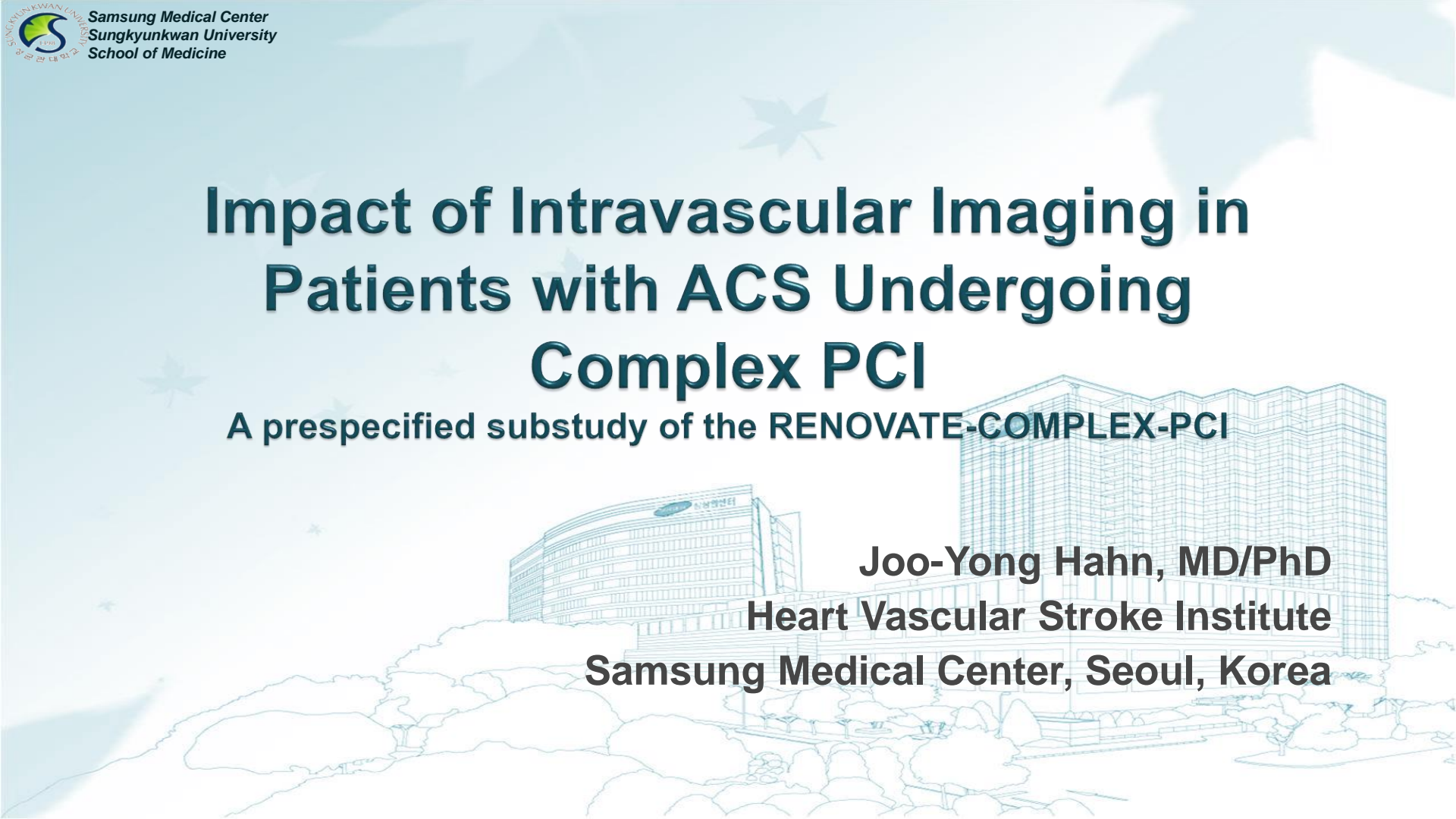


# Impact of Intravascular Imaging in Patients with ACS Undergoing Complex PCI

A prespecified substudy of the RENOVATE-COMPLEX-PCI

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# Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a relevant financial relationship(s) with an ineligible company(ies) listed below.

## Nature of Financial Relationship

Grant/Research Support

Consultant Fees/Honoraria

## Ineligible Company

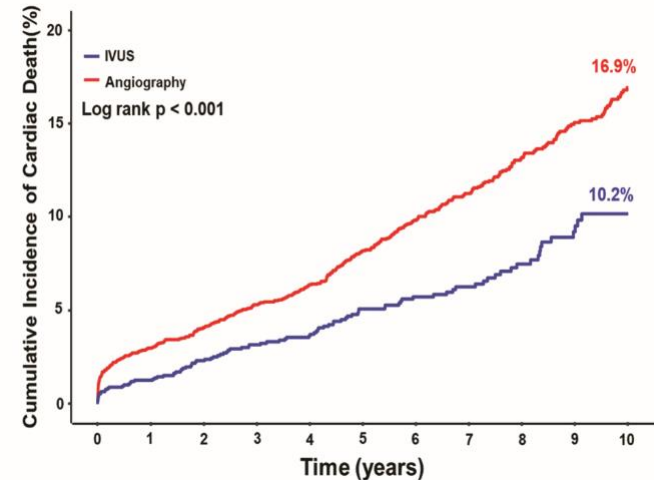
Abbott Vascular, Biosensors, Biotronik, Boston Scientific, Daiichi Sankyo, Donga-ST, Hanmi Pharmaceutical, and Medtronic

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.<sup>1</sup>
  - 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.



1. Choi KH, Song YB, ..., Hahn JY. JACC Cardiovasc Interv. 2019

# 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

Primary end point: target vessel failure  
(a composite of cardiac death, target vessel-related MI, or clinically-driven TVR)



# Inclusion and Exclusion Criteria

## INCLUSION

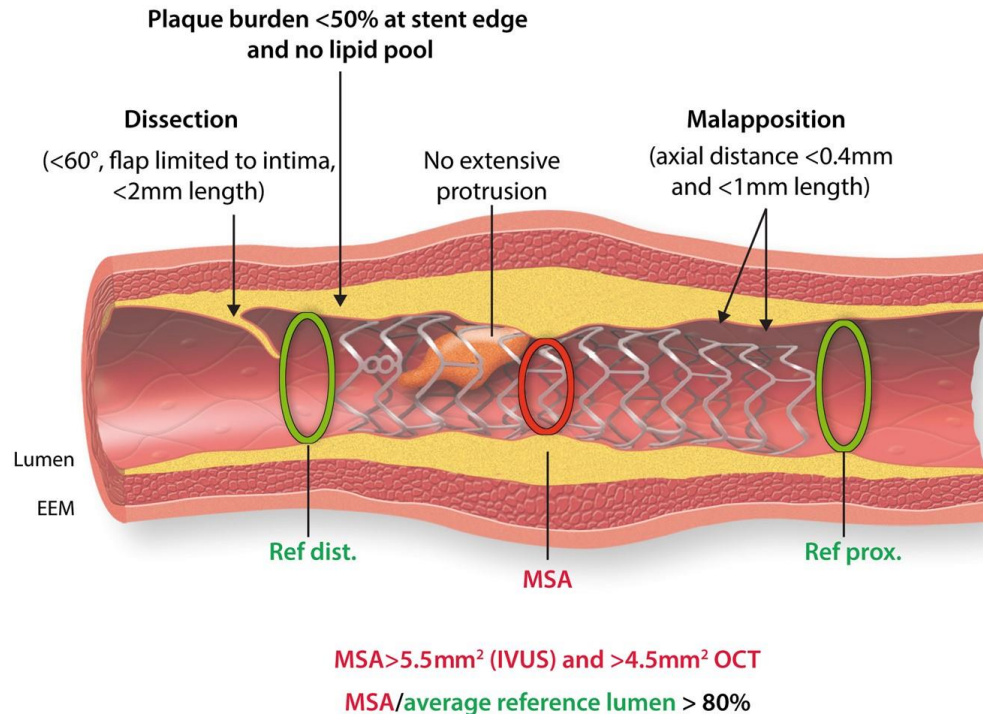
1. Patients ( $\geq 19$  years) with coronary artery disease requiring PCI
2. Patients with a **complex coronary artery lesion** defined as:
  - True bifurcation lesion (Medina 1,1,1/1,0,1/0,1,1) with side branch  $\geq 2.5$ mm
  - Chronic total occlusion ( $\geq 3$  months) as target lesion
  - Unprotected LM disease PCI (LM ostium, body, distal LM bifurcation including non-true bifurcation)
  - Long coronary lesions (implanted stent  $\geq 38$  mm in length)
  - Multi-vessel PCI ( $\geq 2$  vessels treated at one PCI session)
  - Multiple stents needed ( $\geq 3$  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.

# PCI and Intravascular Imaging

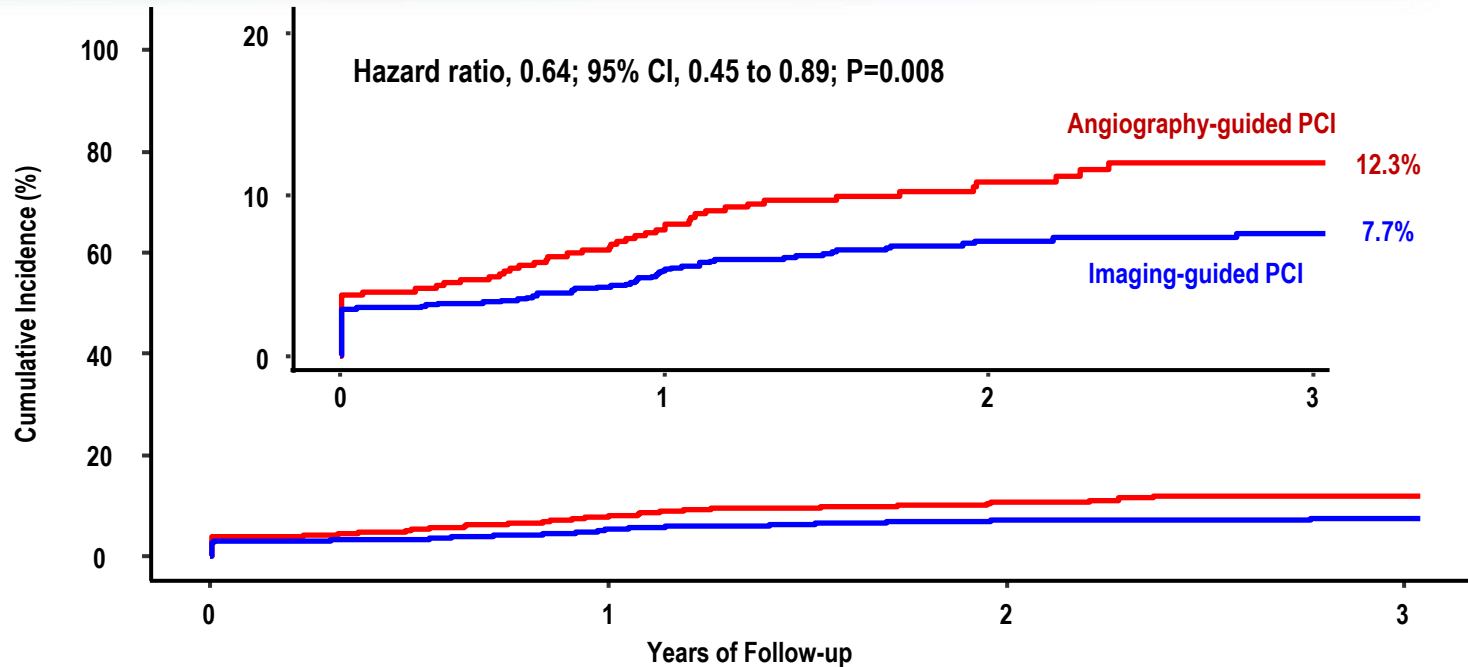
An expert consensus document of the European Association of PCI<sup>1</sup>



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



# Primary End Point: TVF



Number at risk

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





# 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
<b>Primary end point — no. (%)</b>					
Target vessel failure	136 (9.2)	76 (7.7)	60 (12.3)	0.64 (0.45-0.89)	0.008
<b>Secondary end points — no. (%)</b>					
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)	





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

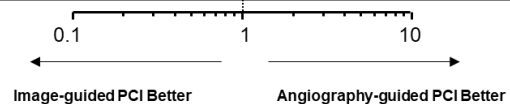
## Intravascular Imaging–Guided or Angiography-Guided Complex PCI

J.M. Lee, K.H. Choi, Y.B. Song, J.-Y. Lee, S.-J. Lee, S.Y. Lee, S.M. Kim, K.H. Yun,  
J.Y. Cho, C.J. Kim, H.-S. Ahn, C.-W. Nam, H.-J. Yoon, Y.H. Park, W.S. Lee,  
J.-O. Jeong, P.S. Song, J.-H. Doh, S.-H. Jo, C.-H. Yoon, M.G. Kang, J.-S. Koh,  
K.Y. Lee, Y.-H. Lim, Y.-H. Cho, J.-M. Cho, W.J. Jang, K.-J. Chun, D. Hong,  
T.K. Park, J.H. Yang, S.-H. Choi, H.-C. Gwon, and J.-Y. Hahn,  
for the RENOVATE-COMPLEX-PCI Investigators\*

# Prespecified Subgroup Analysis



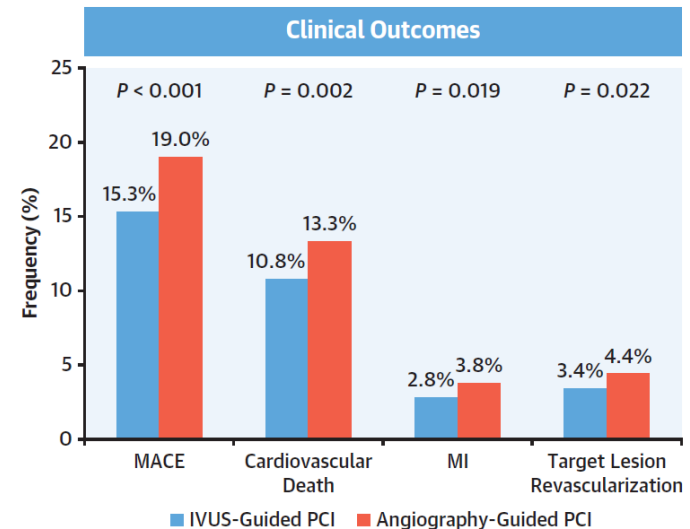
Subgroup	Imaging-guided PCI		Angiography-guided PCI		Hazard ratio (95% CI)
	No. of events / total no. of patients (cumulative incidence, %)				
<b>Overall</b>	76/1092 (7.7%)	60/547 (12.3%)			0.64 (0.45-0.89)
<b>Type of imaging devices</b>					
IVUS	59/800 (8.0%)	60/547 (12.3%)			0.66 (0.46-0.95)
OCT	15/278 (5.8%)	60/547 (12.3%)			0.47 (0.27-0.83)
<b>Initial Presentation</b>					
Stable ischemic heart disease	25/532 (5.0%)	27/275 (10.4%)			0.46 (0.27-0.80)
Acute coronary syndrome	51/560 (10.4%)	33/272 (14.6%)			0.74 (0.48-1.15)
<b>Age</b>					
<65 years	36/517 (7.8%)	23/238 (10.6%)			0.72 (0.42-1.21)
≥65 years	40/575 (7.4%)	37/309 (13.6%)			0.57 (0.36-0.88)
<b>Sex</b>					
Male	66/869 (8.3%)	46/431 (11.7%)			0.70 (0.48-1.02)
Female	10/223 (5.2%)	14/116 (14.5%)			0.35 (0.16-0.80)
<b>Diabetes mellitus</b>					
Presence	45/394 (12.9%)	26/223 (12.3%)			0.97 (0.60-1.57)
Absence	31/698 (4.7%)	34/324 (12.2%)			0.41 (0.25-0.67)
<b>Chronic kidney disease</b>					
Presence	22/203 (13.3%)	19/93 (23.3%)			0.51 (0.27-0.93)
Absence	54/889 (6.4%)	41/454 (9.9%)			0.66 (0.44-0.99)
<b>Left ventricular ejection fraction</b>					
<50%	22/210 (12.0%)	12/84 (15.0%)			0.72 (0.35-1.45)
≥50%	54/882 (6.7%)	48/463 (11.8%)			0.58 (0.39-0.85)



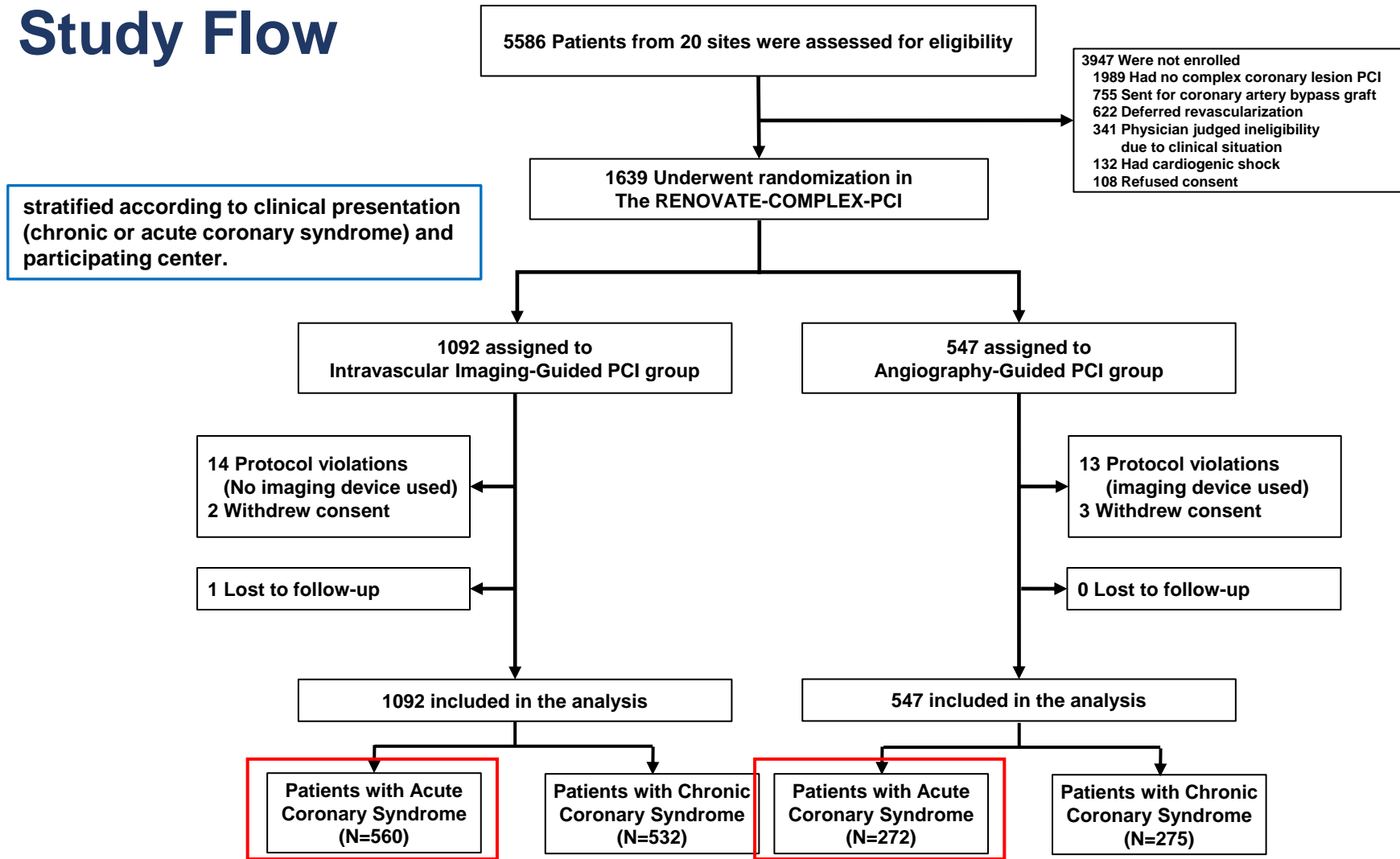


# Intravascular Imaging for ACS

- Procedural optimization by intravascular imaging during complex PCI might have greater influence on the outcomes among patients with ACS rather than CCS because of their vulnerable characteristics with increased thrombogenicity.
- COREA-AMI registry (n=9846)
- But no dedicated RCT for comparison between IVI-guided vs angiography-guided PCI among patients with ACS



# Study Flow



# Baseline Clinical Characteristics

Characteristic	Imaging-guided PCI	Angiography-guided PCI	P value
	(n=560)	(n=272)	
Age, years	64.6 ± 10.8	66.1 ± 10.0	0.06
Male	454 (81.1%)	210 (77.2%)	0.23
Body mass index, kg/m <sup>2</sup>	24.7 ± 3.5	24.8 ± 3.2	0.77
Initial presentation			0.87
Unstable angina	361 (64.5%)	173 (63.6%)	
NSTEMI	171 (30.5%)	87 (32.0%)	
STEMI	28 (5.0%)	12 (4.4%)	
Medical history			
Hypertension	338 (60.4%)	163 (59.9%)	0.97
Diabetes mellitus	189 (33.8%)	105 (38.6%)	0.205
Dyslipidemia	290 (51.8%)	135 (49.6%)	0.61
Current smoking	143 (25.5%)	58 (21.3%)	0.21
Chronic renal insufficiency	99 (17.7%)	42 (15.4%)	0.48
Previous PCI	154 (27.5%)	65 (23.9%)	0.31
Previous MI	41 (7.3%)	25 (9.2%)	0.42
Previous stroke	26 (4.6%)	24 (8.8%)	0.03
Peripheral vascular disease	14 (2.5%)	6 (2.2%)	0.99
Atrial fibrillation	15 (2.7%)	11 (4.0%)	0.40

# Lesion Characteristics

Characteristic	Imaging-guided PCI (n=560)	Angiography-guided PCI (n=272)	P value
<b>Complex coronary lesions</b>			
True bifurcation (Medina 1,1,1 / 1,0,1 / 0,1,1)	120 (21.4%)	62 (22.8%)	0.72
Chronic total occlusion (≥3 months of occlusion)	93 (16.6%)	39 (14.3%)	0.46
Unprotected left main disease	81 (14.5%)	24 (8.8%)	0.03
Long coronary lesion (implanted stent length≥38 mm)	287 (51.2%)	126 (46.3%)	0.21
Multivessel PCI (≥2 major coronary arteries treated)	210 (37.5%)	116 (42.6%)	0.18
Multiple stents implanted (≥3 more stent per patient)	88 (15.7%)	44 (16.2%)	0.94
In-stent restenosis lesion	92 (16.4%)	39 (14.3%)	0.50
Severely calcified lesion (encircling calcium in angiography)	67 (12.0%)	39 (14.3%)	0.40
Ostial coronary lesion	103 (18.4%)	33 (12.1%)	0.03
<b>Number of vessels with disease</b>			0.94
1-vessel disease	187 (33.4%)	92 (33.8%)	
2-vessel disease	212 (37.9%)	105 (38.6%)	
3-vessel disease	161 (28.8%)	75 (27.6%)	

# Procedural Characteristics

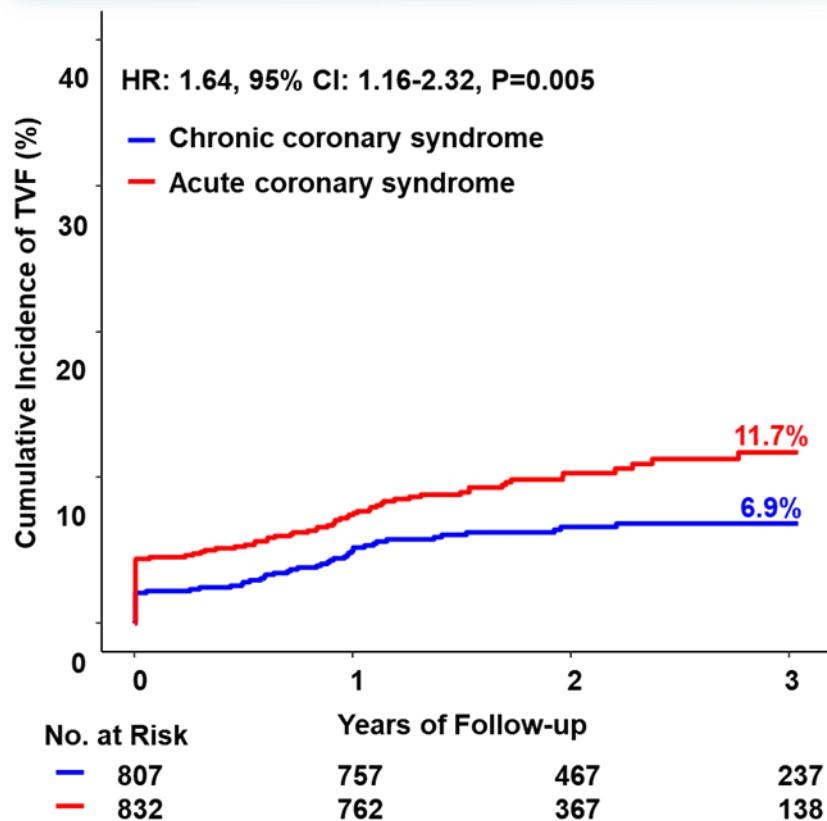
Characteristic	Imaging-guided PCI	Angiography-guided PCI	P value
	(n=560)	(n=272)	
Total no. of target lesions treated	1.5 ± 0.7	1.5 ± 0.7	0.82
Radial access	402 (71.8%)	206 (75.7%)	0.26
Intravascular imaging devices used	554 (98.9%)	10 (3.7%)	<0.001
Intravascular ultrasound	416/554 (75.1%)	10/10 (100%)	
Optical coherence tomography	138/554 (24.9%)	0/10 (0%)	
Adjunctive non-compliant balloon used	423 (75.5%)	167 (61.4%)	<0.001
Rotablation used	16 (2.9%)	8 (2.9%)	0.95
Treatment devices used			0.64
Drug-eluting stent	548 (97.9%)	264 (97.1%)	
Drug-coated balloon angioplasty	12 (2.1%)	8 (2.9%)	
Total no. of devices used per patient	1.8 ± 1.0	1.8 ± 0.9	0.68
Dimensions of devices, mm			
Mean diameter	3.2 ± 0.4	3.1 ± 0.4	0.02
Total length	52.2 ± 32.4	51.6 ± 28.1	0.81
Volume of contrast media used, ml	198.8 ± 127.8	198.3 ± 121.6	0.96
Procedural time, min	79.1 ± 44.4	63.6 ± 33.0	<0.001
Procedural success, no. (%)	550 (98.2%)	267 (98.2%)	0.99
Successful imaging-guided stent optimization	282 (50.4%)	NA	



# Lesion-level Analysis

Characteristic	Imaging-guided PCI (n=560)	Angiography-guided PCI (n=272)	P value
<b>Location of target vessel</b>			0.48
Left main artery	87 (10.6%)	34 (8.6%)	
Left anterior descending artery	360 (43.7%)	183 (46.1%)	
Circumflex artery	157 (19.1%)	67 (16.9%)	
Right coronary artery	219 (26.6%)	113 (28.5%)	
<b>Quantitative coronary angiography</b>			
Pre-PCI QCA			
Proximal RD, mm	3.2 ± 0.5	3.2 ± 0.5	0.006
Distal RD, mm	2.8 ± 0.5	2.8 ± 0.4	0.51
Minimum lumen diameter, mm	0.4 ± 0.4	0.4 ± 0.3	0.16
Diameter stenosis, %	86.6 ± 11.2	87.3 ± 10.4	0.34
Lesion length, mm	27.0 ± 14.9	25.8 ± 14.4	0.19
Post-PCI QCA			
Minimum lumen diameter, mm	2.8 ± 0.5	2.7 ± 0.5	0.04
Diameter stenosis, %	10.1 ± 8.6	10.5 ± 8.0	0.46

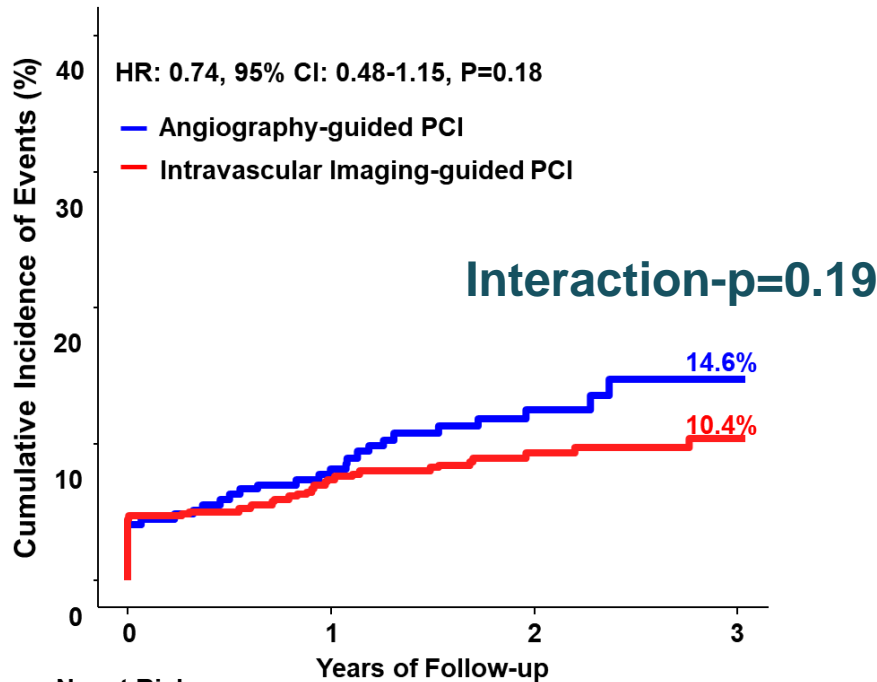
# Outcomes According to Clinical Presentation



End Point	ACS (N=832)	CCS (N=807)
<b>Primary endpoint</b>		
Target vessel failure <sup>†</sup>	84 (11.7%)	52 (6.9%)
<b>Secondary endpoints</b>		
Cardiac death or TV MI	59 (8.0%)	37 (4.9%)
All-cause death	33 (5.6%)	37 (5.7%)
Cardiac death	19 (3.2%)	14 (1.9%)
MI	49 (6.7%)	26 (3.5%)
Target-vessel related MI	43 (5.3%)	25 (3.3%)
Spontaneous MI	7 (0.9%)	10 (1.5%)
Procedure-related MI	36 (4.3%)	16 (2.0%)
Repeat revascularization	51 (8.1%)	36 (5.3%)
TVR	33 (5.0%)	24 (3.3%)
TLR	26 (4.0%)	18 (2.5%)
Definite stent thrombosis	2 (0.2%)	3 (0.4%)
CIN	18 (2.2%)	22 (2.7%)

# Incidence of TVF According to Clinical Presentation

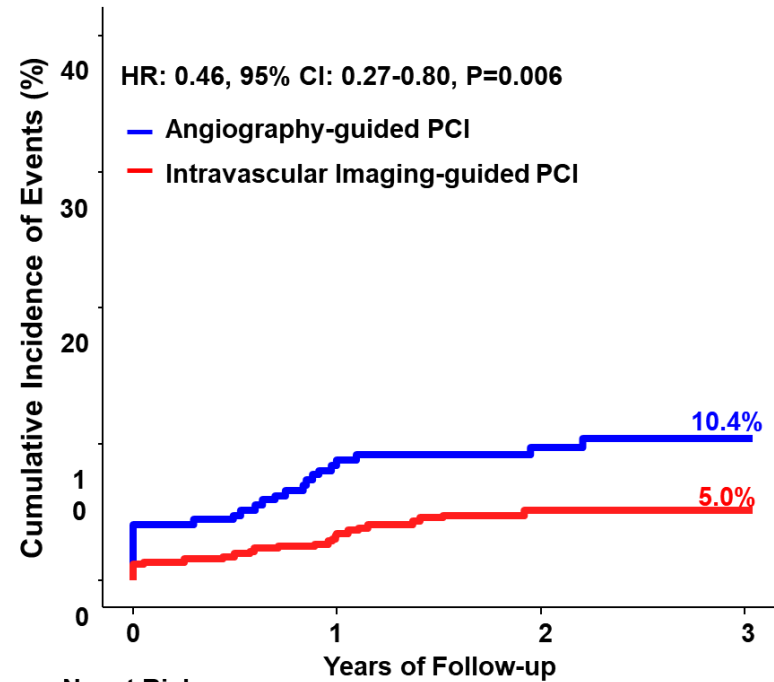
## <Acute Coronary Syndrome>



No. at Risk

—	272	248	110	43
—	560	514	257	95

## <Chronic Coronary Syndrome>



No. at Risk

—	275	248	157	77
—	532	509	310	160

# Primary and Secondary End Points

End Point	Imaging-guided PCI (N=560)	Angiography-guided PCI (N=272)	HR (95% CI)	P value
<b>Primary endpoint</b>				
Target vessel failure*	51 (10.4%)	33 (14.6%)	0.74 (0.48-1.15)	0.18
<b>Secondary endpoints</b>				
Target vessel failure without procedure-related MI	28 (6.3%)	23 (11.1%)	0.58 (0.33-0.99)	0.049
Cardiac death or target-vessel related MI	37 (7.2%)	22 (9.7%)	0.81 (0.48-1.38)	0.44
All-cause death	17 (4.5%)	16 (7.9%)	0.51 (0.26-1.00)	0.05
Cardiac death	8 (1.9%)	11 (5.9%)	0.35 (0.14-0.86)	0.02
MI	34 (7.0%)	15 (6.2%)	1.10 (0.60-2.01)	0.77
Target-vessel related MI	30 (5.5%)	13 (4.8%)	1.12 (0.59-2.15)	0.73
Spontaneous MI	5 (1.0%)	2 (0.7%)	1.20 (0.23-6.19)	0.83
Procedure-related MI	25 (4.5%)	11 (4.0%)	1.11 (0.54-2.25)	0.78
Repeat revascularization	31 (7.4%)	20 (9.5%)	0.73 (0.48-1.28)	0.28
Target vessel revascularization	20 (4.5%)	13 (5.9%)	0.73 (0.36-1.46)	0.37
Target lesion revascularization	15 (3.5%)	11 (5.0%)	0.64 (0.30-1.40)	0.27
Definite stent thrombosis	1 (0.2%)	1 (0.4%)	0.49 (0.03-7.75)	0.61
Contrast induced nephropathy	11 (2.0%)	7 (2.6%)	0.77 (0.30-1.97)	0.58

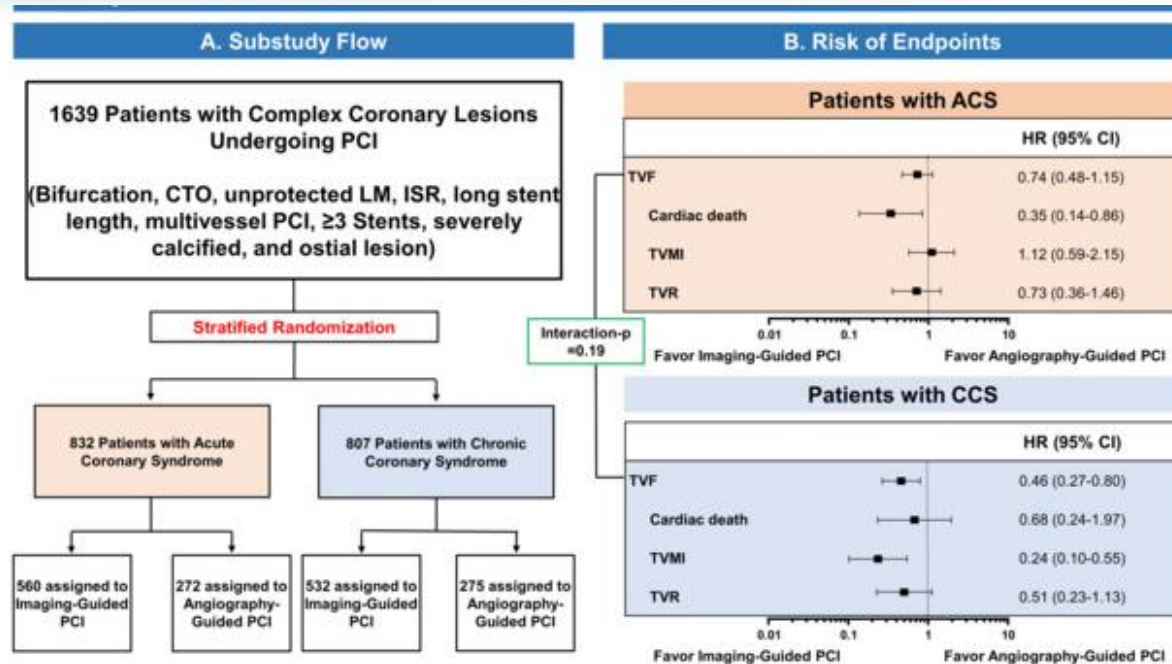


# Limitations

- Although it was pre-specified and randomization was stratified according to clinical presentation, it is a subgroup analysis of a randomized clinical trial. With regard to sample size, this analysis was underpowered for the evaluation of differences in the primary endpoint between the allocation groups in each clinical presentation.
- Second, although all clinical end points were assessed by members of independent clinical event adjudication committee, operators were not blinded to treatment allocation.

# Intravascular Imaging-guided PCI in Acute or Chronic Coronary Syndrome

## <A pre-specified, stratified subgroup analysis from the RENOVATE-COMPLEX-PCI>



- Over median 2.1-year follow-up, no significant interaction was observed between the benefits of intravascular imaging and clinical presentation in the risk of TVF ( $P_{\text{interaction}}=0.19$ )
- Stent optimization by intravascular imaging was particularly important for ACS patients; among those randomized to intravascular imaging-guided PCI, risk of TVF was 6.5% for optimized vs. 14.1% for unoptimized, HR: 0.49, 95% CI: 0.27-0.87,  $P=0.02$ . No such difference was observed for CCS patients.