executive committee members tried to maximize the potential benefit of intravascular imaging-guided PCI in the treatment of complex coronary artery lesions. While we did not collect the exact proportion of PCI cases done with intravascular imaging guidance from all the participating centers, the adoption rate of intravascular imaging-guided PCI in Korea is about 27.5% to 28.6% according to the Korean Percutaneous Coronary Intervention (K-PCI) Registry, which includes 92 participating centers.[9] Considering the adoption rate of intravascular imaging-guided PCI in Korea, a 2:1 randomization ratio should not introduce bias when interpreting the trial results.

Definition of clinical events

Death

Death, as defined by the Academic Research Consortium, is as follows:[10]

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

Cardiac death: Any death due to a proximate cardiac cause (eg, myocardial infarction, low-output failure, fatal arrhythmia), unwitnessed death and death from unknown cause, and all procedure-related deaths, including those related to concomitant treatment, were classified as cardiac death.

Noncardiac 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

The definition of myocardial infarction used in this trial was based on the Third Universal Definition of Myocardial Infarction for spontaneous myocardial infarction,[11] and the definition of Society for Cardiovascular Angiography and Interventions for procedure-related myocardial infarction.[12]

Spontaneous myocardial infarction

Myocardial infarction was considered to be present when there was evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia.[11] Under these conditions any one of the following criteria meets the diagnosis for myocardial infarction:

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

- Symptoms of ischemia
- New or presumed new significant ST-segment T-wave 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) 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) Stent thrombosis associated with myocardial infarction 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 1 value above the 99th percentile upper reference limit.

Procedure-related myocardial infarction

Procedure-related myocardial infarction was defined as follows:[12]

1) In patients with normal baseline CK-MB, myocardial infarction was considered to have occurred when the peak CK-MB measured within 48 hours of the procedure rose to at least 10 times the local laboratory upper reference limit; or to at least 5 times the upper reference limit with new pathologic Q-waves in at least 2 contiguous leads or new persistent LBBB; or, in the absence of CK-MB measurements and a normal baseline cardiac troponin (cTn), a cTn (I or T) level measured within 48 hours of the PCI rose to at least 70 times the local laboratory upper reference limit; or at least 35 times the upper reference limit with new pathological Q-waves in at least 2 contiguous leads, or new persistent LBBB

2) In patients with an elevated baseline CK-MB (or cTn) in whom the biomarkers were stable or falling, the definition was based on when CK-MB (or cTn) rose by an absolute increment equal to those levels recommended above from the most recent preprocedure level.

3) In patients with an elevated baseline CK-MB (or cTn) in whom the biomarker levels were not shown to be stable or falling, the definition was based on when CK-MB (or cTn) rose by an absolute increment equal to those levels recommended above plus new ST-segment elevation or depression plus signs consistent with a clinically relevant MI, such as new onset or worsening heart failure or sustained hypotension.

Revascularization

A coronary revascularization procedure could be either a PCI or a coronary artery bypass grafting surgery. Revascularization is defined by the Academic Research Consortium[10] as follows:

The revascularized coronary segments were subclassified as:

Target lesion: A target lesion was defined as a lesion revascularized in the index procedure (or during a planned or provisional staged procedure). The LM target lesion extends from the left main stem ostium to the end of the 5 mm proximal segments of the left anterior descending and left circumflex arteries as well as the ramus intermedius if the latter vessel has a vessel diameter of at least 2 mm.

Target vessel: The target vessel was defined as the entire major coronary vessel proximal and distal to the target lesion including upstream and downstream branches and the target lesion itself. The LM and any vessel originating from the LM, or its major branches was, by definition, considered a target vessel for the purposes of this trial.

Target vessel nontarget lesion: The target vessel nontarget lesion was a lesion in the epicardial vessel or branch or graft that contains the target lesion; however, this lesion was outside of the target lesion by at least 5 mm distal or proximal to the target lesion determined by quantitative coronary angiography.

Nontarget vessel: The nontarget vessel was any vessel that did not undergo attempts at revascularization at the index procedure but was subsequently revascularized.

Target lesion revascularization: Target lesion revascularization was defined as any repeat PCI of the target lesion or bypass surgery of the target vessel performed for restenosis or another complication of the target lesion. All target lesion revascularizations were classified prospectively as clinically indicated or not clinically indicated by the investigator prior to repeat angiography. An independent angiographic core laboratory verified that the severity of the percent diameter stenosis met the requirements for clinical indication and overruled cases where investigator reports were not in agreement. The target lesion was defined as the treated segment from 5 mm proximal to the stent to 5 mm distal to the stent.

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

Nontarget lesion revascularization: Any revascularization in a lesion other than the target lesion was considered a nontarget lesion revascularization.

Nontarget vessel revascularization: Any revascularization in a vessel other than the target vessel was considered a nontarget vessel revascularization.

All revascularization events were adjudicated as either clinically driven or nonclinically driven. Revascularization was considered clinically driven if the diameter stenosis of the revascularized coronary segment was at least 50% on quantitative coronary angiography and any of the following criteria for ischemia were met:

- A positive functional study corresponding to the area served by the target lesion; or
- Ischemic ECG changes at rest in a distribution consistent with the target vessel; or
- Typical ischemic symptoms related to the target lesion; or
- Positive invasive physiologic test (fractional flow reserve ≤ 0.80 or instantaneous wave-free ratio ≤ 0.89); or
- The presence of stenosis with at least 70% diameter stenosis, even in the absence of other criteria

Stent thrombosis

Stent thrombosis is defined by the Academic Research Consortium[10] as follows:

1) Timing: *a)* acute, *b)* subacute, *c)* late, and *d)* very late

Acute stent thrombosis[a]	0-24 hours after stent implantation
Subacute stent thrombosis[a]	More than 24 hours to 30 days after stent implantation
Late stent thrombosis[b]	More than 30 days to 1 year after stent implantation
Very late stent thrombosis[b]	More than 1 year after stent implantation

[a] Acute/subacute can also be replaced by early stent thrombosis. Early stent thrombosis (0-30 days) is currently used to define stent thrombosis occurring from day 0 to day 30 by the international interventional cardiology community.

[b] This definition includes "primary" as well as "secondary" late stent thrombosis; "secondary" late stent thrombosis was defined as stent thrombosis that occurred after a target segment revascularization.

2) Stent thrombosis categories: *a)* definite, *b)* probable, and *c)* possible

Definite stent thrombosis: Definite stent thrombosis was considered to have occurred on either angiographic or pathologic confirmation.

Angiographic confirmation of stent thrombosis: The presence of an intracoronary thrombus that originated in the stent or in the segment 5 mm proximal or distal to the stent and the presence of at least 1 of the following criteria within a 48-hour time window:

- Acute onset of ischemic symptoms at rest; or
- New ischemic ECG changes that suggested acute ischemia; or
- Typical rise and fall in cardiac biomarkers (refer to the definition of spontaneous myocardial infarction); or
- Nonocclusive thrombus: intracoronary thrombus was defined as a (spherical, ovoid, or irregular) noncalcified filling defect or lucency surrounded by contrast material (on 3 sides or within a coronary stenosis) observed in multiple projections during coronary angiography, or the persistence of contrast material within the lumen, or a visible embolization of intraluminal material downstream.
- Occlusive thrombus: defined as Thrombolysis in Myocardial Infarction (TIMI) grade 0 flow (no flow of contrast after the thrombotic stenosis) or TIMI grade 1 flow (flow past the thrombotic stenosis not filling the vessel entirely) within the stent or proximal to a stent up to the most adjacent proximal side branch or main branch (if the stent originated 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.

[2] Probable stent thrombosis: The clinical definition of probable stent thrombosis was considered to have occurred after intracoronary stenting in the following cases:

- Any unexplained death within the first 30 days; or
- Irrespective of the time after the index procedure, any myocardial infarction that was 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.

[3] Possible stent thrombosis: The clinical definition of possible stent thrombosis was considered to have occurred with any unexplained death from 30 days after intracoronary stenting until the end of trial follow-up.

Contrast-induced nephropathy

Contrast-induced nephropathy was defined as an increase in serum creatinine of at least 0.5 mg/dL or at least 25% from baseline within 48 to 72 hours after exposure to a contrast agent.[10]

Protocol for intravascular imaging device use and angiography-guided PCI

PCI was performed using standard techniques. The drug-eluting stents used were either biodegradable polymer-coated everolimus-eluting stents (Synergy, Boston Scientific Corporation, San Jose, CA, USA) or biocompatible polymer-coated everolimus-eluting stents (Xience, Abbott Vascular, St. Paul, MN, USA). The trial limited stent choice to these drug-eluting stents due to the well-validated efficacy and safety profiles of biodegradable polymer-coated everolimus-eluting stents and biocompatible polymer-coated everolimus-eluting stents,[13] the fact that these 2 stents have the highest market share in Korea, and the availability of these drug-eluting stents in all participating centers.

In patients assigned to intravascular imaging-guided PCI, the choice of intravascular imaging device (IVUS or OCT) was at the operators' discretion. While the use of intravascular imaging was allowed at any step of the PCI procedure (prior to intervention, during PCI, and after stent implantation or angioplasty when performed as a standalone procedure), evaluation after PCI using intravascular imaging was mandated for optimization of the stented segment.

Standard protocols for image acquisition were used with the IVUS (Opticross^{TM}, Boston Scientific Corporation, San Jose, CA, USA) or OCT (Dragonfly^{TM}, Abbott Vascular, St. Paul, MN, USA) devices. Before advancing the intravascular imaging catheter, intracoronary nitroglycerin (100 to 200 μg) was administered. For IVUS, the transducer was pulled back automatically at a speed of 0.5 mm per second. For OCT, preheated contrast media at 37°C was flushed through the guiding catheter at a rate of 2 to 4 mL per second for approximately 3 to 6 seconds using an injector pump to obtain the OCT images. However, the final choice of pullback speed for the IVUS device and the injection rate and amount of contrast media used during OCT imaging were also left to the operators' discretion. If a staged procedure was performed during the same hospitalization, it was strongly recommended that the operator follow the initially allocated imaging or angiography guidance strategy.

Protocols for selecting the reference segments for the lesion, choosing selecting the appropriate size of the stent, and stent optimization were prespecified based on previous reports in the literature.[14] In brief, proximal and distal reference sites were determined at cross-sections adjacent to the target lesion (at least 5 mm apart) that had the largest lumen and a plaque burden of less than 50% on IVUS. Using OCT, proximal and distal reference sites were also determined at cross-sections adjacent to the target lesion (at least 5 mm apart) that had the most normal appearance and were free of lipid-containing plaque. The criteria used to determine optimal stent expansion were a residual angiographic diameter stenosis (defined by percent diameter stenosis; ([mean reference vessel diameter – minimum lumen diameter]/mean reference vessel diameter) x 100) of less than 10% and a minimum stent area (defined by the lumen area measured by intravascular imaging devices at the site of the narrowest lumen inside the stented segment) greater than 80% of the average reference lumen area or an absolute minimum stent area greater than 5.5 mm^2 on IVUS or 4.5 mm^2 on OCT for a stenosis, except if the lesion was in the left main coronary artery. For a left main stenosis, an absolute minimum stent area greater than 7 mm^2 for the distal left main coronary artery and greater than 8 mm^2 for the proximal left main coronary artery were used as optimization criteria, respectively.[14]

An optimized procedural result in the intravascular imaging-guided PCI group was defined as sufficient stent expansion without major stent malapposition and edge dissection. Specific definitions are provided in the table below.

Major stent malapposition was defined as an acute malapposition with the distance of at least 0.4 mm between the vessel wall and the stent, with a longitudinal length of more than 1 mm. Major edge dissection was defined as a dissection occurring within 5 mm from the edge of the stent, extending to the medial layer with a dissection angle of at least 60° of the circumference of the vessel or at least 3 mm in length of the dissection flap. If any of the above findings were identified by the intravascular imaging devices, additional procedures, including adjunctive postdilatation or additional stent implantation followed by further intravascular imaging, were recommended to optimize the final results.

To avoid perforation, the noncompliant balloon diameter was recommended to be no larger than the nearest reference vessel diameter or up to 0.5 mm larger than the mean reference lumen diameter after PCI, based on findings from intravascular imaging. The maximal inflation pressure of the noncompliant balloon was left to the operator; however, it was recommended that the noncompliant balloon be inflated to a pressure above the nominal rated pressure for the balloon. If a major edge dissection was identified by intravascular imaging, additional stent implantation was recommended; the stent size selected was based on findings from the intravascular imaging study. After additional procedural optimization, the intravascular imaging study should be repeated until the acquisition of the optimized results, as described above. However, operators could decide to consider the procedure finished if they believed that there was a potential risk of complications associated with further procedural optimization interventions.

	IVUS	**OCT**
Reference sites	Largest size vessel lumen; Plaque burden <50%; At least 5 mm away from the target lesion	Most normal looking segment; No lipid-containing plaque; At least 5 mm away from the target lesion
Stent sizing	Vessel diameter (external elastic membrane) is measured at the proximal and distal reference sites. The averaged value of the proximal and distal reference external elastic membrane diameter is used to determine the stent diameter.	Vessel diameter is measured at the distal reference sites (in cases where ≥180° of the external elastic membrane can be identified). Stent diameter is determined using the mean external elastic membrane diameter at the distal reference, rounded down to the nearest 0.25 mm. For example, if the mean external elastic membrane reference diameter is measured as 3.15 mm,

	IVUS	OCT
		then a 3.0 mm stent diameter will be selected. OR The lumen diameter is measured at the distal reference sites (in cases where ≥ 180° of the external elastic membrane cannot be identified). Stent diameter is determined using the mean lumen diameter at the distal reference, rounded up to the nearest 0.25 mm. For example, if the mean distal reference lumen diameter is 2.55 mm, then a 2.75 mm stent diameter will be selected.
Stent length	By measuring the distance from the distal to the proximal reference site.	
Stent optimization		
● **Stent expansion**	Visually assess that the residual angiographic diameter stenosis is < 10% "AND" ● Nonleft main coronary artery lesions: in-stent minimal stent lumen area > 80% of the average reference lumen area "OR" a minimal stent area of >5.5 mm^2 on IVUS and > 4.5 mm^2 on OCT. ● Left main coronary artery lesions: minimal stent luminal area of >7 mm^2 for a distal left main coronary artery stenosis and > 8 mm^2 for a proximal left main coronary artery stenosis on IVUS.	
● **Stent apposition**	No major malapposition (defined as an acute malapposition of ≥ 0.4 mm with longitudinal extension > 1 mm) of the stent over its entire length against the vessel wall.	
● **Edge dissection**	No major edge dissection in the proximal or distal reference segments, defined as a location that is 5 mm from the edge of the stent, extends to the medial layer with potential to provoke flow disturbances (defined as ≥ 60° of the circumference of the vessel at the site of a dissection or ≥ 3 mm in length of the dissection flap).	
Stent optimization technique	**If any of above findings are identified, additional procedural intervention, including additional postdilatation of the stent or additional stent implantation is recommended.** For additional postdilatation of the stent, the diameter of the noncompliant balloon should not be larger than the IVUS or OCT	

	IVUS	OCT
	determined mean reference external elastic membrane diameter assessed after stenting of 1 or both segments (proximal or distal), or if the external elastic membrane cannot be measured, no more than 0.5 mm larger than the mean reference segment lumen diameter of 1 or both segments (proximal or distal) nearest to the dilation site.	

Among patients assigned to the angiography-guided PCI group, stent optimization was assessed and performed based on angiographic findings. A stent was considered optimized if the angiographic residual diameter stenosis was less than 10% by visual estimation and there was no flow-limiting dissection (type C through F dissection). When underexpansion of the stent was suspected based on angiography, adjunctive balloon dilatation using noncompliant balloons was recommended. To avoid perforation, the noncompliant balloon diameter was recommended to be no larger than the nearest reference vessel diameter, or up to 0.5 mm larger than the mean reference lumen diameter after PCI. The maximal inflation pressure of the noncompliant balloon was left to the operator's discretion; however, it was recommended that the noncompliant balloon inflation pressure be at least above the nominal rated pressure of the balloon. Additional procedural optimization was recommended until the optimized results (as described above) were obtained. Operators could decide to consider the procedure finished if they believed that there was a potential risk of complications associated with additional procedural optimization interventions.

After the index PCI procedure, dual antiplatelet therapy was recommended for at least 3 to 6 months in patients with stable ischemic heart disease and 6 to 12 months in those with acute coronary syndrome, regardless of allocated arms.[15,16] However, the loading, maintenance dose, and duration of dual antiplatelet therapy were left to the physicians' discretion. Regardless of patient assignment, guideline-directed medical therapy was recommended according to the current American College of Cardiology/ American Heart Association/ Society of Coronary Angiographers and Interventionalists or the European Society of Cardiology/European Association for Cardiothoracic Surgery guidelines.[17,18] All coronary angiograms and intravascular imaging data were analyzed by the independent core laboratories.

Supplementary Tables

Supplementary Table 1. Baseline characteristics of patients according to TIMI risk score for secondary prevention

	Low-risk by TRS-2P < 3 (n = 1247)	High-risk by TRS-2P ≥ 3 (n = 392)	*P*
Characteristics			
Age, y	63.8 ± 9.6	71.2 ± 9.8	< .001
Male sex	1009 (80.9)	291 (74.2)	.005
Body mass index, kg/m²	24.8 ± 3.2	24.7 ± 3.4	.547
Initial presentation			.084
Stable ischemic heart disease	621 (49.8)	186 (47.4)	
Unstable angina	414 (33.2)	120 (30.6)	
Acute myocardial infarction	212 (17.0)	86 (21.9)	
Medical history			
Hypertension	636 (51.0)	369 (94.1)	< .001
Diabetes mellitus	324 (26.0)	293 (74.7)	< .001
Dyslipidemia	602 (48.3)	238 (60.7)	< .001
Current smoking	185 (14.8)	122 (31.1)	< .001
Family history of premature CAD	81 (6.5)	17 (4.3)	.147
Chronic kidney disease	91 (7.3)	205 (52.3)	< .001
Previous PCI	266 (21.3)	129 (32.9)	< .001
Previous myocardial infarction	76 (6.1)	41 (10.5)	.005
Previous stroke	40 (3.2)	72 (18.4)	< .001
Peripheral artery disease	12 (1.0)	32 (8.2)	< .001
LV ejection fraction, %	59.9 ± 10.7	55.0 ± 13.4	< .001
Discharge medication			
Aspirin	1222 (98.0)	384 (98.0)	.999
$P2Y_{12}$ inhibitor			
Any	1220 (97.8)	383 (97.7)	.999
Clopidogrel	896 (71.9)	320 (81.6)	< .001
Ticagrelor	167 (13.4)	42 (10.7)	.194
Prasugrel	157 (12.6)	21 (5.4)	< .001
Oral anticoagulant	52 (4.2)	23 (5.9)	.206
Statin	1203 (96.5)	364 (92.9)	.004

Beta blocker	503 (40.3)	207 (52.8)	< .001
ACE inhibitor or ARB	679 (54.5)	266 (67.9)	< .001

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; CAD, coronary artery disease; LV, left ventricular; PCI, percutaneous coronary intervention.

Data are presented as No. (%) or mean ± standard deviation.

Supplementary Table 2. Baseline angiographic and procedural characteristics of patients according to TIMI risk score for secondary prevention

Characteristics	Low-risk by TRS-2P < 3 (n = 1247)	High-risk by TRS-2P ≥ 3 (n = 392)	*P*
Target lesion characteristics			
Complex coronary lesions			
Chronic total occlusion	245 (19.6)	74 (18.9)	.793
True bifurcation	284 (22.8)	75 (19.1)	.147
Unprotected left main disease	140 (11.2)	52 (13.3)	.315
Long coronary lesion	685 (54.9)	213 (54.3)	.882
Multivessel PCI	457 (36.6)	165 (42.1)	.060
Multiple stents implanted	229 (18.4)	76 (19.4)	.704
In-stent restenosis lesion	152 (12.2)	84 (21.4)	< .001
Severely calcified lesion	158 (12.7)	73 (18.6)	.004
Ostial coronary lesion	194 (15.6)	57 (14.5)	.684
Number of complex coronary lesions ≥ 3	366 (29.4)	139 (35.5)	.026
Arteries with stenosis			<.001
1-vessel disease	444 (35.6)	82 (20.9)	
2-vessel disease	457 (36.6)	164 (41.8)	
3-vessel disease	346 (27.7)	146 (37.2)	
Procedural characteristics			
Total no. of target lesions treated	1.5 ± 0.7	1.5 ± 0.7	.294
Radial access	1015 (81.4)	238 (60.7)	<.001
Intravascular imaging devices used	831 (66.6)	260 (66.3)	.957
Intravascular ultrasound	601/831 (72.3)	212/260 (81.5)	.004
Optical coherence tomography	230/831 (27.7)	48/260 (18.5)	.004
Adjunctive noncompliant balloon used	879 (70.5)	255 (65.1)	.049
Rotablation used	35 (2.8)	18 (4.6)	.114
Treatment devices used			.185
Drug-eluting stent	1217 (97.6)	377 (96.2)	
Drug-coated balloon angioplasty	30 (2.4)	15 (3.8)	
Total no. of devices used per patient	1.9 ± 1.0	2.0 ± 1.1	.044
Dimensions of devices, mm			
Total length	54.9 ±32.4	57.6 ±33.0	.153
Mean diameter	3.1 ± 0.4	3.1 ± 0.4	.172
Volume of contrast media used, mL	213.6 ±114.6	187.5 ±120.3	<.001
Procedural time, min	73.2 ±41.1	79.2 ±50.6	.031
Procedural success	1241 (99.5)	387 (98.7)	.185

PCI, percutaneous coronary intervention.

The data are presented as No. (%) or mean ± standard deviation.

Supplementary Table 3. Lesion-level analysis of intravascular imaging according to TIMI risk score for secondary prevention

Characteristics	IVUS-guided PCI (n = 1188)[a]			OCT-guided PCI (n = 361)		
	Low-risk (n = 889)	High-risk (n = 299)	*P*	Low-risk (n = 296)	High-risk (n = 65)	*P*
Location of target lesion			.087			.118
Left main artery	111 (12.5)	38 (12.7)		12 (4.1)	3 (4.6)	
Left anterior descending artery	376 (42.3)	111 (37.1)		165 (55.7)	26 (40.0)	
Circumflex artery	176 (19.8)	52 (17.4)		50 (16.9)	13 (20.0)	
Right coronary artery	226 (25.4)	98 (32.8)		69 (23.3)	23 (35.4)	
Profile of intravascular imaging use			.899			.257
Pre-PCI evaluation only	4 (0.4)	2 (0.7)		10 (3.4)	0 (0)	
Post-PCI evaluation only	209 (23.5)	70 (23.4)		73 (24.7)	14 (21.5)	
Both pre- and post-PCI evaluation	676 (76.0)	227 (75.9)		213 (72.0)	51 (78.5)	
Pre-PCI analysis						
Proximal reference						
External elastic membrane area, mm^2	17.6 ± 5.4	17.5 ± 5.2	.702	14.3 ± 4.5	11.3 ± 3.6	.015
Lumen area, mm^2	10.6 ± 3.9	9.8 ± 3.5	.008	8.6 ± 3.0	7.7 ± 2.8	.108
Plaque burden, %	39.6 ± 10.9	43.8 ± 10.8	<.001	38.2 ± 8.8	39.4 ± 7.6	.635
Minimal lumen area, mm^2	2.4 ± 0.9	2.3 ± 0.9	.809	1.8 ± 1.2	1.7 ± 0.8	.276
Maximal plaque burden at MLA, mm^2	80.6 ± 7.1	81.8 ± 6.6	.032	NA	NA	
Distal reference						
External elastic membrane area, mm^2	10.6 ± 4.8	11.2 ± 5.3	.109	8.7 ± 3.6	8.0 ± 3.4	.431
Lumen area, mm^2	6.9 ± 2.9	6.7 ± 2.8	.231	5.7 ± 2.6	5.6 ± 2.3	.788
Plaque burden, %	31.9 ± 12.2	37.1 ± 13.7	<.001	35.6 ± 9.9	35.0 ± 9.0	.821
Lesion length, mm	32.9 ± 18.6	34.8 ± 18.8	.200	33.2 ± 13.9	30.6 ± 11.7	.268
Dimensions of devices, mm						
Mean diameter	3.15 ± 0.47	3.07± 0.44	.011	3.1 ± 0.4	3.2 ± 0.5	.181
Total length	38.5 ± 20.3	40.0 ± 19.6	.281	38.0 ± 18.1	33.4 ± 15.8	.061
Post-PCI analysis						
Stent expansion, %	71.9 ± 17.3	70.8 ± 16.2	.328	74.8 ± 18.6	79.8 ± 18.9	.068
Minimum stent area, mm^2	5.9 ± 2.1	5.5 ± 1.9	.010	5.2 ± 1.9	5.4 ± 2.0	.616
Prespecified optimization criteria[b]						
Plaque burden at stent landing zone < 50%	829 (93.3)	261 (87.3)	.002	NA	NA	NA
Optimal stent expansion[c]	551 (62.0)	171 (57.2)	.162	217 (73.3)	54 (83.1)	.136
Edge dissection						
Any edge dissection	27 (3.0)	9 (3.0)	.999	37 (12.5)	10 (15.4)	.673
Major edge dissection[d]	6 (0.7)	1 (0.3)	.819	8 (2.7)	4 (6.2)	.306

Stent malapposition						
Any stent malapposition	37 (4.2)	14 (4.7)	.827	54 (18.2)	19 (29.2)	.068
Major stent malapposition[e¶]	3 (0.3)	7 (2.3)	.004	23 (7.8)	8 (12.3)	.348
Optimized results (met all the above criteria)	518 (58.3)	141 (47.2)	.001	193 (65.2)	45 (69.2)	.634

The data are presented as No. (%) or mean ± standard deviation.

[a] Among the total 1623 lesions in the intravascular imaging-guided PCI group, core laboratory analysis could not be performed for 74 lesions due to insufficient lesion coverage, suboptimal image quality, manual pullback of the IVUS catheter, or lack of raw data of intravascular imaging.

[b] Protocols for selecting reference segment, selecting appropriated size of stent, and stent optimization were prespecified and are described in the Supplementary Appendix.

[c] Optimal stent expansion was defined as visually assess residual angiographic diameter stenosis <10% and in-stent minimum stent area (MSA) >80% of the average reference lumen area or absolute MSA >5.5 mm^2 (IVUS) and >4.5 mm^2 (OCT). For left main stenosis, MSA >7 mm^2 for distal left main and >8 mm^2 for proximal left main was used as optimization criteria.

[d] Major edge dissection was defined as 5mm 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 ≥3 mm in length of dissection flap).

[e] Major malapposition was defined as an acute malapposition of ≥ 0.4 mm with longitudinal extension >1 mm of the stent over its entire length against the vessel wall.

Supplementary Table 4. Lesion-level analysis of imaging-guided PCI and angiography-guided PCI according to TIMI risk score for secondary prevention

Characteristics	Low-risk by TRS-2P < 3 (n = 1841)			High-risk by TRS-2P ≥ 3 (n = 597)		
	Imaging-guided PCI (n = 1224)	Angiography-guided PCI (n = 617)	*P*	Imaging-guided PCI (n = 399)	Angiography-guided PCI (n = 198)	*P*
Location of target vessel			.493			.837
Left main artery	123 (10.0)	51 (8.3)		41 (10.3)	22 (11.1)	
Left anterior descending artery	554 (45.3)	298 (48.3)		147 (36.8)	78 (39.4)	
Circumflex artery	238 (19.4)	119 (19.3)		75 (18.8)	32 (16.2)	
Right coronary artery	309 (25.2)	149 (24.1)		136 (34.1)	66 (33.3)	
Quantitative coronary angiography						
Pre-PCI QCA						
Proximal reference vessel diameter, mm	3.2 ± 0.5	3.1 ± 0.5	< .001	3.2 ± 0.5	3.1 ± 0.5	.599
Distal reference vessel diameter, mm	2.8 ± 0.5	2.7 ± 0.4	.256	2.7 ± 0.5	2.7 ± 0.5	.924
Minimum lumen diameter, mm	0.44 ± 0.36	0.45 ± 0.37	.730	0.42 ± 0.37	0.42 ± 0.36	.997
Diameter stenosis, %	85.3 ± 11.5	85.1 ± 11.7	.664	85.9 ± 11.6	85.8 ± 11.6	.920
Lesion length, mm	28.4 ± 15.8	26.4 ± 14.1	.006	28.2 ± 16.3	28.1 ± 16.9	.945
Post-PCI QCA[*]						
Minimum lumen diameter, mm	2.8 ± 0.5	2.7 ± 0.5	.002	2.7 ± 0.5	2.7 ± 0.5	.684
Diameter stenosis, %	9.5 ± 8.2	9.8 ± 8.7	.432	10.6 ± 10.9	10.4 ± 8.2	.804
Post-PCI residual stenosis<10%	835/1176 (71.0)	415/599 (69.3)	.486	263/384 (68.5)	125/187 (66.8)	.764
Adjunctive noncompliant balloon used	756 (61.8)	287 (46.5)	< .001	224 (56.1)	84 (42.4)	.002
Rotablation used	28 (2.3)	9 (1.5)	.308	14 (3.5)	8 (4.0)	.925
Treatment devices used			.572			.613
Drug-eluting stent	1158 (94.6)	579 (93.8)		369 (92.5)	180 (90.9)	
Drug-coated balloon angioplasty	66 (5.4)	38 (6.2)		30 (7.5)	18 (9.1)	
Total no. of devices used per treated lesion	1.3 ± 0.5	1.2 ± 0.5	.011	1.3 ± 0.5	1.4 ± 0.6	.191
Dimensions of devices, mm						

Total length	38.1 ± 19.7	36.2 ± 17.5	.039	37.6 ± 19.0	39.1 ± 21.0	.355
Mean diameter	3.1 ± 0.5	3.0 ± 0.4	< .001	3.1 ± 0.5	3.0 ± 0.5	.809
Procedural success	1208 (98.7)	612 (99.2)	.475	393 (98.5)	194 (98.0)	.901

PCI, percutaneous coronary intervention; QCA, quantitative coronary angiography.

The data are presented as No. (%) or mean ± standard deviation.

*Quantitative coronary angiography after PCI was not available for 92 lesions in 84 patients.

Supplementary Table 5. Clinical endpoints of patients with low and high ischemic risk

Endpoints	Low-risk by TRS-2P < 3 (n = 1247)	High-risk by TRS-2P ≥ 3 (n = 392)	Hazard ratio (95%CI)	*P*
Primary endpoint				
Target vessel failure	83 (7.2)	53 (15.5)	2.13 (1.51-3.00)	< .001
Secondary endpoints				
Target vessel failure without procedure-related MI	52 (4.8)	36 (11.3)	2.31 (1.51-3.53)	< .001
Cardiac death or target vessel-related MI	52 (4.5)	44 (12.5)	2.79 (1.87-4.17)	< .001
Cardiac death or spontaneous target vessel-related MI	20 (1.9)	27 (8.3)	4.48 (2.51-7.99)	<.001
All-cause death	29 (3.2)	41 (13.3)	4.67 (2.90-7.52)	< .001
Cardiac death	12 (1.1)	21 (6.5)	5.76 (2.83-11.71)	< .001
Myocardial infarction	44 (3.8)	31 (9.1)	2.31 (1.46-3.66)	< .001
Target vessel-related MI	42 (3.5)	26 (6.9)	2.02 (1.24-3.29)	.005
Spontaneous MI	9 (0.9)	8 (2.3)	2.98 (1.15-7.73)	.025
Procedure-related MI	33 (2.6)	19 (4.8)	1.85 (1.05-3.25)	.033
Nontarget vessel related MI	3 (0.3)	5 (2.2)	5.50 (1.31-23.01)	.020
Repeat revascularization	62 (6.0)	25 (8.7)	1.36 (0.86-2.17)	.192
Target vessel revascularization	41 (3.8)	16 (5.2)	1.31 (0.74-2.34)	.359
Target lesion revascularization	31 (2.9)	13 (4.1)	1.41 (0.74-2.69)	.302
Nontarget vessel revascularization	32 (3.3)	10 (3.8)	1.04 (0.51-2.13)	.903
Definite stent thrombosis	1 (0.1)	4 (1.1)	13.16 (1.47-117.71)	.021
Cerebrovascular accident	13 (1.2)	7 (2.3)	1.79 (0.72-4.49)	.213
Contrast-induced nephropathy	19 (1.5)	21 (5.4)	3.55 (1.91-6.61)	< .001

CI, confidence interval; MI, myocardial infarction; PCI, percutaneous coronary intervention.
Values are expressed as No. (%). Cumulative incidences of events are presented as Kaplan-Meier estimates.

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