10-Year Final Report of PRECOMBAT Trial: Deep Dive

Duk-Woo Park, MD

Professor, Heart Institute, Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea

CVRF

Disclosure

Institutional grant/research funding to CardioVascular Research Foundation (CVRF, Korea) and/or Asan Medical Center from Daiichi-Sankyo, Abbott, Boston Scientific, Medtronics, Edwards, Biosensor, ChongKunDang Pharm and Daewoong Pharm,

CVRF

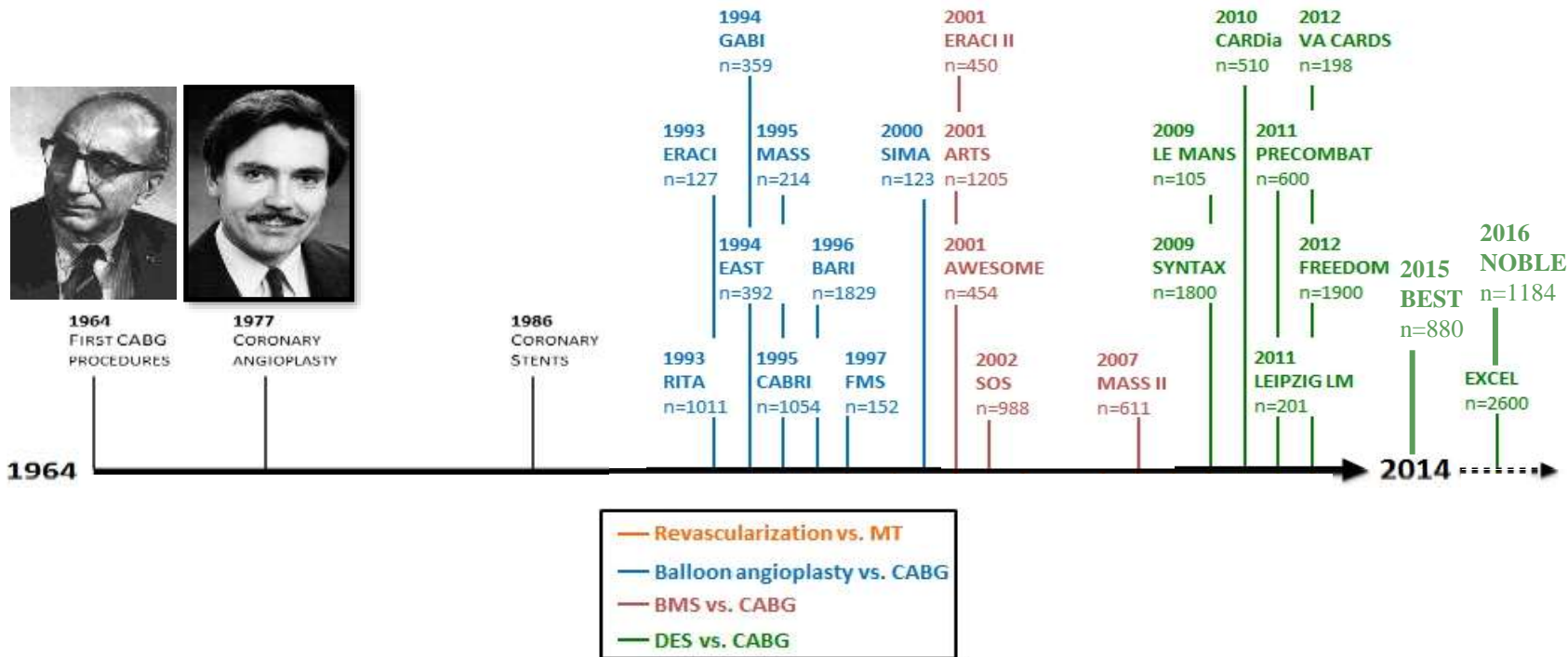# Long Journey of Left Main PCI

CENTRAL ILLUSTRATION Secular Changes of Treatment Effect and Guideline Recommendations in Relation to Medical Advances of Each Treatment Stratum for Left Main Coronary Artery Disease

Diminishing Outcome Gap between PCI and CABG in LM Disease Over Time
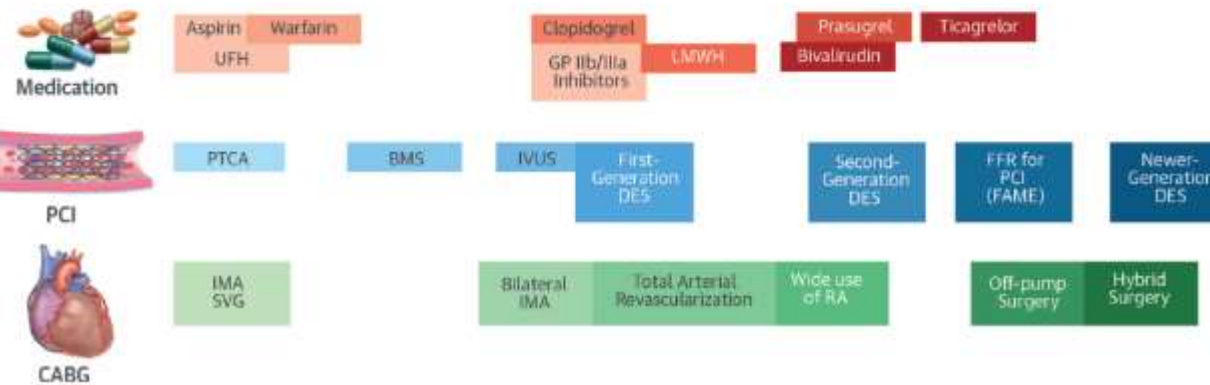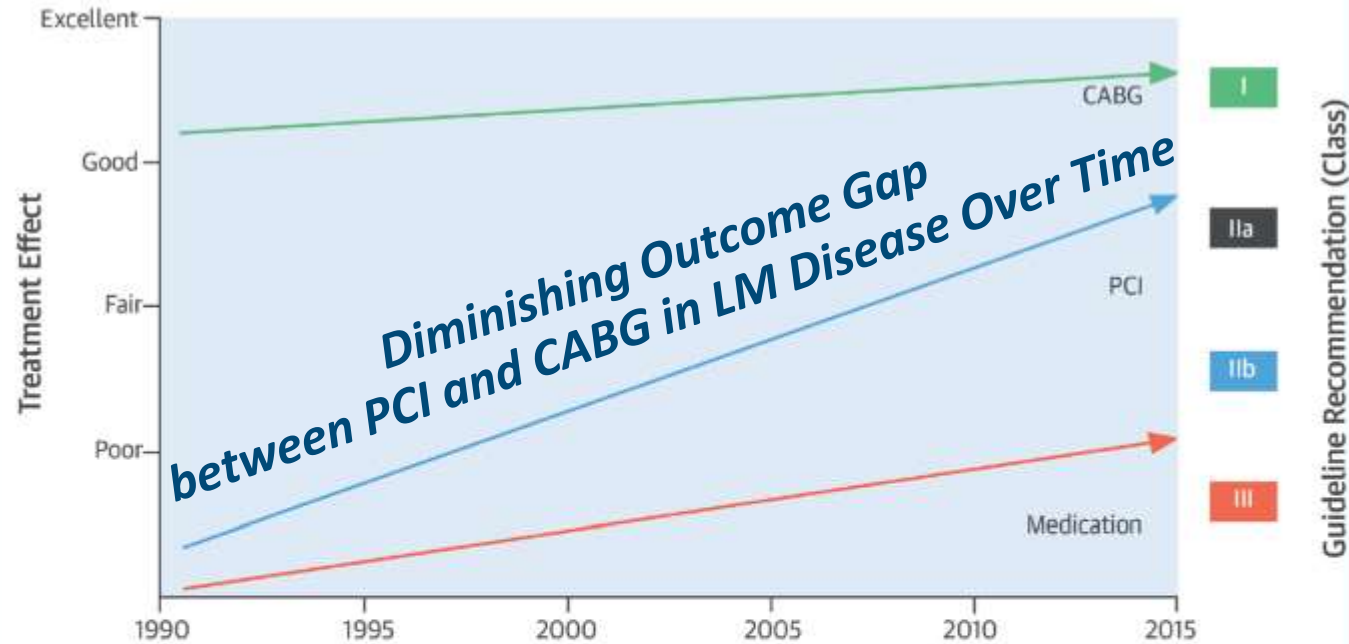
Lee, P.H. et al. J Am Coll Cardiol. 2016;68(11):1233–46.

PH Lee, DW Park, SJ Park et al, JACC. 2016;68:1233-46.

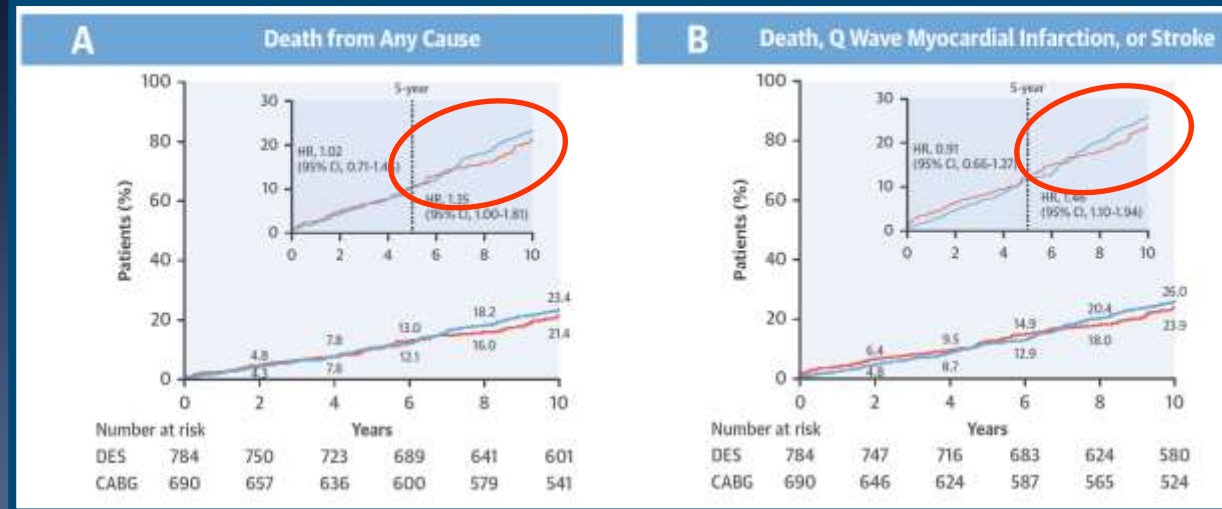# RCTs on Revascularization

Continuous Big Match

PCI vs. CABG in LM Disease, *2020*

However, The Game Is Just Begun !

One Remained Important Issue:
We Are Demanding Very Long-Term
(ie,10-Year) Results of PCI and CABG for LM disease

Why We Need Very Long-Term Data?: There Were Some Signals...
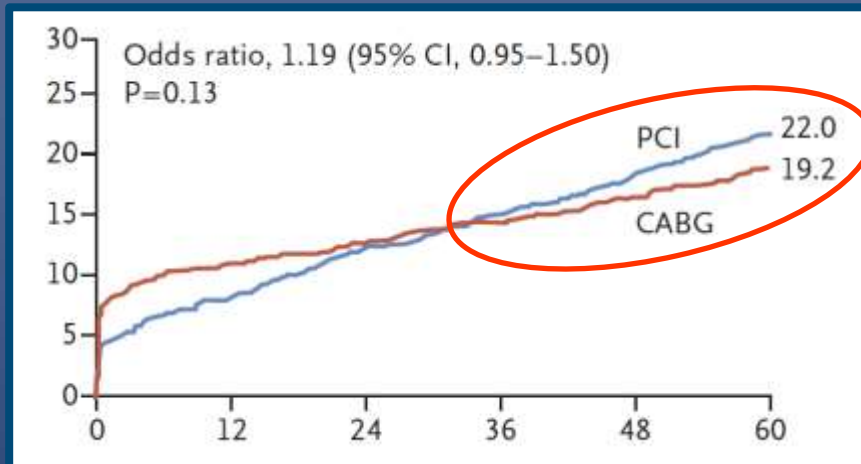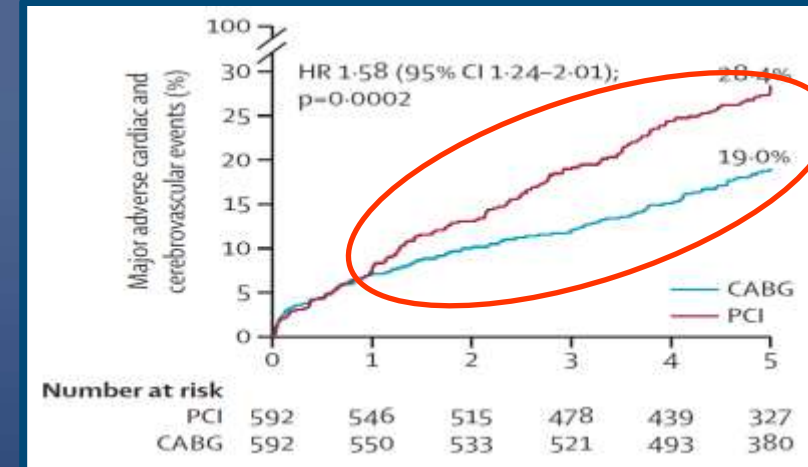
Background and Study Purpose

- Data are still limited on very long-term (beyond 5 years) outcomes of PCI or CABG in patients with left main coronary artery (LMCA) disease in RCTs.

- Given that some studies reported a trend of late catch-up or crossover in primary outcome favoring CABG over PCI over time, there remains uncertainty about long-term outcomes it warrants additional longer-term follow-up studies.

PRECOMBAT: Trial Design

1454 patients with LMCA disease from April 2004 to August 2009 in 13 major centers, Korea

Clinical and anatomic eligibility considered by the cardiologists and surgeons

Yes

No
(N=854)

Randomized (N=600)

Enrollment registry

Stratified by participating center

R

PCI (Cypher) (N=300)

CABG (N=300)
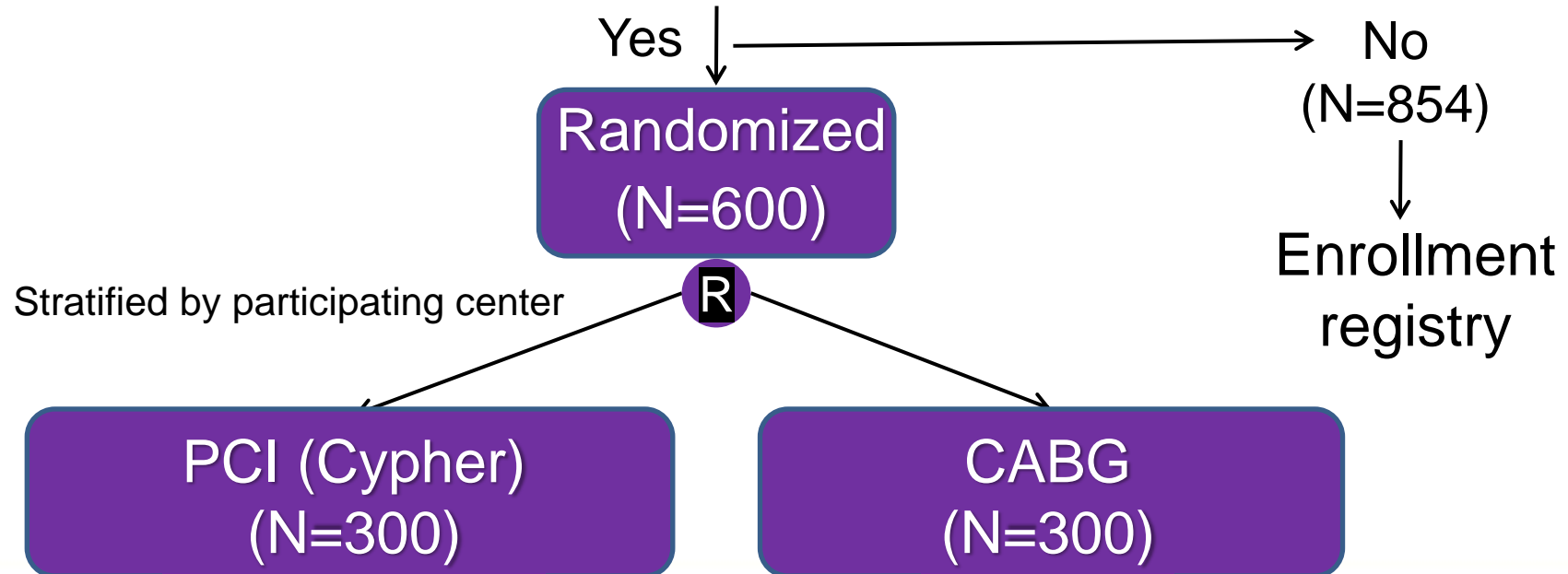
Follow-up: 1 month, 6 months, 1 year, annually through 5 years
Primary endpoint: Major adverse cardiac or cerebrovascular events (MACCE)

PRECOMBAT Trial at 2 Year and at 5 Year

Primary endpoint: MACCE (a composite of death from any cause, MI, stroke, or ischemia-driven target-vessel revascularization)

2-Year Report
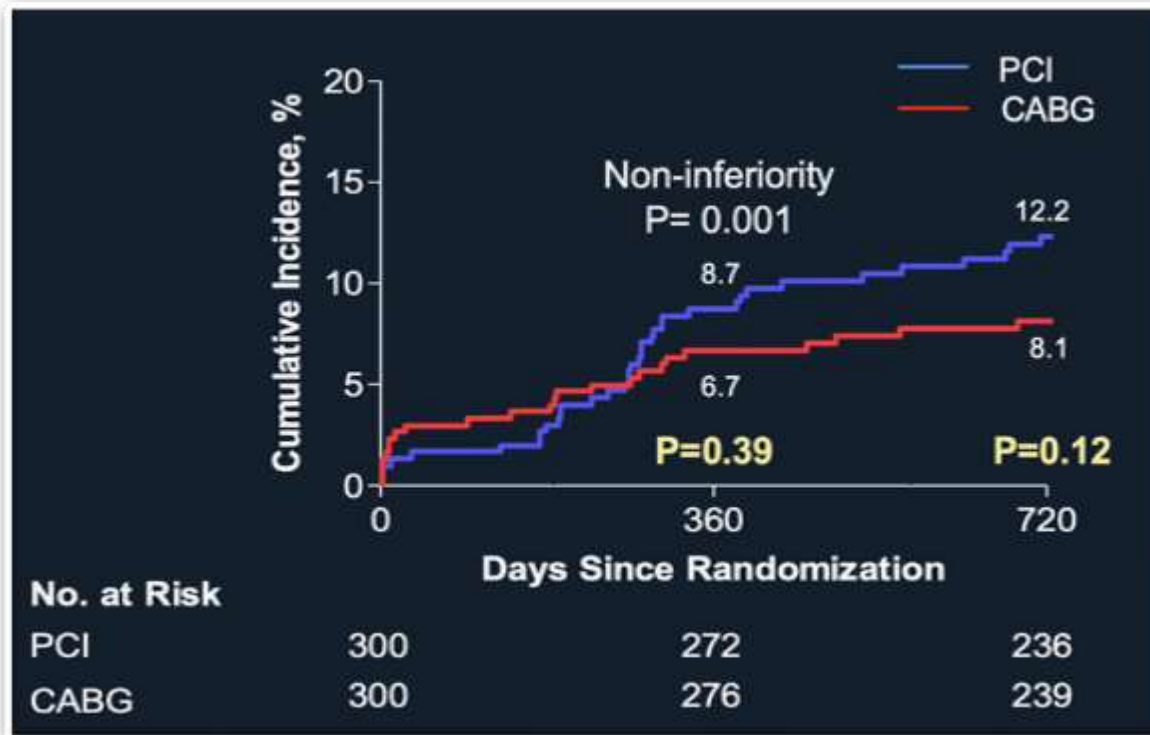
5-Year Report
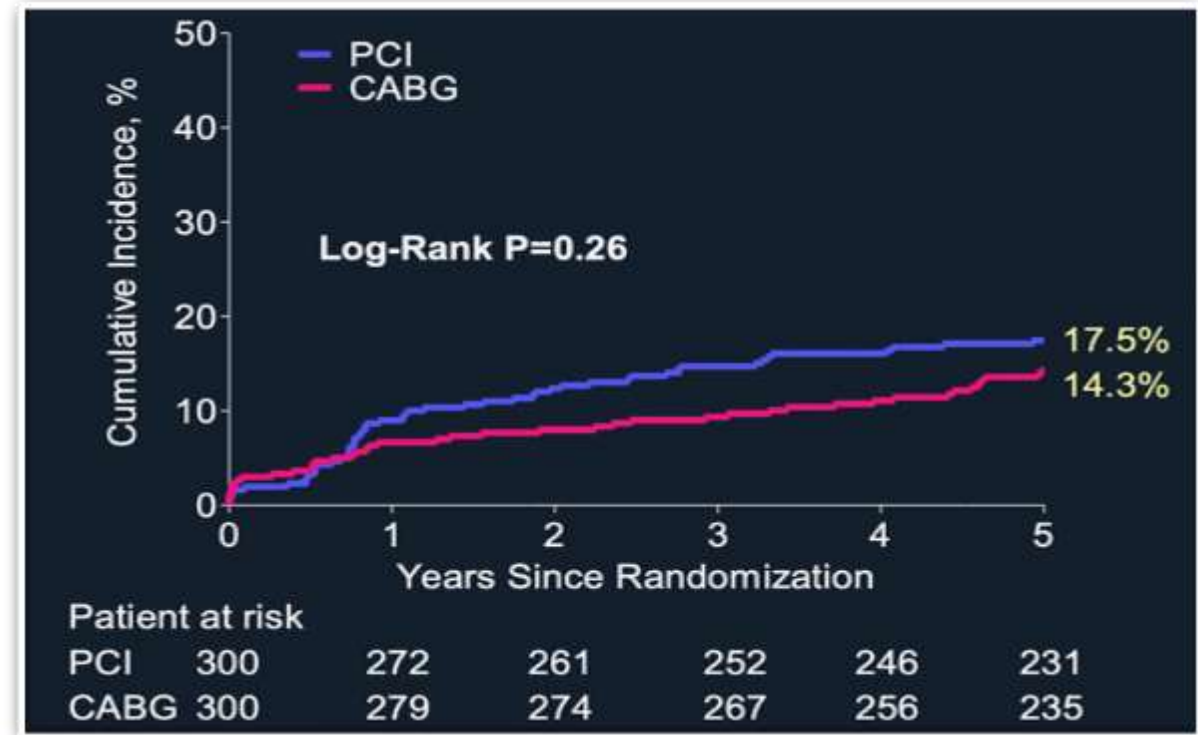
Major Inclusion Criteria

- ≥ 18 years of age.
- Significant *de novo* ULMCA stenosis (>50%)
- Left main lesion and lesions outside ULMCA (if present) <u>potentially comparably treatable with PCI and CABG,</u> determined by physician and operators
- Objective evidence of ischemia or ischemic symptom with angina or NSTEMI

Major Exclusion Criteria

- Any contraindication to DAPT
- Any previous PCI within 1 year
- Previous CABG
- Chronic total occlusion > 1
- AMI within 1 week
- Shock or LV EF < 30%
- Planed surgery
- Disabled stroke
- Other comorbidity, such as CRF, liver disease, etc

Primary Outcome

- Cumulative rate of major adverse cardiac or cerebrovascular events (MACCE) at 10-year after randomization

  – Death from any cause

  – Myocardial infarction

  – Stroke

  – Ischemia-driven TVR

Definition

- Myocardial Infarction

  ≤48 H: new Q waves and CK-MB ≥ 5 times

  >48 H: Any CK-MB elevation and

  ischemic symptoms/signs

- Stroke: confirmed by imaging and neurologist

- TVR (target-vessel revascularization)

  - Ischemia-driven: angiographic stenosis >50% and ischemic symptom/sign or angiographic stenosis >70%

Major Secondary Outcomes

- Individual components of the primary composite outcome,
- A composite of death, MI, or stroke,
- Any revascularization, or
- Definite stent thrombosis or symptomatic graft occlusion.

10-Year Follow-Up

- Although the PRECOMBAT was initially planned to complete FU at 5 years in the original protocol, all participating centers agreed to participate in an investigator-driven extension of follow-up of 10 years.

- Information on adverse clinical events and survival data was obtained through (electronic) healthcare record review and national death registry checks of the Korean National Health Insurance Service (NHIS) database.

- The NHIS is a single-payer program of a universal health coverage system and provides mandatory health care for all Korean citizens, with an enrollment rate of more than 97%.

Baseline Clinical Characteristics

	PCI (N=300)	CABG (N=300)
Age, years	61.8±10.0	62.7±9.5
Male gender	228 (76.0)	231 (77.0)
Body-mass index	24.6±2.7	24.5±3.0
Diabetes mellitus		
Any	102 (34.0)	90 (30.0)
Requiring insulin	10 (3.3)	9 (3.0)
Hypertension	163 (54.3)	154 (51.3)
Hyperlipidemia	127 (42.3)	120 (40.0)
Current smoker	89 (29.7)	83 (27.7)
Previous PCI	38 (12.7)	38 (12.7)
Previous myocardial infarction	13 (4.3)	20 (6.7)
Previous congestive heart failure	0 (0)	2 (0.7)

*Data are presented as mean ± SD or n (%)

Baseline Clinical Characteristics

	PCI (N=300)	CABG (N=300)
Chronic renal failure	4 (1.3)	1(0.3)
Peripheral vascular disease	15 (5.0)	7 (2.3)
Chronic pulmonary disease	6 (2.0)	10 (3.3)
Family history of CAD	31 (10.3)	19 (6.3)
Clinical manifestation		
Stable angina or silent ischemia	160 (53.3)	137 (45.7)
Unstable angina	128 (42.7)	144 (48.0)
Recent myocardial infarction	12 (4.0)	19 (6.3)
Ejection fraction, %	61.7±8.3	60.6±8.5
Electrocardiographic findings		
Sinus rhythm	286 (96.6)	289 (97.3)
Atrial fibrillation	5 (1.7)	5 (1.7)
Others	5 (1.7)	3 (1.0)
EuroSCORE	2.6±1.8	2.8±1.9

*Data are presented as mean ± SD or n (%)

Baseline Angiographic Characteristics

	PCI (N=300)	CABG (N=300)
Extent of disease vessel		
LM only	27 (9.0)	34 (11.3)
LM plus 1-vessel	50 (16.7)	53 (17.7)
LM plus 2-vessel	101 (33.7)	90 (30.0)
LM plus 3-vessel	122 (40.7)	123 (41.0)
Bifurcation left main involvement	200 (66.9)	183 (62.2)
SYNTAX score	24.4±9.4	25.8±10.5
Low (≤22)	131 / 291 (45.0)	109 / 275 (39.6)
Intermediate (23 to 32)	102 / 291 (35.1)	98 / 275 (35.6)
High (≥33)	58 / 291 (19.9)	68 / 275 (24.7)
Complete revascularization	205 (68.3)	211 (70.3)

*Data are presented as mean ± SD or n (%)

Procedural or Operative Characteristics

PCI (N=300)		CABG (N=300)	
Stents number in LM	1.6±0.8	Grafts per patient	2.7±0.9
Stent length in LM, mm	44.0±31.9	Arterial grafts	2.1±0.9
Stents per pt	2.7±1.4	Vein graft	0.7±0.8
Stent length per pt, mm	60.0±42.1	Use of LIMA	233 (93.6)
IVUS guidance	250 (91.2)	Off-pump surgery	155 (63.8)
Bifurcation treatment			
1-stent technique	87 (46.3)		
2-stent technique			
Crush	33 (17.9)		
Kissing	33 (17.9)		
T stent	25 (13.6)		
V stent	4 (2.2)		
Final kissing balloon	129 (70.1)		

*Data are presented as mean ± SD or n (%)

10-Year Follow-Up of PRECOMBAT Trial

1454 Patients assessed for eligibility

854 Ineligible
    335 enrolled in CABG registry
    475 enrolled in PCI registry
    44 underwent medical treatment

600 Patients underwent randomization

300 Were assigned to receive PCI
276 Received assigned treatment
24 Did not receive assigned treatment
24 Underwent CABG

300 Were assigned to receive CABG
248 Received assigned treatment
52 Did not receive assigned treatment
51 Underwent PCI
1 Underwent medical treatment

300 From sites that participated in 10-year FU
288 With complete FU data at 10 years (96%)
241 Followed-up and alive
47 Died
12 With incomplete follow-up data at 10 years
12 Lost to follow-up

300 From sites that participated in 10-year FU
288 With complete FU data at 10 years (96%)
244 Followed-up and alive
44 Died
12 With incomplete follow-up data at 10 years
12 Lost to follow-up

300 Were included in primary analysis

300 Were included in primary analysis

Primary Endpoint of MACCE: ITT Population

HR 1.25
(95% CI 0.93 – 1.69)

29.8%
24.7%

Patients (%)

Years since procedure
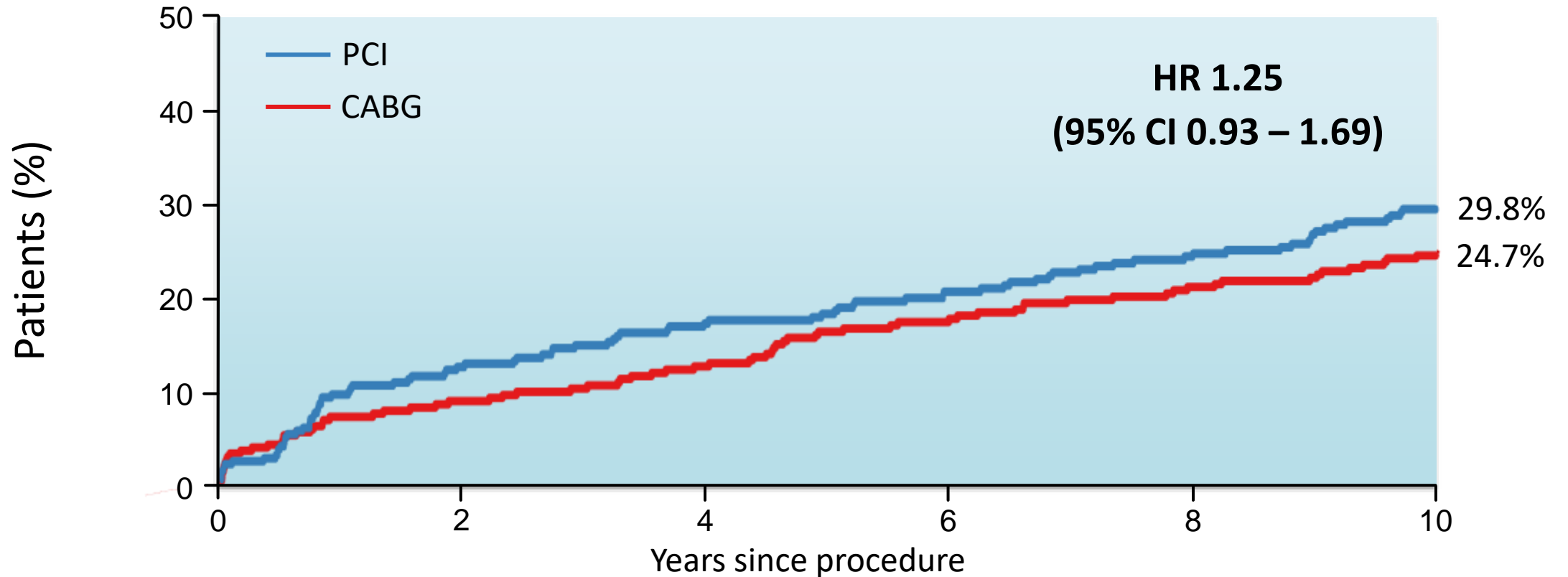
Number at risk

PCI	300	256	239	226	214	195
CABG	300	265	253	237	227	210

Primary endpoint: MACCE (death, MI, stroke, or ischemia-driven TVR)

Composite of Death, MI, or Stroke
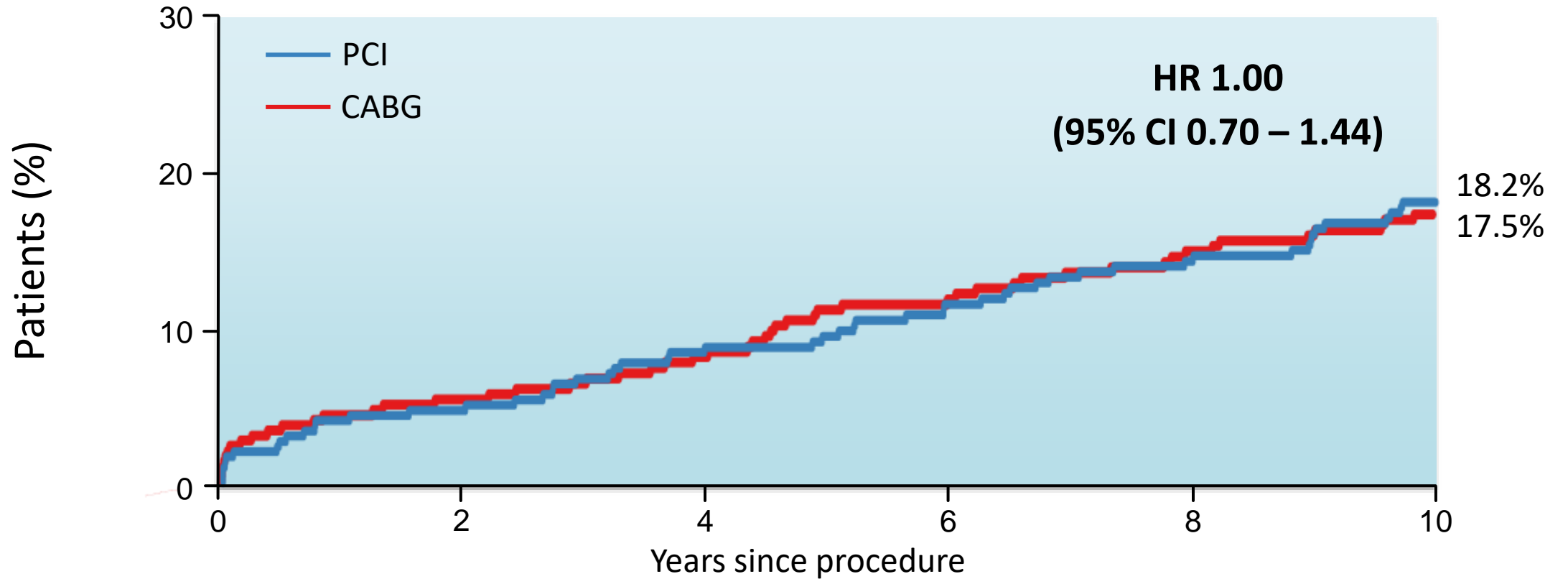
Death from Any Cause

Patients (%) — y-axis: 0, 10, 20, 30

Years since procedure — x-axis: 0, 2, 4, 6, 8, 10

Legend:
- PCI
- CABG

HR 1.13
(95% CI 0.75 – 1.70)

14.5%
13.8%
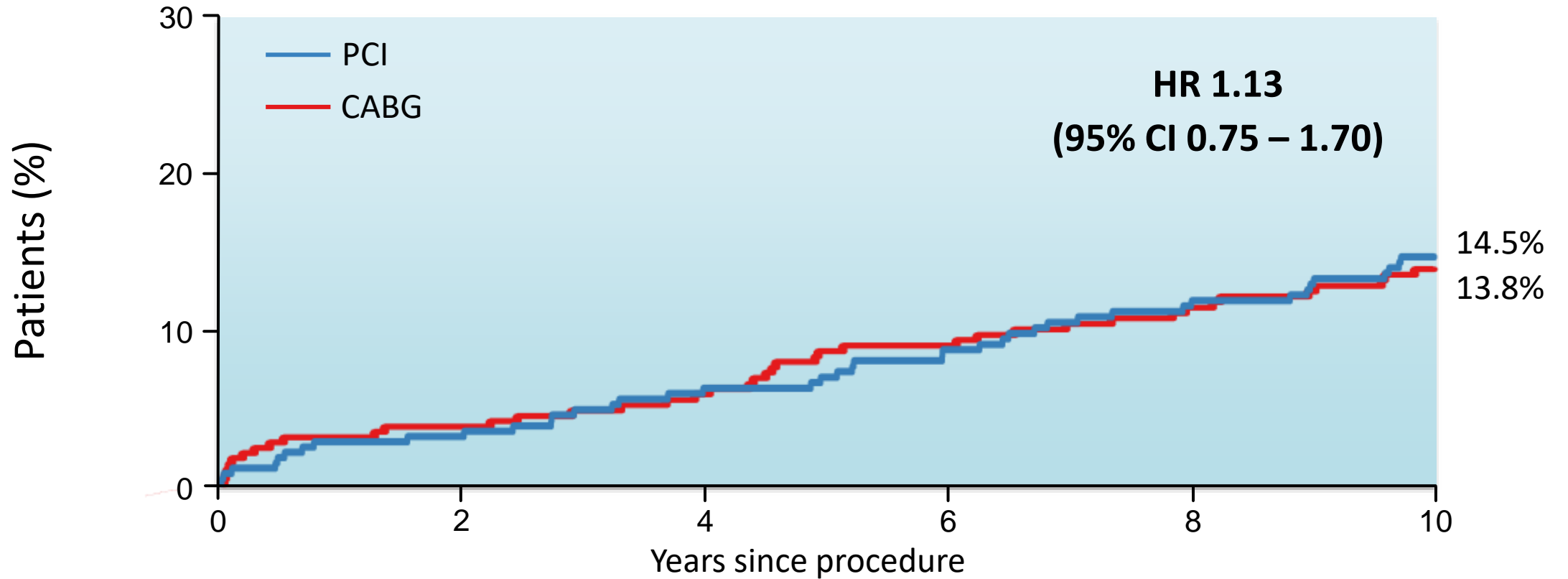
Number at risk

PCI	300	284	272	262	253	237
CABG	300	279	272	262	254	238

Ischemic-Driven Target-Vessel Revascularization

PCI
CABG

HR 1.98
(95% CI 1.21 – 3.21)

16.1%

8.0%

Patients (%)

Years since procedure
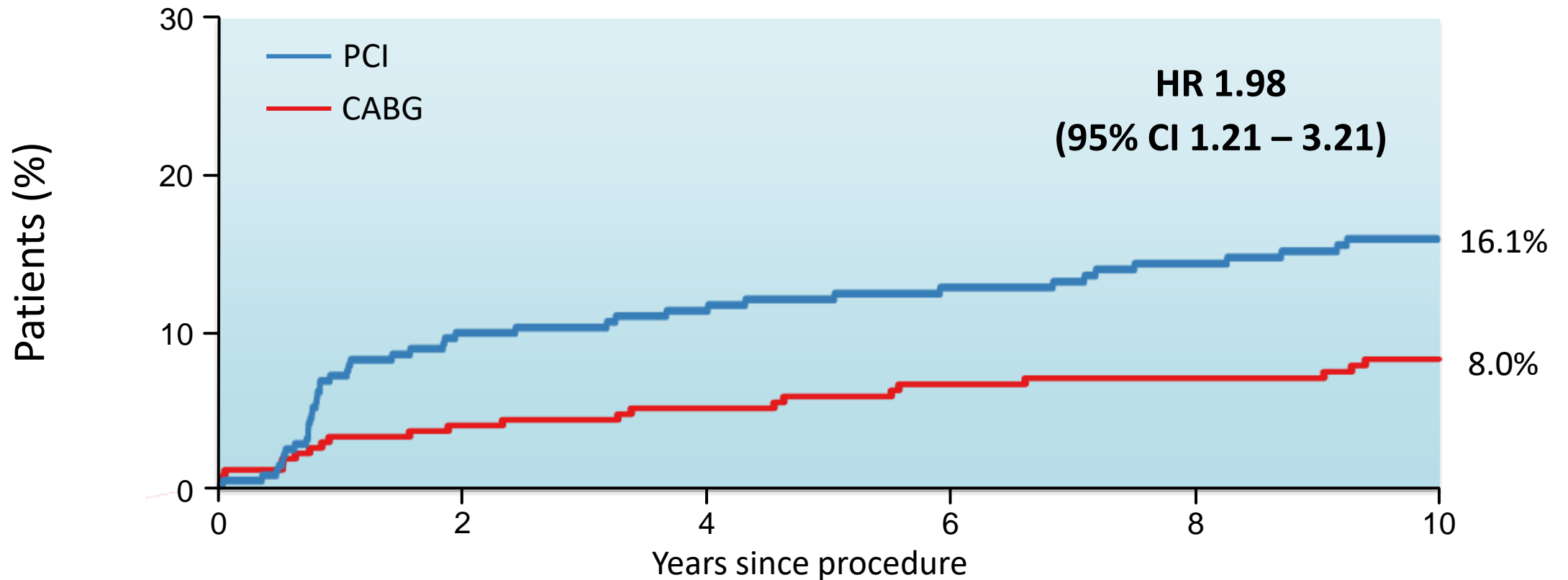
Number at risk						
PCI	300	255	240	227	214	199
CABG	300	270	260	246	237	220

Primary and Secondary Outcomes at 10 Years

Outcomes	PCI (N=300)	CABG (N=300)	Risk Difference (95% CI)	HR (95% CI)*
MACCE	87 (29.8%)	72 (24.7%)	5.2 (-2.1 to 12.4)	1.25 (0.93–1.69)
Death, MI, or stroke	53 (18.2%)	51 (17.5)	0.7 (-5.6 to 6.9)	1.00 (0.70–1.44)
Death from any cause	42 (14.5%)	40 (13.8%)	0.7 (-5.0 to 6.4)	1.13 (0.75–1.70)
Cardiovascular cause	22 (7.8%)	25 (8.7%)	-0.9 (-5.5 to 3.6)	0.96 (0.56–1.65)
Non-cardiovascular cause	11 (3.9%)	8 (2.9%)	1.0 (-2.0 to 4.0)	1.55 (0.63–3.81)
Undetermined cause	9 (3.4%)	7 (2.7%)	0.8 (-2.2 to 3.7)	1.27 (0.50–3.22)
MI	9 (3.2%)	8 (2.8%)	0.4 (-2.4 to 3.2)	0.76 (0.32–1.82)
Q-wave	4 (1.4%)	4 (1.4%)	-0.02 (-1.9 to 1.9)	0.82 (0.22–3.06)
Non-Q-wave	5 (1.8%)	4 (1.4%)	0.4 (-1.7 to 2.5)	0.71 (0.22–2.26)
Stroke	5 (1.9%)	6 (2.2%)	-0.3 (-2.7 to 2.1)	0.71 (0.22–2.23)
Ischemia-driven TVR	45 (16.1%)	22 (8.0%)	8.1 (2.8 to 13.5)	1.98 (1.21–3.21)
Any revascularization	59 (21.3%)	29 (10.6%)	10.7 (4.6 to 16.7)	2.04 (1.33–3.11)
Stent thrombosis or symptomatic graft occlusion	4 (1.4%)	10 (3.7%)	-2.3 (-4.9 to 0.3)	0.56 (0.20–1.55)

ACC.20 TOGETHER WITH WORLD CONGRESS OF CARDIOLOGY

*Hazard ratios (HR) are for the PCI group as compared with the CABG group

Key Subgroup Analyses: Forest Plot for Primary Endpoint

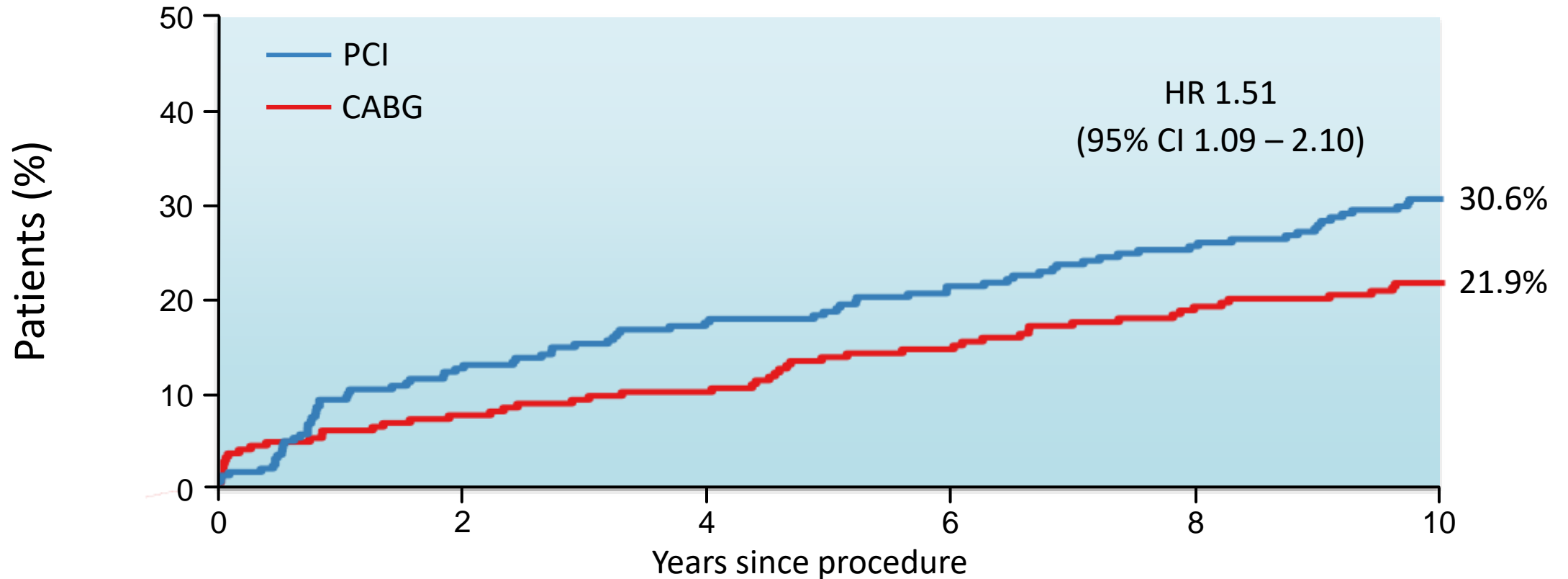| Subgroup	PCI	CABG	Hazard Ratio (95% CI)		P value for Interaction
	no. /total no. (%)				
Overall	87/300 (29.8)	72/300 (24.7)		1.25 (0.93–1.69)	
Age					0.99
<65	42/171 (25.0)	27/151 (18.2)		1.32 (0.84–2.08)	
≥65	45/129 (36.3)	45/149 (31.4)		1.30 (0.87–1.95)	
Sex					0.95
Male	68/228 (30.6)	54/231 (24.0)		1.24 (0.87–1.75)	
Female	19/72 (27.1)	18/69 (26.9)		1.12 (0.60–2.09)	
Diabetes					0.70
Yes	37/102 (36.8)	24/90 (27.3)		1.25 (0.76–2.05)	
No	50/198 (26.1)	48/210 (25.6)		1.16 (0.79–1.69)	
Clinical presentation					0.89
Non-acute coronary syndrome	42/160 (26.7)	30/137 (22.8)		1.35 (0.87–2.11)	
Acute coronary syndrome	45/140 (33.4)	42/163 (26.2)		1.29 (0.86–1.95)	
Left main involvement					0.54
Ostium and shaft	23/99 (23.6)	23/111 (21.2)		1.12 (0.65–1.91)	
Distal bifurcation	64/200 (33.1)	48/183 (28.1)		1.32 (0.91–1.90)	
Extent of diseased vessel					0.048
Left main only	4/27 (15.1)	5/34 (14.9)		1.55 (0.40–5.95)	
Left main with 1-vessel disease	6/50 (13.4)	10/53 (19.8)		0.67 (0.25–1.76)	
Left main with 2-vessel disease	30/101 (30.1)	26/90 (29.9)		0.89 (0.53–1.51)	
Left main with 3-vessel disease	47/122 (40.0)	31/123 (25.6)		1.82 (1.16–2.86)	
Syntax score					0.63
≤22	27/131 (21.6)	23/109 (22.2)		1.01 (0.59–1.73)	
22-32	32/102 (31.8)	21/98 (22.2)		1.61 (0.92–2.81)	
≥33	26/58 (46.2)	24/68 (45.7)		1.18 (0.67–2.09)	
Complete revascularization					0.45
Yes	57/205 (28.3)	53/211 (25.7)		1.14 (0.79–1.65)	
No	30/95 (33.2)	19/89 (22.2)		1.57 (0.90–2.73)	

0.1   1   10

← PCI Better   CABG Better →

Primary Endpoint of MACCE: As-Treated Analysis

HR 1.51
(95% CI 1.11 – 2.06)

31.6%

21.8%

Years since procedure

Patients (%)

PCI
CABG
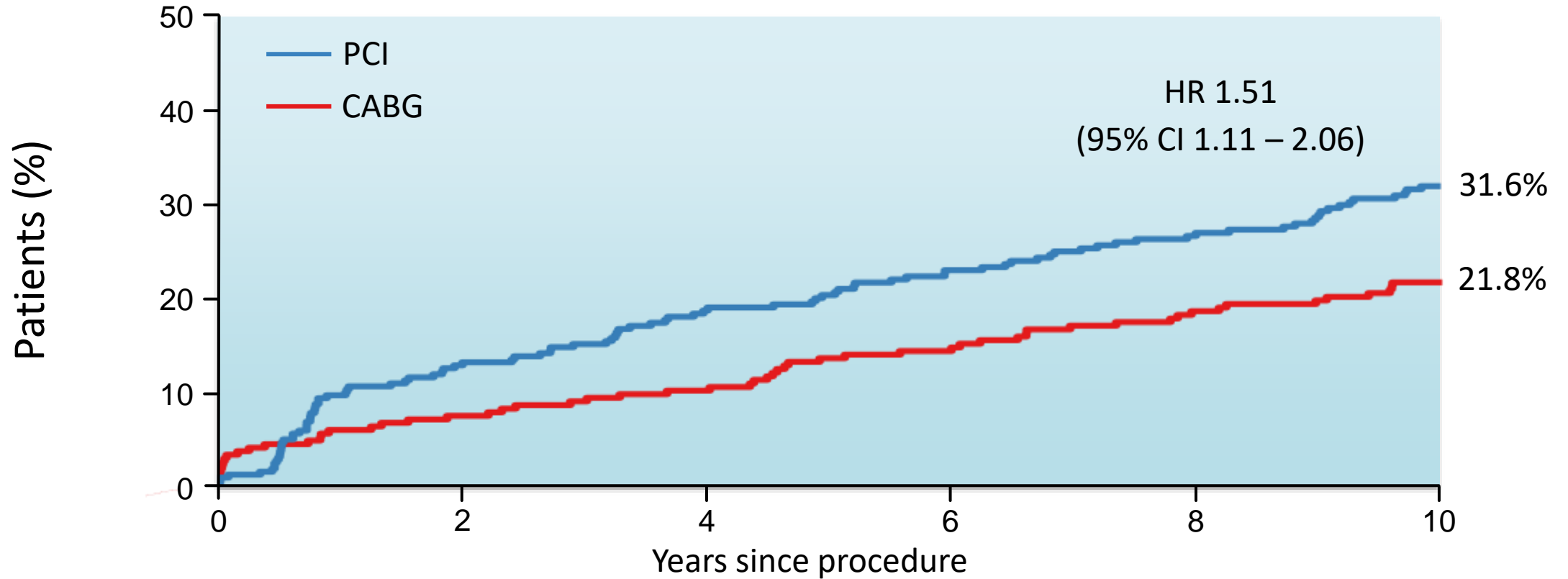
Number at risk						
PCI	327	275	254	238	226	206
CABG	272	245	237	224	214	199

Primary Endpoint of MACCE: Per-Protocol Analysis

Kaplan-Meier curves of Patients (%) versus Years since procedure comparing PCI (blue) and CABG (red).

HR 1.51
(95% CI 1.09 – 2.10)

PCI: 30.6%
CABG: 21.9%

Number at risk

	0	2	4	6	8	10
PCI	276	234	218	205	193	176
CABG	248	223	216	203	193	180

Circulation

Ten-Year Outcomes After Drug-Eluting Stents Versus Coronary Artery Bypass Grafting for Left Main Coronary Disease
Extended Follow-Up of the PRECOMBAT Trial

Editorial, see p 1447

BACKGROUND: Long-term comparative outcomes after percutaneous coronary intervention (PCI) with drug-eluting stents and coronary-artery bypass grafting (CABG) for left main coronary artery disease are highly debated.

METHODS: In the PRECOMBAT trial (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease), patients with unprotected left main coronary artery disease were randomly assigned to undergo PCI with sirolimus-eluting stents (n=300) or CABG (n=300) in 13 hospitals in Korea from April 2004 to August 2009. The follow-up was extended to at least 10 years for all patients (median, 11.3 years). The primary outcome was the incidence of major adverse cardiac or cerebrovascular events (composite of death from any cause, myocardial infarction, stroke, or ischemia-driven target-vessel revascularization).

RESULTS: At 10 years, a primary outcome event occurred in 29.8% of the PCI group and in 24.7% of the CABG group (hazard ratio [HR] with PCI vs CABG, 1.25 [95% CI, 0.93–1.69]). The 10-year incidence of the composite of death, myocardial infarction, or stroke (18.2% vs 17.5%; HR 1.00 [95% CI, 0.70–1.44]) and all-cause mortality (14.5% vs 13.8%; HR 1.13 [95% CI, 0.75–1.70]) were not significantly different between the PCI and CABG groups. Ischemia-driven target-vessel revascularization was more frequent after PCI than after CABG (16.1% vs 8.0%; HR 1.98 [95% CI, 1.21–3.21]).

Duk-Woo Park, MD*
Jung-Min Ahn, MD*
Hanbit Park, MD
Sung-Cheol Yun, PhD
Do-Yoon Kang, MD
Pil Hyung Lee, MD
Young-Hak Kim, MD
Do-Sun Lim, MD
Seung-Woon Rha, MD
Gyung-Min Park, MD
Hyeon-Cheol Gwon, MD
Hyo-Soo Kim, MD
In-Ho Chae, MD
Yangsoo Jang, MD
Myung-Ho Jeong, MD
Seung-Jea Tahk, MD
Ki Bae Seung, MD
Seung-Jung Park, MD
On behalf of the PRECOMBAT Investigators

ACC.20 TOGETHER WITH WORLD CONGRESS OF CARDIOLOGY

Circulation

Ten-Year Follow-Up of Left Main Coronary Artery Revascularization

Still Equipoise Between Percutaneous Interventions and Surgery?

Article, see p 1437

Fernando Alfonso, MD, PhD
Adnan Kastrati, MD, PhD

Left main coronary artery disease (LMCAD) remains a therapeutic challenge with important prognostic implications attributable to the large amount of subtended myocardium.[1,2] The current European clinical practice guidelines on coronary revascularization provide the same level of recommendation (class IA) for percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) for patients with LMCAD with low anatomic complexity (SYNTAX [Synergy between PCI with Taxus and Cardiac Surgery] score ≤22).[2] However, CABG is considered superior to PCI (class IA versus IIIB) for patients with LMCAD and severe complexity.[2] This represents a paradigm shift consider-

Alfonso et al. Circulation. 2020;141:1447–1451
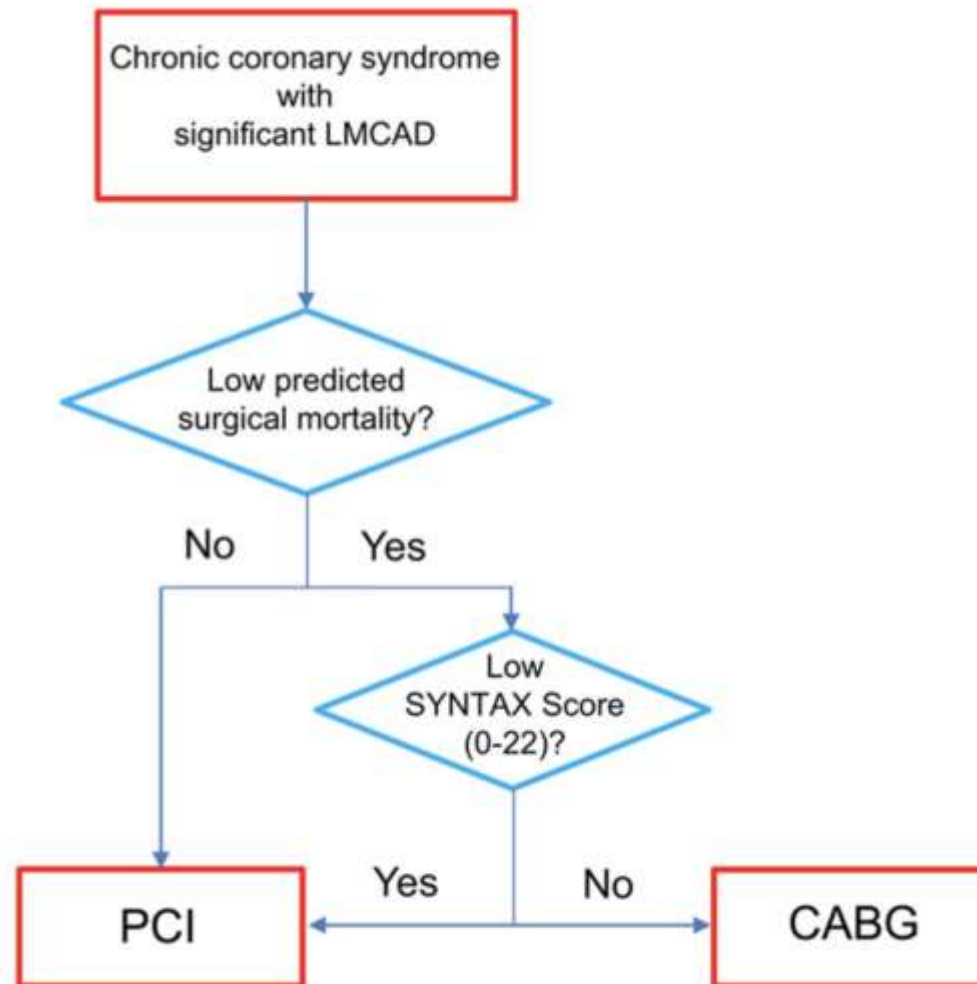
Proposed Heart-Team Decision-Making

A **CLINICAL CHARACTERISTICS:**
- Age
- Diabetes
- Left ventricular function
- STS score (better than EuroSCORE II)

ANATOMIC FEATURES:
- Completeness of revascularization
- Distal bifurcation involvement:
  - LAD and LCX ostial disease
  - LCX size. Dominance (RCA vs. LCX)
- Number of concomitant diseased vessels (1,2,3)
- SYNTAX Score and SYNTAX-2
- Specific adverse features of lesions in major vessels: (*)
  - Number of lesions
  - Lesion length
  - Chronic total occlusion
  - Major bifurcation
  - Severe calcification

B
Chronic coronary syndrome with significant LMCAD → Low predicted surgical mortality? — No → PCI / Yes → Low SYNTAX Score (0-22)? — Yes → PCI / No → CABG

Alfonso et al. Circulation. 2020;141:1447–1451

Summary

- In ten-year follow-up of the PRECOMBAT trial of patients with LMCA disease randomized to PCI or CABG, there was no significant difference in the incidence of MACCE, mortality, and serious composite outcome.
- Given that extended follow-up data of landmark clinical trials (SYNTAX, PRECOMBAT, EXCEL and NOBLE) are available, further **IPD meta-analysis** will provide more strong scientific evidence and useful insights to better inform the clinical decision-making process to select the optimal revascularization modality for these patients.