Disclosure

➤ ## Grant support

- National Evidence-based Healthcare Collaborating Agency, Ministry of Health & Welfare, Republic of Korea
- Abbott Vascular, Biosensors, Biotronik, Boston Scientific, Daiichi Sankyo, Donga-ST, Hanmi Pharmaceutical, and Medtronic

➤ ## Consulting Fees/Honoraria

- Abbott Vascular, Amgen, Astra Zeneca, Biosensors, Biotronik, Boston Scientific, Daiichi Sankyo, MSD Korea, Novartis, Pfizer, and Sanofi-Aventis

Background

- Previous trials (CTO-IVUS, AVIO, HOME-DES-IVUS, IVUS-XPL, and ULTIMATE) have shown lower rates of major adverse clinical events after intravascular ultrasound (IVUS)-guided percutaneous coronary intervention (PCI) than after angiography-guided PCI but have not been considered definitive owing to limited sample size, short follow-up duration, or the inclusion of highly selected coronary-lesion subsets.

- Our group has already reported the long-term benefit of the use of IVUS in patients undergoing complex PCI in an observational study.[1]
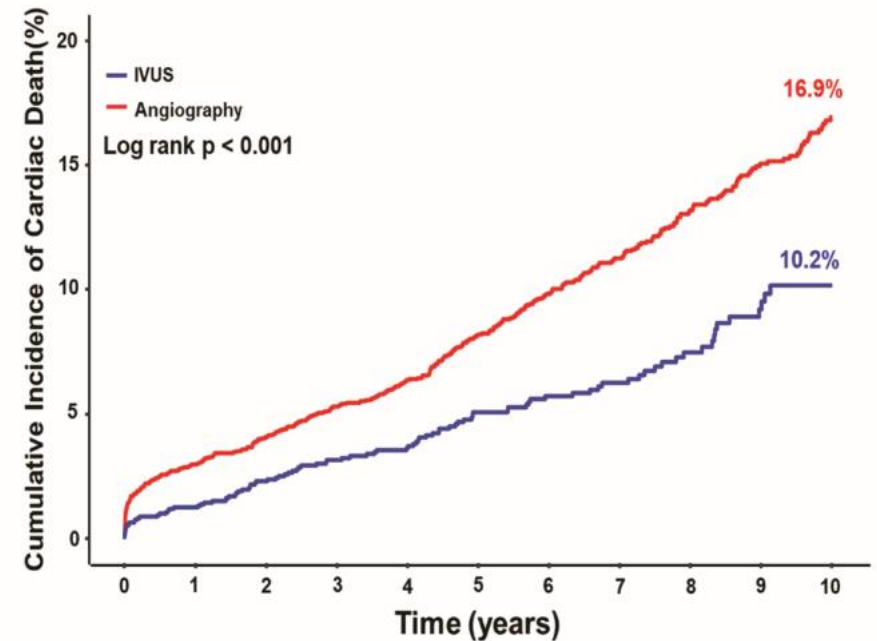
1. Choi KH, Song YB, ..., Hahn JY. JACC Cardiovasc Interv. 2019

Guidelines for Coronary Artery Revascularization

2021 ACC/AHA/SCAI

COR	LOE	Recommendations
2a	B-R	1. In patients undergoing coronary stent implantation, IVUS can be useful for procedural guidance, particularly in cases of left main or complex coronary artery stenting, to reduce ischemic events.[1-10]
2a	B-R	2. In patients undergoing coronary stent implantation, OCT is a reasonable alternative to IVUS for procedural guidance, except in ostial left main disease.[11-13]
2a	C-LD	3. In patients with stent failure, IVUS or OCT is reasonable to determine the mechanism of stent failure.[14-17]

2018 ESC/EACTS

Recommendations	Class[a]	Level[b]
IVUS or OCT should be considered in selected patients to optimize stent implantation.[603,612,651–653]	IIa	B
IVUS should be considered to optimize treatment of unprotected left main lesions.[35]	IIa	B

A randomized trial with adequate sample size is needed to confirm the benefit of intravascular imaging-guided PCI in patients with complex coronary artery lesions.

RENOVATE-COMPLEX-PCI: Study Objective

- To investigate whether intravascular imaging-guided PCI using IVUS or optical coherence tomography (OCT) would improve clinical outcomes compared with angiography-guided PCI in patients with complex coronary artery lesions.

Working Hypothesis

Intravascular imaging-guided PCI would reduce target vessel failure (a composite of cardiac death, target vessel-related myocardial infarction, and target vessel revascularization), compared with angiography-guided PCI in treatment of patients with complex coronary artery lesions.

Study Design
RENOVATE-COMPLEX-PCI (NCT03381872)

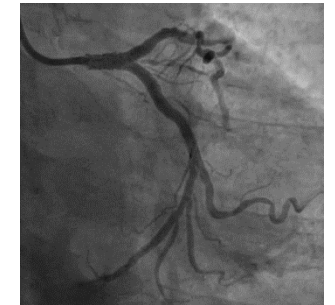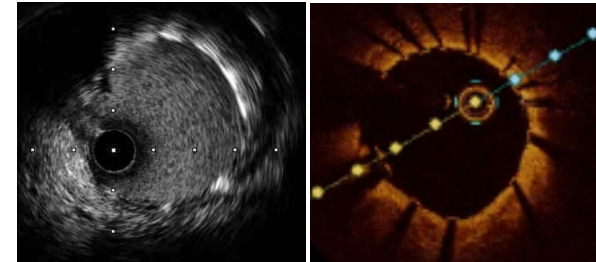An investigator-initiated, prospective, multicenter, randomized, open-label trial at 20 sites in Korea

Patients with Complex Coronary Artery Lesions Undergoing PCI

Randomization (2:1) for Treatment Strategy of Target Lesions

Imaging-Guided Strategy

Angiography-Guided Strategy

For patients who had been assigned to the intravascular imaging group, the choice of IVUS or OCT was made at the operators' discretion.

Inclusion and Exclusion Criteria
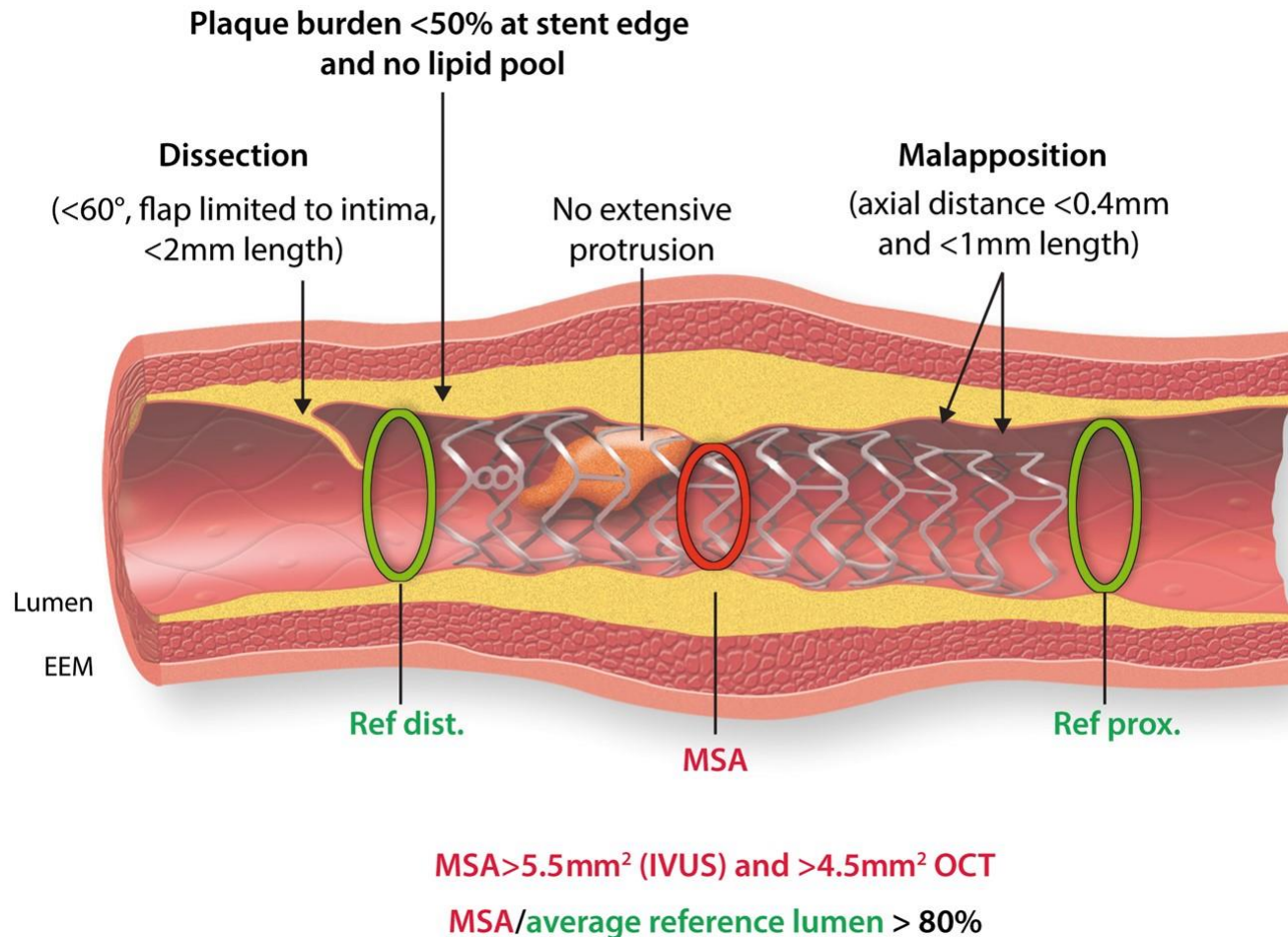
INCLUSION

1. Patients (≥ 19 years) with coronary artery disease requiring PCI
2. Patients with a **complex coronary artery lesion** defined as:
   - True bifurcation lesion (Medina 1,1,1/1,0,1/0,1,1) with side branch ≥2.5mm
   - Chronic total occlusion (≥3 months) as target lesion
   - Unprotected LM disease PCI (LM ostium, body, distal LM bifurcation including non-true bifurcation)
   - Long coronary lesions (implanted stent ≥38 mm in length)
   - Multi-vessel PCI (≥2 vessels treated at one PCI session)
   - Multiple stents needed (≥3 more stent per patient)
   - In-stent restenosis lesion as target lesion
   - Severely calcified lesion (encircling calcium in angiography)
   - Ostial coronary lesion (LAD, LCX, RCA)

KEY EXCLUSION

1. Target lesions not amenable to PCI by operators' decision
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. Non-cardiac co-morbid conditions are present with life expectancy <1 year or that may result in protocol non-compliance (per site investigator's medical judgment)
7. Unwillingness or inability to comply with the procedures described in this protocol.

Criteria of PCI Optimization by Intravascular Imaging

An expert consensus document of the European Association of PCI[1]

Plaque burden <50% at stent edge and no lipid pool

Dissection
(<60°, flap limited to intima, <2mm length)

No extensive protrusion

Malapposition
(axial distance <0.4mm and <1mm length)

Lumen

EEM

Ref dist.

MSA

Ref prox.

MSA>5.5mm² (IVUS) and >4.5mm² OCT
MSA/average reference lumen > 80%

- Standardized protocols for selection of reference size, stent size, and length
- In left main lesions, MSA >7 mm² for a distal left main coronary artery stenosis and >8 mm² for a proximal left main coronary artery stenosis
- Intravascular imaging could be used at any time during the PCI procedure but was mandated after stent implantation to determine whether the stented segment was optimized.
- If stent optimization did not occur, additional dilation of the stent or additional stent implantation was recommended, and repeat evaluation on intravascular imaging was mandated.

1. Raber L, Mintz GS, Koskinas KC, et al. Eur Heart J 2018;39:3281-300.
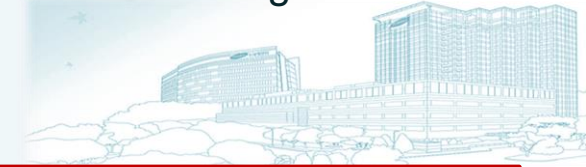
Study End Points

Primary End Point

- **Target vessel failure**

  - A composite of cardiac death, target vessel-related MI, or clinically-driven target vessel revascularization.

Secondary End Points

- Target vessel failure without procedure-related MI
- Cardiac death or target vessel-related MI
- Target vessel-related MI with or without procedure-related MI
- Non-target vessel-related MI
- Any MI with or without procedure-related MI
- Target lesion revascularization

- Target vessel revascularization
- Any revascularization (clinically-driven)
- Definite stent thrombosis
- Total amount of contrast
- Incidence of contrast-induced nephropathy
- Total procedural time
- Total medical cost (not reported in this publication)

Definition of Clinical Events

- Spontaneous MI according to 3rd Universal Definition[1]
- Other clinical events according to ARC-2 criteria[3]

- Procedure-related MI according to SCAI Definition[2]

1. Garcia-Garcia HM, McFadden EP, Farb A, et al. Circulation 2018;137:2635-50. 2. Thygesen K, Alpert JS, Jaffe AS, et al. Circulation 2012;126:2020-35. 3. Moussa ID, Klein LW, Shah B, et al. J Am Coll Cardiol 2013;62:1563-70.

Study Flow

5586 Patients from 20 sites were assessed for eligibility
(From May 2018 to May 2021)

3947 Were not enrolled
  1989 Had no complex coronary lesion PCI
  755 Sent for coronary artery bypass graft
  622 Deferred revascularization
  341 Physician judged ineligibility
      due to clinical situation
  132 Had cardiogenic shock
  108 Refused consent

1639 Underwent randomization

1092 assigned to
Intravascular Imaging-Guided PCI group

547 assigned to
Angiography-Guided PCI group

14 Protocol violations
  (No imaging device used)
2 Withdrew consent

13 Protocol violations
  (imaging device used)
3 Withdrew consent

1 Lost to follow-up

0 Lost to follow-up

1092 included in the analysis
(the intention-to-treat population)

547 included in the analysis
(the intention-to-treat population)

Baseline Clinical Characteristics

Characteristics	Total (N=1639)	Imaging-guided PCI (N=1092)	Angio-guided PCI (N=547)
Age — yr	65.6±10.2	65.3±10.3	66.0±10.0
Male — n (%)	1300 (79.3)	869 (79.6)	431 (78.8)
Initial presentation — no. (%)			
Stable ischemic heart disease	807 (49.2)	532 (48.7)	275 (50.3)
Acute coronary syndrome	832 (50.8)	560 (51.3)	272 (49.7)
Unstable angina	534 (32.6)	361 (33.1)	173 (31.6)
Acute myocardial infarction	298 (18.2)	199 (18.2)	99 (18.1)
Non-ST-segment elevation myocardial infarction	258 (15.7)	171 (15.7)	87 (15.9)
ST-segment elevation myocardial infarction	40 (2.4)	28 (2.6)	12 (2.2)
Medical history — no. (%)			
Hypertension	1005 (61.3)	682 (62.5)	323 (59.0)
Diabetes mellitus	617 (37.6)	394 (36.1)	223 (40.8)
Dyslipidemia	840 (51.3)	560 (51.3)	280 (51.2)
Current smoking	307 (18.7)	212 (19.4)	95 (17.4)
Chronic renal insufficiency	296 (18.1)	203 (18.6)	93 (17.0)
Previous PCI	395 (24.1)	268 (24.5)	127 (23.2)
Previous myocardial infarction	117 (7.1)	75 (6.9)	42 (7.7)
LV ejection fraction —(%)	58.7±11.6	58.4±11.9	59.3±11.0

Baseline Angiographic and Procedural Characteristics

Characteristics	Total (N=1639)	Imaging-guided PCI (N=1092)	Angio-guided PCI (N=547)
Complex coronary lesions — no. (%)			
True bifurcation lesion with side branch ≥2.5mm	359 (21.9)	233 (21.3)	126 (23.0)
Chronic total occlusion (≥3 months)	319 (19.5)	220 (20.1)	99 (18.1)
Unprotected left main coronary artery disease	192 (11.7)	138 (12.6)	54 (9.9)
Long coronary lesion (implanted stent ≥38 mm in length)	898 (54.8)	617 (56.5)	281 (51.4)
Multivessel PCI (≥2 vessels treated at one PCI session)	622 (37.9)	409 (37.5)	213 (38.9)
Multiple stents (≥3 more stent per patient)	305 (18.6)	208 (19.0)	97 (17.7)
In-stent restenosis	236 (14.4)	158 (14.5)	78 (14.3)
Severely calcified (encircling calcium in angiography)	231 (14.1)	157 (14.4)	74 (13.5)
Ostial coronary lesion (LAD, LCX, RCA)	251 (15.3)	182 (16.7)	69 (12.6)
Number of vessels with disease — no. (%)			
1-vessel disease	526 (32.1)	342 (31.3)	184 (33.6)
2-vessel disease	621 (37.9)	420 (38.5)	201 (36.7)
3-vessel disease	492 (30.0)	330 (30.2)	162 (29.6)
Procedural characteristics			
Radial artery access — no. (%)	1253 (76.4%)	827 (75.7%)	426 (77.9%)
Intravascular imaging devices used — no./total no. (%) †	1091/1639 (66.6)	1078/1092 (98.7)	13/547 (2.4)
Intravascular ultrasound	813/1091 (74.5)	800/1078 (74.2)	13/13 (100.0)
Optical coherence tomography	278/1091 (25.5)	278/1078 (25.8)	0/13 (0.0)
Volume of contrast media used — ml	207.3±116.5	214.2±118.5	193.7±111.3
Procedural time — min	65.0 (47.0-89.0)	70.0 (51.0-95.0)	53.5 (40.0-75.0)
Procedural success — no. (%)	1613 (98.4)	1073 (98.3)	540 (98.7)

Primary End Point: TVF

Hazard ratio, 0.64; 95% CI, 0.45 to 0.89; P=0.008

Angiography-guided PCI — 12.3%

Imaging-guided PCI — 7.7%

Cumulative Incidence (%)

Years of Follow-up
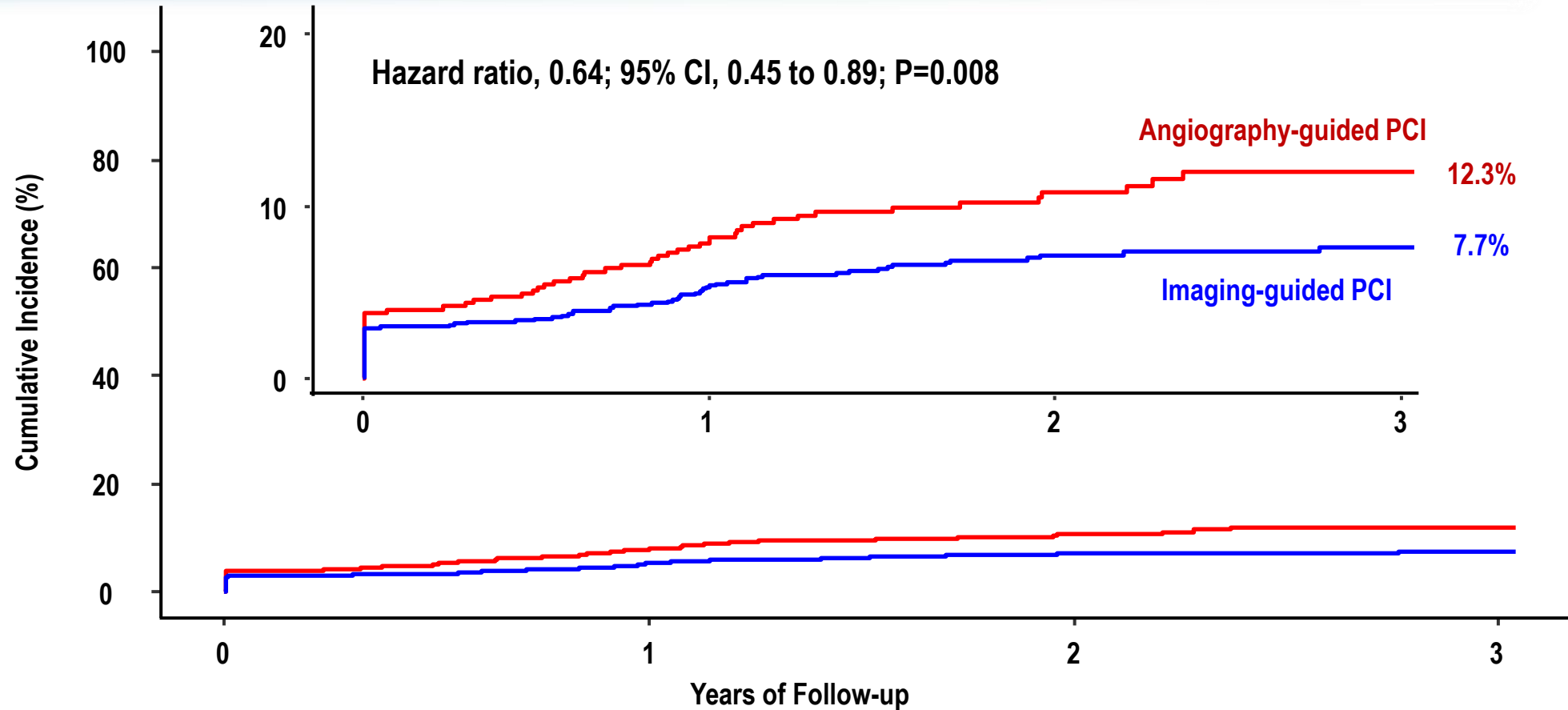
Number at risk

Angiography-guided PCI	547	496	280	120
Imaging-guided PCI	1092	1023	591	255

Complex PCI 2023

Primary and Secondary End Points

End Point	Total (N=1639)	Imaging-guided PCI (N=1092)	Angiography-guided PCI (N=547)	Hazard Ratio (95% CI)*	P Value
Primary end point — no. (%)					
Target vessel failure	136 (9.2)	76 (7.7)	60 (12.3)	0.64 (0.45-0.89)	0.008
Secondary end points — no. (%)					
Target vessel failure without procedure-related MI	88 (6.3)	48 (5.1)	40 (8.7)	0.59 (0.39-0.90)	
Cardiac death or target-vessel related MI	96 (6.4)	53 (5.3)	43 (8.5)	0.63 (0.42-0.93)	
All-cause death	70 (5.6)	42 (5.3)	28 (6.4)	0.71 (0.44–1.15)	
Cardiac death	33 (2.4)	16 (1.7)	17 (3.8)	0.47 (0.24-0.93)	
Myocardial infarction	75 (5.0)	43 (4.4)	32 (6.2)	0.78 (0.48-1.25)	
Target-vessel related MI	68 (4.3)	38 (3.7)	30 (5.6)	0.74 (0.45-1.22)	
Spontaneous MI	17 (1.2)	8 (0.9)	9 (1.8)	0.66 (0.23-1.90)	
Procedure-related MI	52 (3.2)	30 (2.7)	22 (4.0)	0.77 (0.43-1.35)	
Non-target vessel related MI	8 (0.8)	5 (0.8)	3 (0.8)	1.24 (0.24-6.40)	
Repeat revascularization	87 (6.6)	55 (6.3)	32 (7.1)	0.95 (0.60-1.48)	
Target vessel revascularization	57 (4.1)	32 (3.4)	25 (5.5)	0.69 (0.40-1.18)	
Target lesion revascularization	44 (3.2)	24 (2.6)	20 (4.4)	0.66 (0.36-1.22)	
Definite stent thrombosis	5 (0.3)	1 (0.1)	4 (0.7)	0.25 (0.02-2.75)	
Contrast induced nephropathy†	40 (2.4)	26 (2.4)	14 (2.6)	0.99 (0.51-1.92)	

Conclusion

- *Among patients with complex coronary artery lesions,* intravascular imaging-guided PCI reduced a composite of cardiac death, target vessel-related myocardial infarction, or clinically driven target vessel revascularization compared with angiography-guided PCI.

- The RENOVATE-COMPLEX-PCI supports the intravascular imaging-guided PCI in patients with complex coronary lesions.

Thank You Very Much!

Samsung Medical Center

RENOVATE-COMP

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intravascular Imaging–Guided or Angiography-Guided Complex PCI

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Complex PCI 2023

Prognostic Impact of Operator Experience and IVUS Guidance on Long-Term Clinical Outcomes

Samsung Medical Center Institutional Registry
2003.03 ~ 2015.12

Patients who undergo PCI (n=13,313)

Excluded (n=7,308)
Patients who had a non-complex coronary lesion (n=5,209)
Patients who treated with bare-metal stent (n=309)
Patients who treated with balloon angioplasty only (n=536)
Duplicated cases (n=1,228)
Optical coherence tomography-guided PCI (n=26)

6,005 Patients who have a complex coronary artery lesion undergoing PCI with DES

* Definition of complex lesions
① Bifurcation lesion with side branch ≥2.5mm size
② Chronic total occlusion (≥3 months) as target lesion
③ PCI for unprotected left main disease
④ Implanted stent length ≥38mm
⑤ Multi-vessel PCI (≥2 vessels treated at one PCI session)
⑥ Multiple stent needed (≥3 more stent per patient)
⑦ In-stent restenosis lesion as target lesion
⑧ Severely calcified lesion (using rotablation)

Less Experienced Operator
(Lifetime Independent Experience with PCI ≤ 5 Years) (n=2200)

Experienced Operator
(Lifetime Independent Experience with PCI > 5 Years) (n=3805)

IVUS Guidance (n=546)

Angiography Guidance (n=1654)

IVUS Guidance (n=1128)

Angiography Guidance (n=2677)

Complex PCI 2023

Ten-Year Risk of Cardiac Death or TVMI According to Operator Experience

Samsung Medical Center

A. Categorical Value

Less Experienced (≤ 5 years)
Experienced (>5 years)

Adjusted HR* 0.779, 95% CI 0.663-0.915, p=0.002
Log-rank p<0.001

Cumulative Incidence of Events (%)
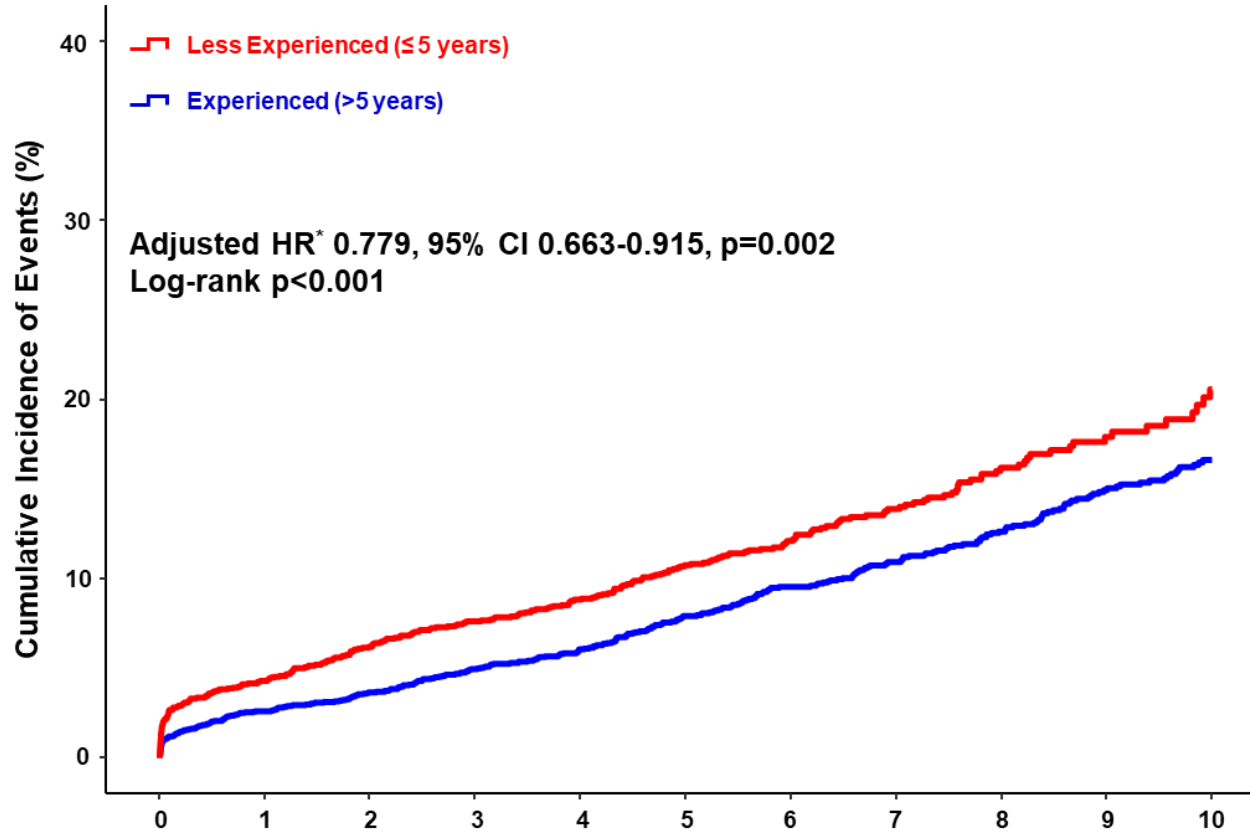
Time (Years)

No. at risk

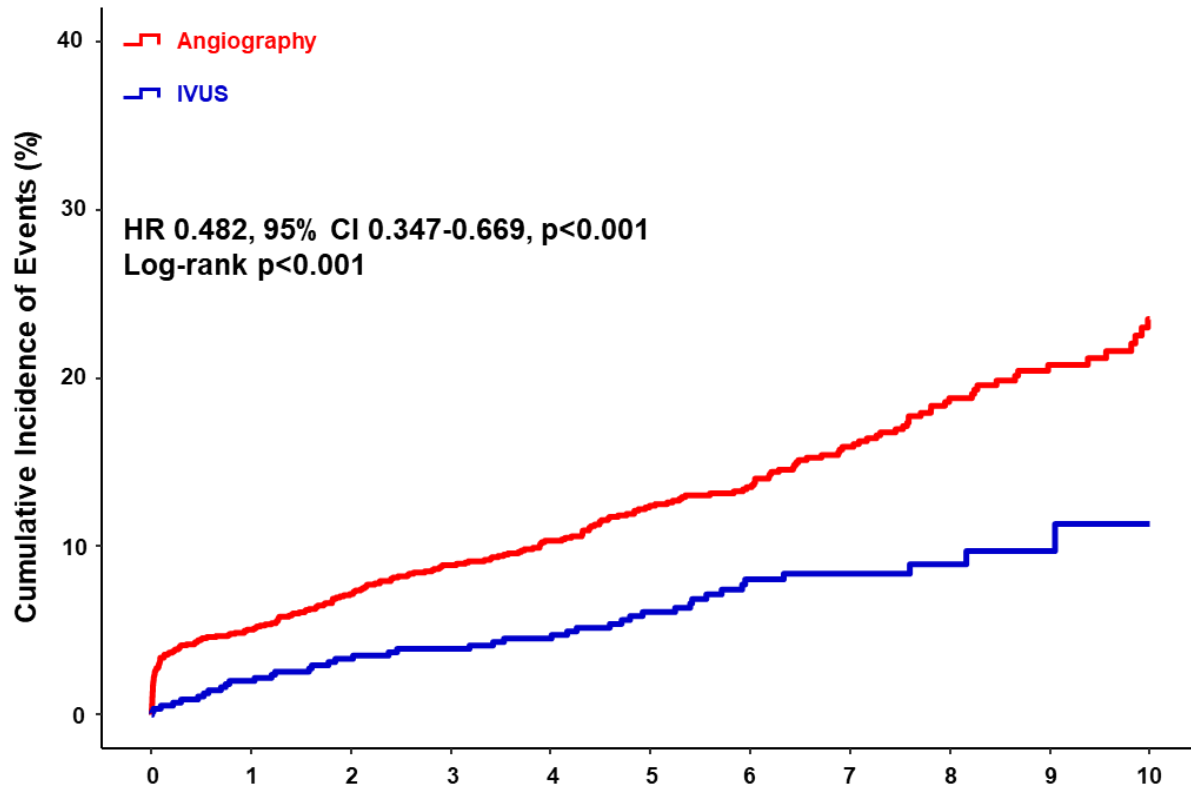|											
Less Experienced	2200	2036	1839	1685	1512	1271	984	716	481	290	180
Experienced	3805	3486	3004	2498	2126	1807	1556	1315	1082	839	607

B. Continuous Value

Relative Risk of Cardiac Death or Target-Vessel MI

Per 1-year increase, Adjusted HR*
0.968, 95% CI 0.952-0.985, p<0.001

Operator Experience (Year)

Complex PCI 2023
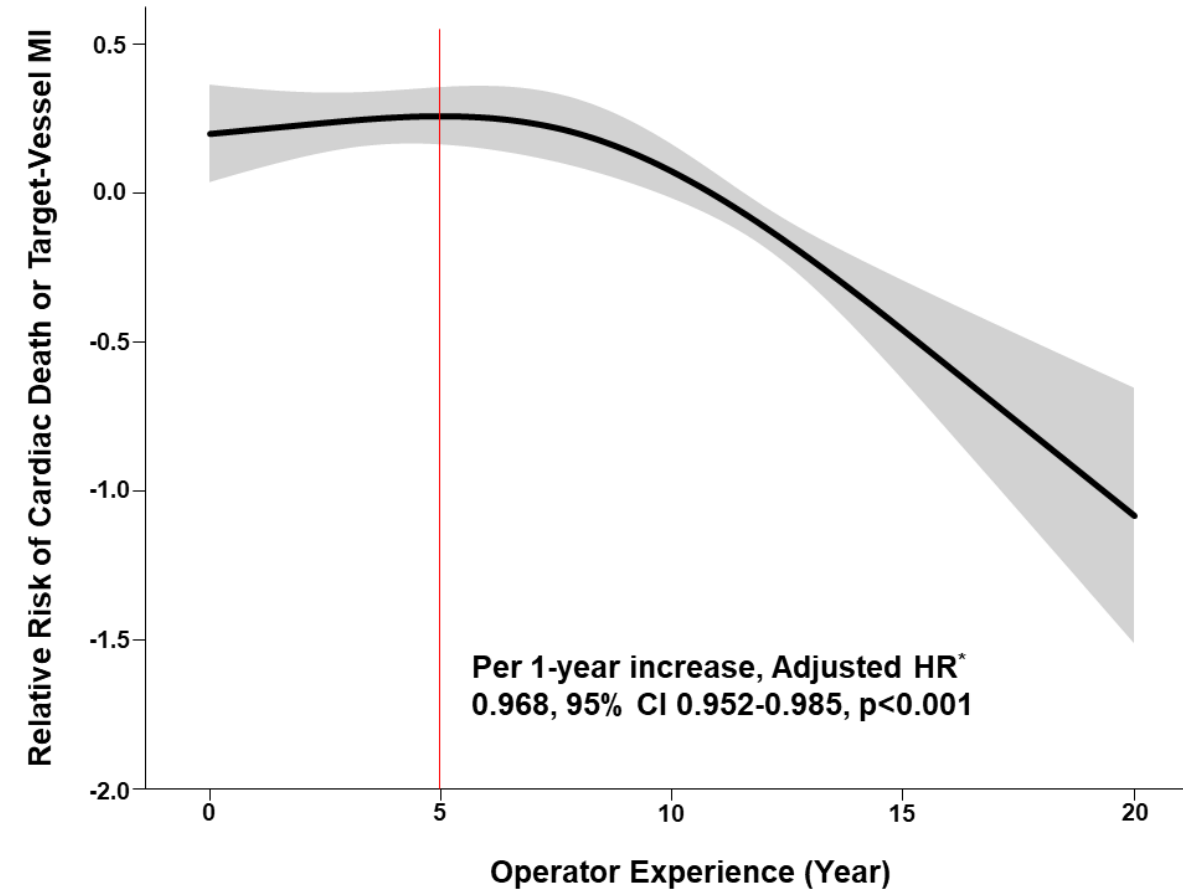
Cardiac Death or TVMI Between IVUS and Angiography Guidance According to Operator Experience

A. Less Experienced Operator

- Angiography
- IVUS

HR 0.482, 95% CI 0.347-0.669, p<0.001
Log-rank p<0.001

Cumulative Incidence of Events (%)

Time (Years)

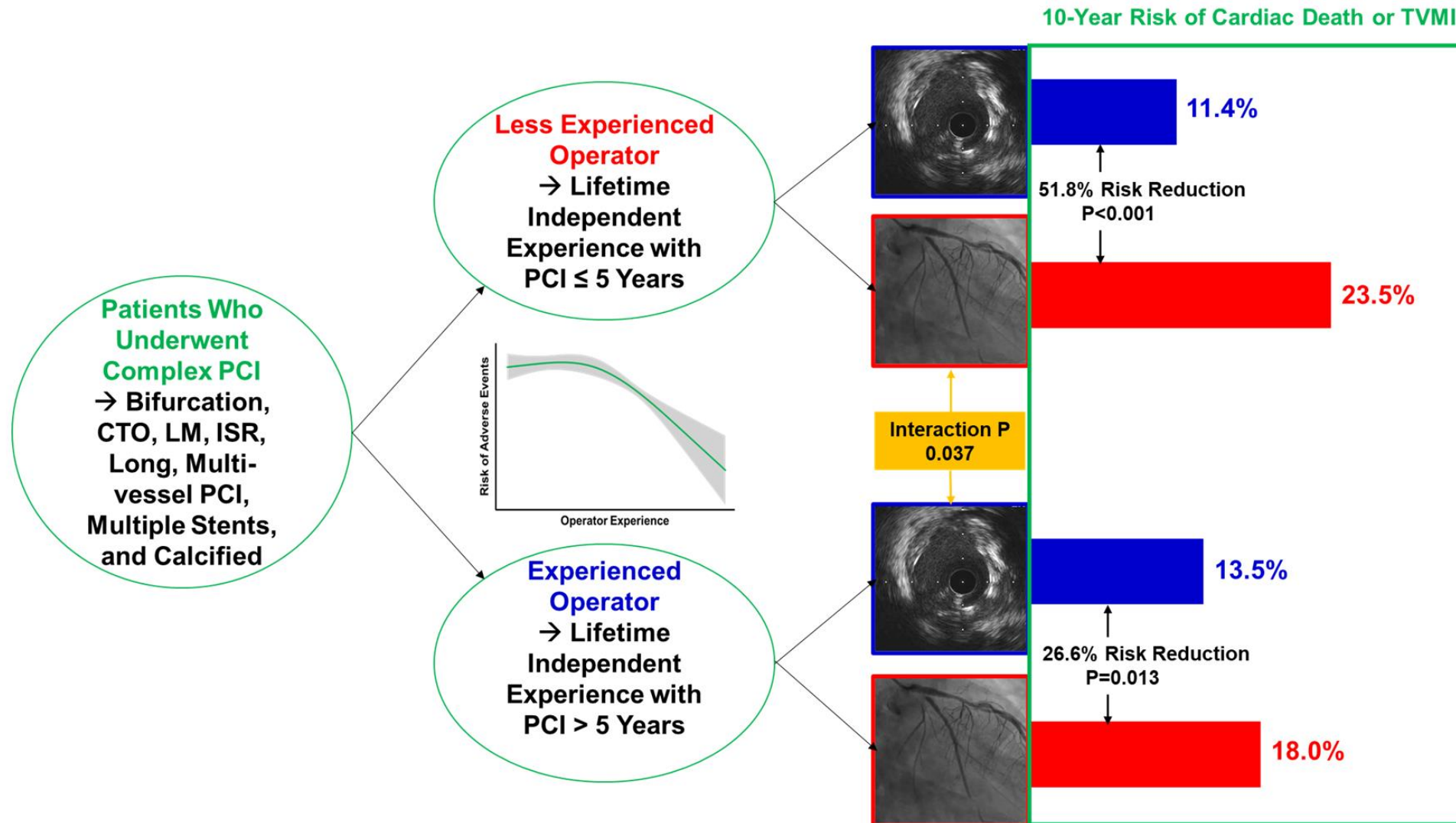| No. at risk											
Angiography	1654	1507	1345	1211	1066	889	686	505	353	227	153
IVUS	546	529	494	474	446	382	298	211	128	63	27

B. Experienced Operator

- Angiography
- IVUS

HR 0.734, 95% CI 0.575-0.937, p=0.013
Log-rank p=0.013

Cumulative Incidence of Events (%)
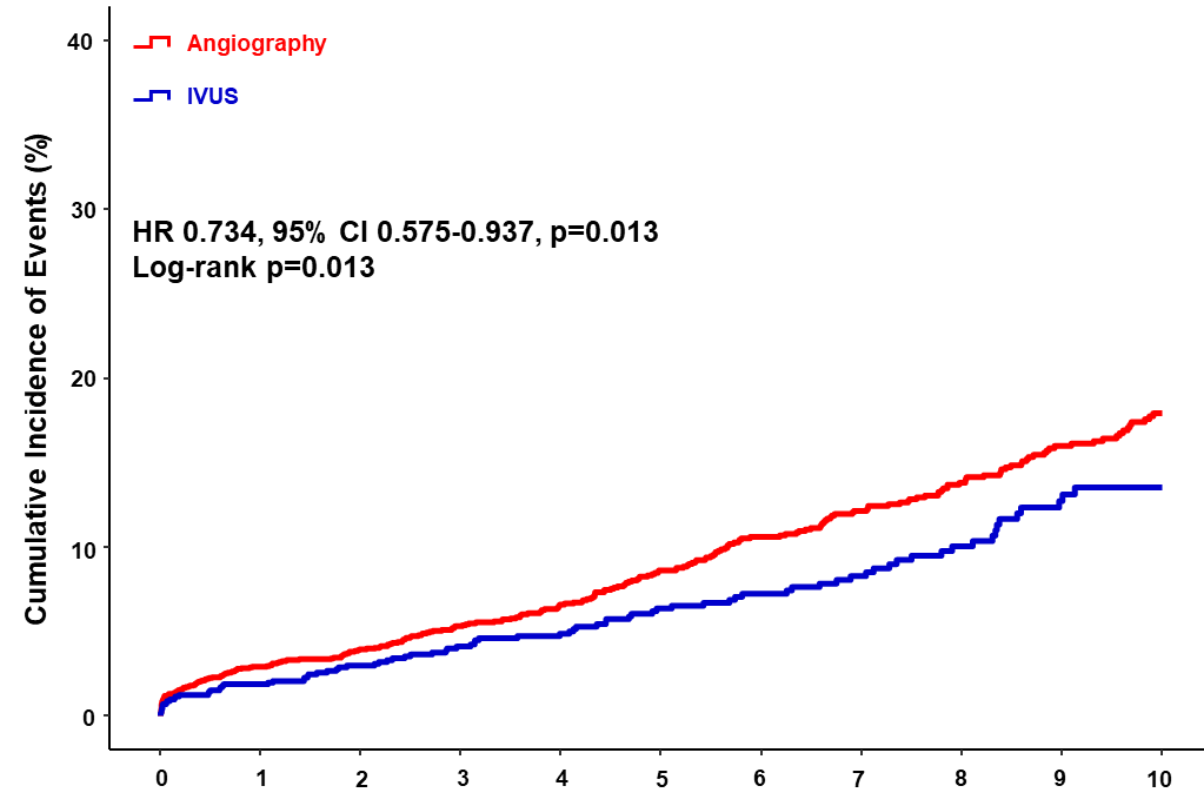
Time (Years)

No. at risk											
Angiography	2677	2438	2084	1701	1439	1223	1059	913	776	615	460
IVUS	1128	1048	920	797	687	584	497	402	306	224	147

Interaction P= 0.037

Complex PCI 2023

Differential Benefits of IVUS Guidance According to Operator Experience During Complex PCI

10-Year Risk of Cardiac Death or TVMI

Patients Who Underwent Complex PCI → Bifurcation, CTO, LM, ISR, Long, Multi-vessel PCI, Multiple Stents, and Calcified

Less Experienced Operator → Lifetime Independent Experience with PCI ≤ 5 Years

Experienced Operator → Lifetime Independent Experience with PCI > 5 Years

Risk of Adverse Events / Operator Experience

Interaction P 0.037

11.4%
51.8% Risk Reduction P<0.001
23.5%

13.5%
26.6% Risk Reduction P=0.013
18.0%

감사합니다.
Thank you for your attention.