Randomized Trial of Stents versus Bypass Surgery for Left Main Coronary Artery Disease

Five-Year Outcomes of PRECOMBAT Study

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On behalf of the PRECOMBAT Investigators

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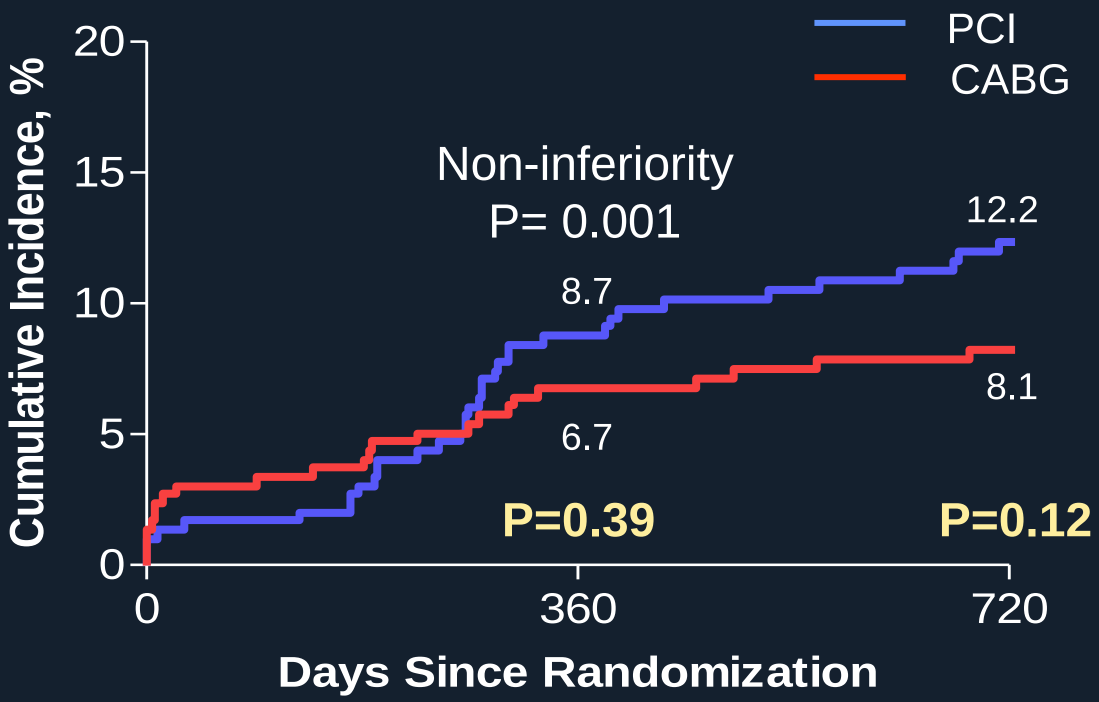
Introduction

- Recent guidelines considered PCI to be a potential alternative to CABG for unprotected left main coronary artery stenosis, based on several large registries and randomized trials.
- However, the durable effect of PCI remains in debate and limited data exist regarding the long-term comparison between PCI and CABG.

PRECOMBAT Study

Death, MI, Stroke or iTVR



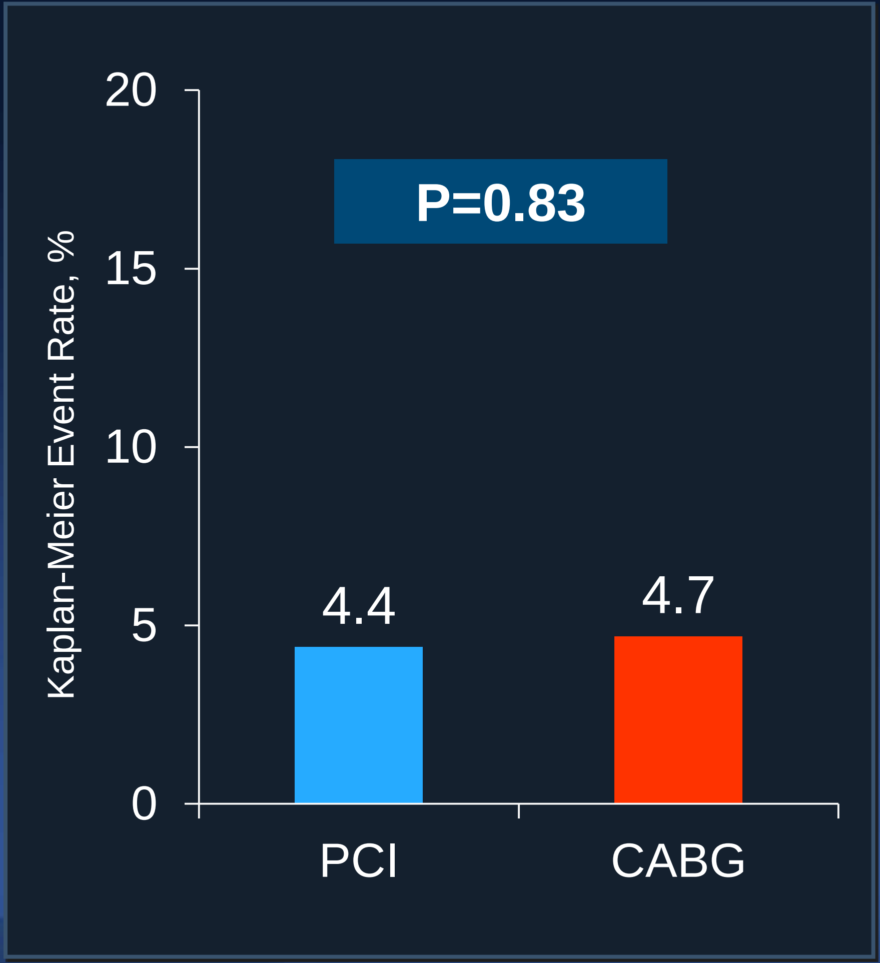
No. at Risk

PCI	300	272	236
CABG	300	276	239

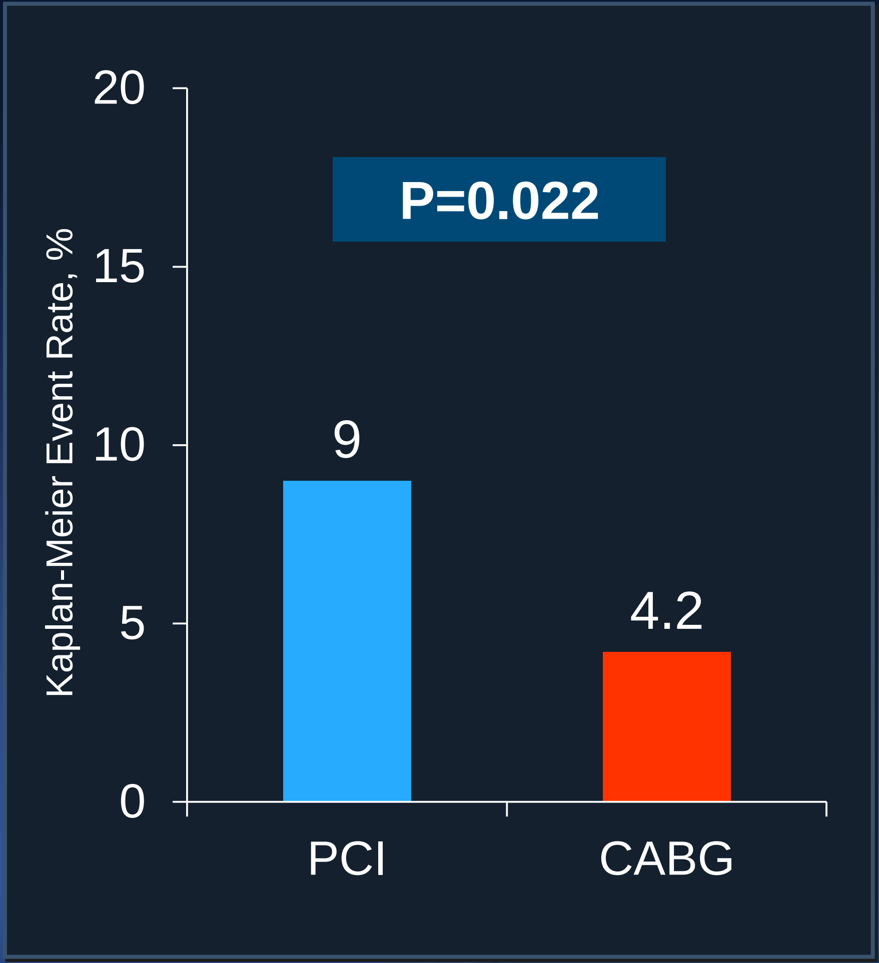
Park SJ, Kim YH, et al N Engl J Med 2011;364:1718-27

PRECOMBAT Study at 2 Year

Death, MI, or Stroke



iTVR



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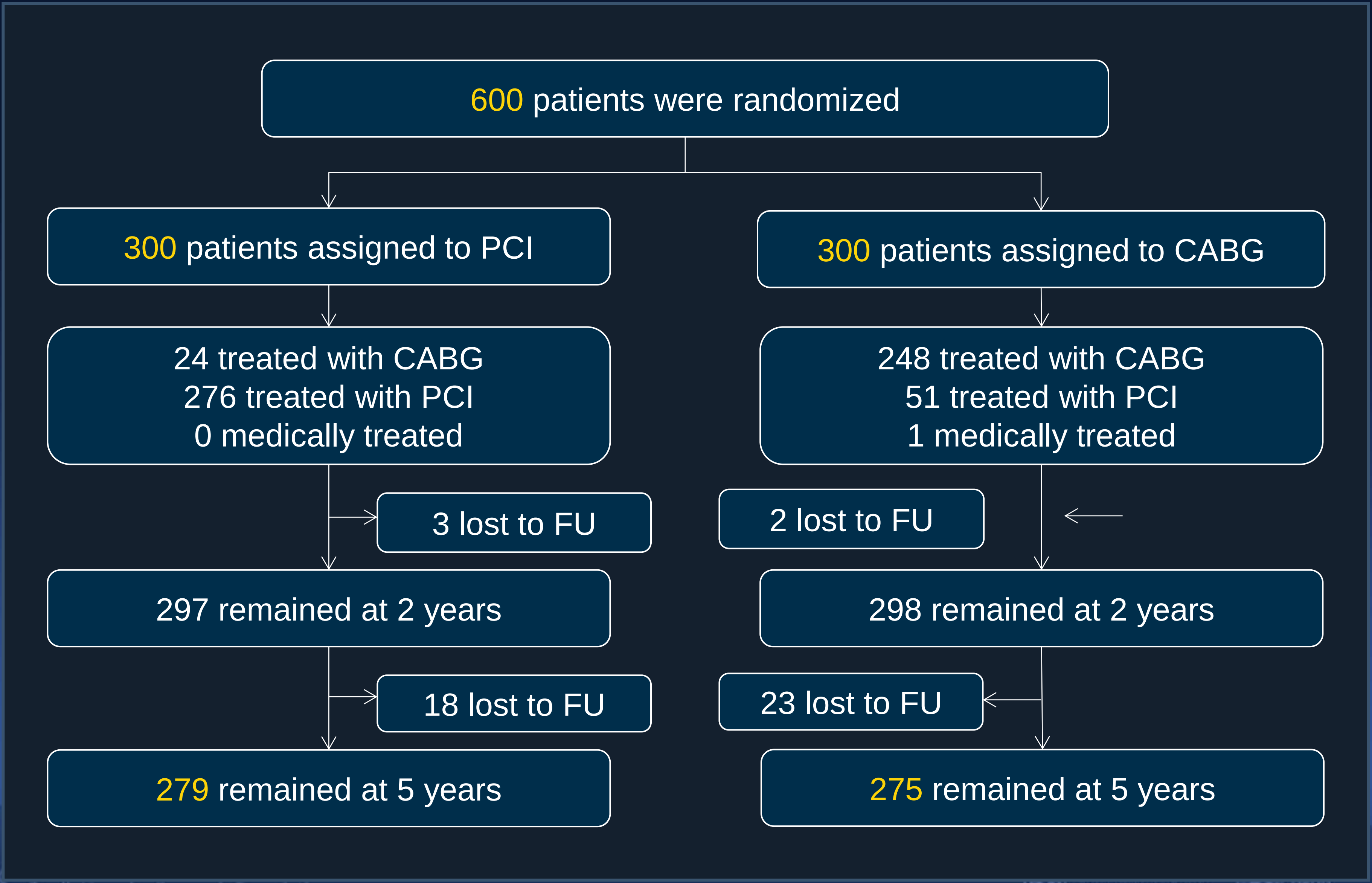
5 Year Follow-up of PRECOMBAT Study



600 patients were randomized

300 patients assigned to PCI

24 treated with CABG
276 treated with PCI
0 medically treated

3 lost to FU

297 remained at 2 years

18 lost to FU

279 remained at 5 years

300 patients assigned to CABG

248 treated with CABG
51 treated with PCI
1 medically treated

2 lost to FU

298 remained at 2 years

23 lost to FU

275 remained at 5 years

Participating Centers

Site	Investigator
Asan Medical Center	Seung-Jung Park
Korea University Anam Hospital	Do-Sun Lim
Korea University Guro Hospital	Seung-Woon Rha
Ulsan University Hospital	Sang-Gon Lee
Samsung Medical Center	Hyeon-Cheol Gwon
Seoul National University Hospital	Hyo-Soo Kim
Seoul National University Hospital, Bundang	In-Ho Chae
Yonsei University Severance Hospital	Yangsoo Jang
Chonnam National University Hospital	Myung-Ho Jeong
Ajou University Medical Center	Seung-Jea Tahk
Catholic University of Korea, St. Mary's Hospital	Ki Bae Seung

Major Inclusion Criteria

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

Major Exclusion Criteria

- Any contraindication to dual antiplatelet therapy
- 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

Study Procedures

- **Sirolimus-Eluting Cypher stent** for all lesions
- Strong recommendation of IVUS-guidance
- Other adjunctive devices at the operator’s discretion
- Use of LIMA to LAD anastomosis
- Off- or on-pump surgery at the operator’s discretion
- DAPT at least for 6 months after PCI
- Standard medical treatment after PCI and CABG

Primary End Point

- Cumulative rate of major adverse cardiac or cerebrovascular events (MACCE) at 5-year after randomization

  - Death from any cause
  - Myocardial infarction
  - Stroke
  - Ischemia-driven target vessel revascularization

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
- Target Vessel Revascularization
  - Ischemia-driven: ischemic symptom/sign or
    angiographic stenosis > 70%
  - Clinical-driven: ischemia symptom or sign

Statistical Analysis

- Kaplan-Meier method to estimate cumulative event rates, and log-rank test to compare them
- Cox proportional hazards model to calculate hazard ratios and 95% confidence intervals
- Subgroups analysis performed using the Cox regression model with tests for interaction.
- Primary analysis based on an intention-to-treat principle.

Baseline Clinical Characteristics

	PCI (N=300)	CABG (N=300)	P value
Age, years	61.8±10.0	62.7±9.5	0.24
Male sex	228 (76.0)	231 (77.0)	0.77
Body mass index	24.6±2.7	24.5±3.0	0.74
Medically treated diabetes			
Any	102 (34.0)	90 (30.0)	0.29
Requiring insulin	10 (3.3)	9 (3.0)	0.82
Hypertension	163 (54.3)	154 (51.3)	0.46
Hyperlipidemia	127 (42.3)	120 (40.0)	0.56
Current smoker	89 (29.7)	83 (27.7)	0.59
Previous PCI	38 (12.7)	38 (12.7)	1.0
Previous myocardial infarction	13 (4.3)	20 (6.7)	0.21
Previous congestive heart failure	0 (0)	2 (0.7)	0.16

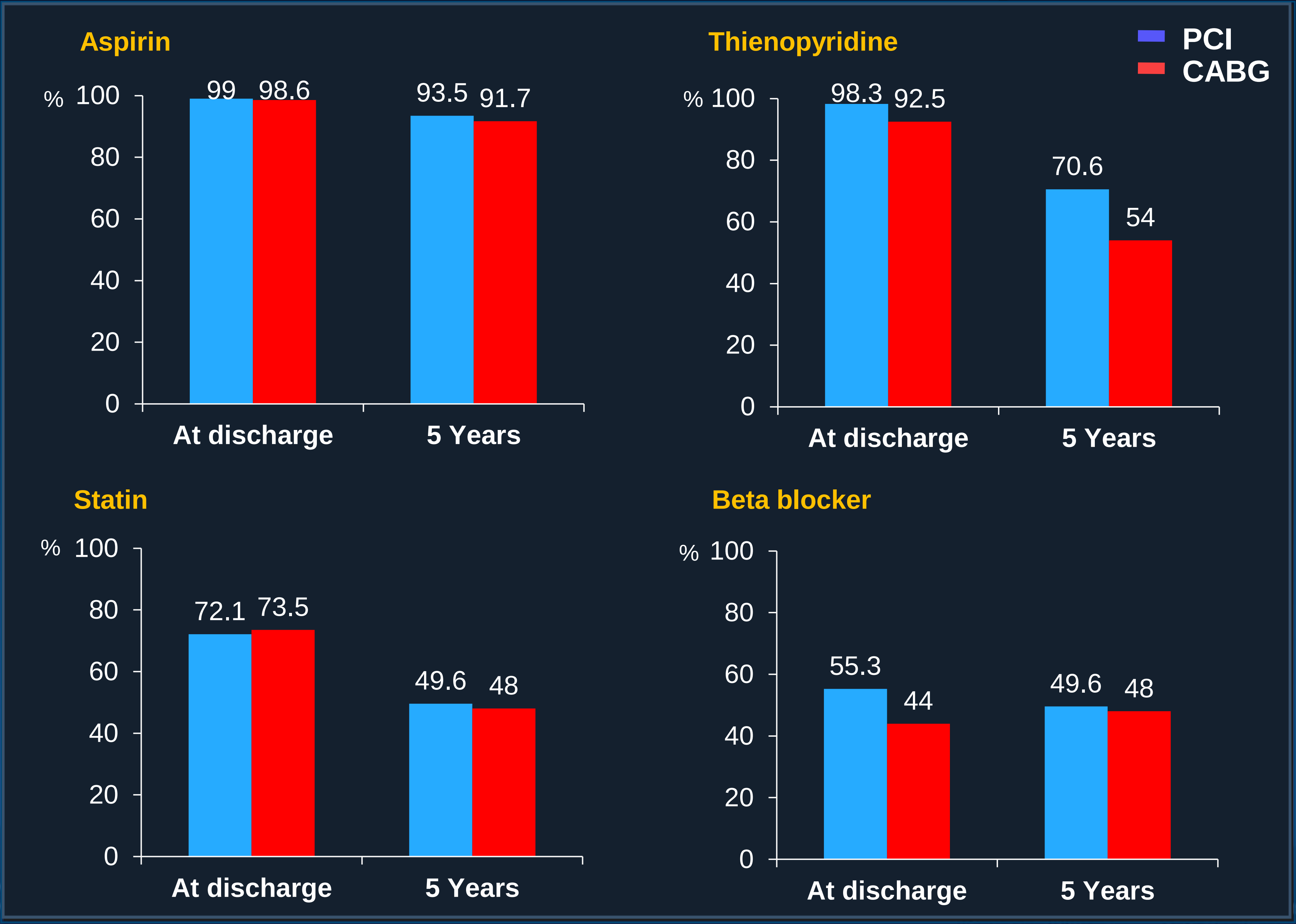
Baseline Clinical Characteristics

	PCI (N=300)	CABG (N=300)	P value
Chronic renal failure	4 (1.3)	1(0.3)	0.37
Peripheral vascular disease	15 (5.0)	7 (2.3)	0.08
Chronic pulmonary disease	6 (2.0)	10 (3.3)	0.31
Clinical manifestation			0.12
Stable angina or asymptomatic	160 (53.3)	137 (45.7)	
Unstable angina	128 (42.7)	144 (48.0)	
Recent acute myocardial infarction	12 (4.0)	19 (6.3)	
Ejection fraction, %	61.7±8.3	60.6±8.5	0.12
EuroSCORE value	2.6±1.8	2.8±1.9	0.16
Electrocardiographic findings			0.77
Sinus rhythm	286 (96.6)	289 (97.3)	
Atrial fibrillation	5 (1.7)	5 (1.7)	
Others	5 (1.7)	3 (1.0)	

Baseline Angiographic Characteristics

	PCI (N=300)	CABG (N=300)	P value
Extent of disease vessel			0.68
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)	0.24
Diameter stenosis of left main, %			0.12
> 50 and ≤ 70	160 (53.3)	141 (47.0)	
> 70	140 (46.7)	159 (53.0)	
Right coronary artery disease	149 (49.7)	159 (53.0)	0.41
Restenotic lesion	1 (0.3)	2 (0.7)	0.56
Chronic total occlusion	2 (0.7)	2 (0.7)	1.0
SYNTAX score	24.4±9.4	25.8±10.5	0.09

Medication at Follow-Up



Procedural Characteristics

PCI (N=300)

Stents number in LM	1.6±0.8
Stent length in LM, mm	44.0±31.9
Stents per pt	2.7±1.4
Stent length per pt, mm	60.0±42.1
IVUS guidance	250 (91.2)
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)

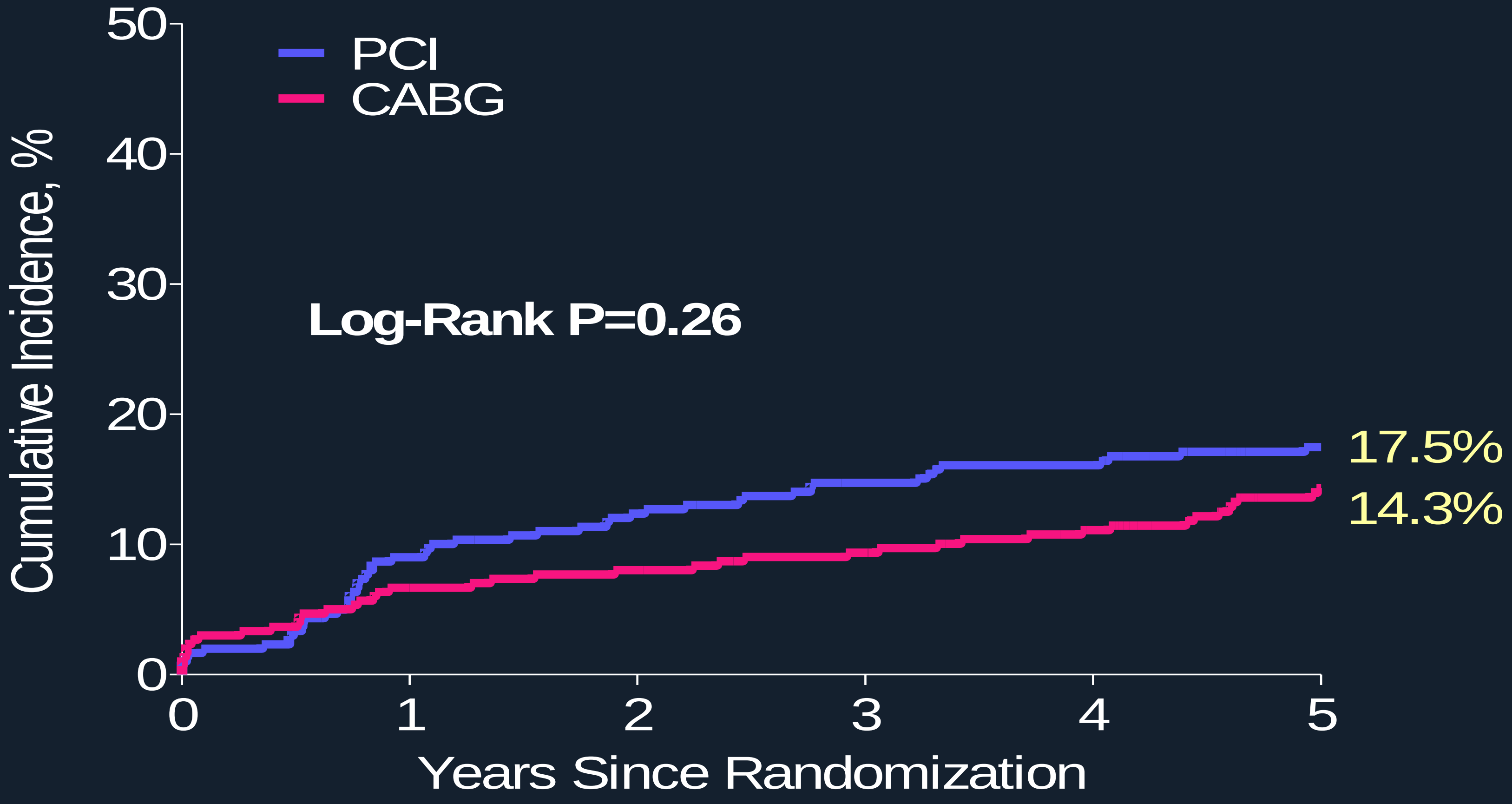
CABG (N=300)

Grafts per patient	2.7±0.9
Arterial grafts	2.1±0.9
Vein graft	0.7±0.8
Use of LIMA	233 (93.6)
Off-pump surgery	155 (63.8)

	PCI	CABG	P
Complete revascularization	205 (68.3)	211 (70.3)	0.60

Long-Term Outcomes

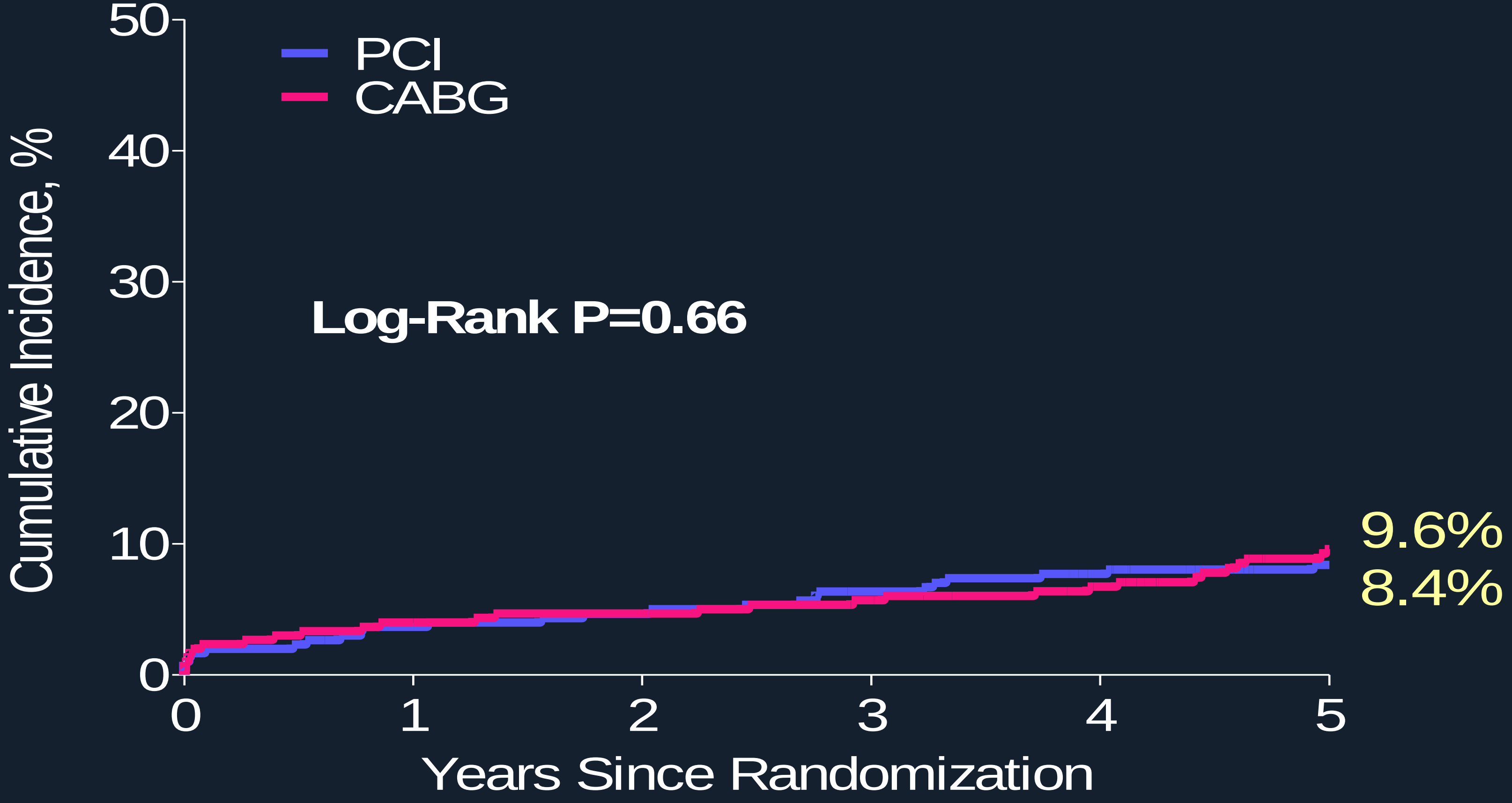
Primary End Point of MACCE



Patient at risk

PCI	300	272	261	252	246	231
CABG	300	279	274	267	256	235

Death, MI or Stroke

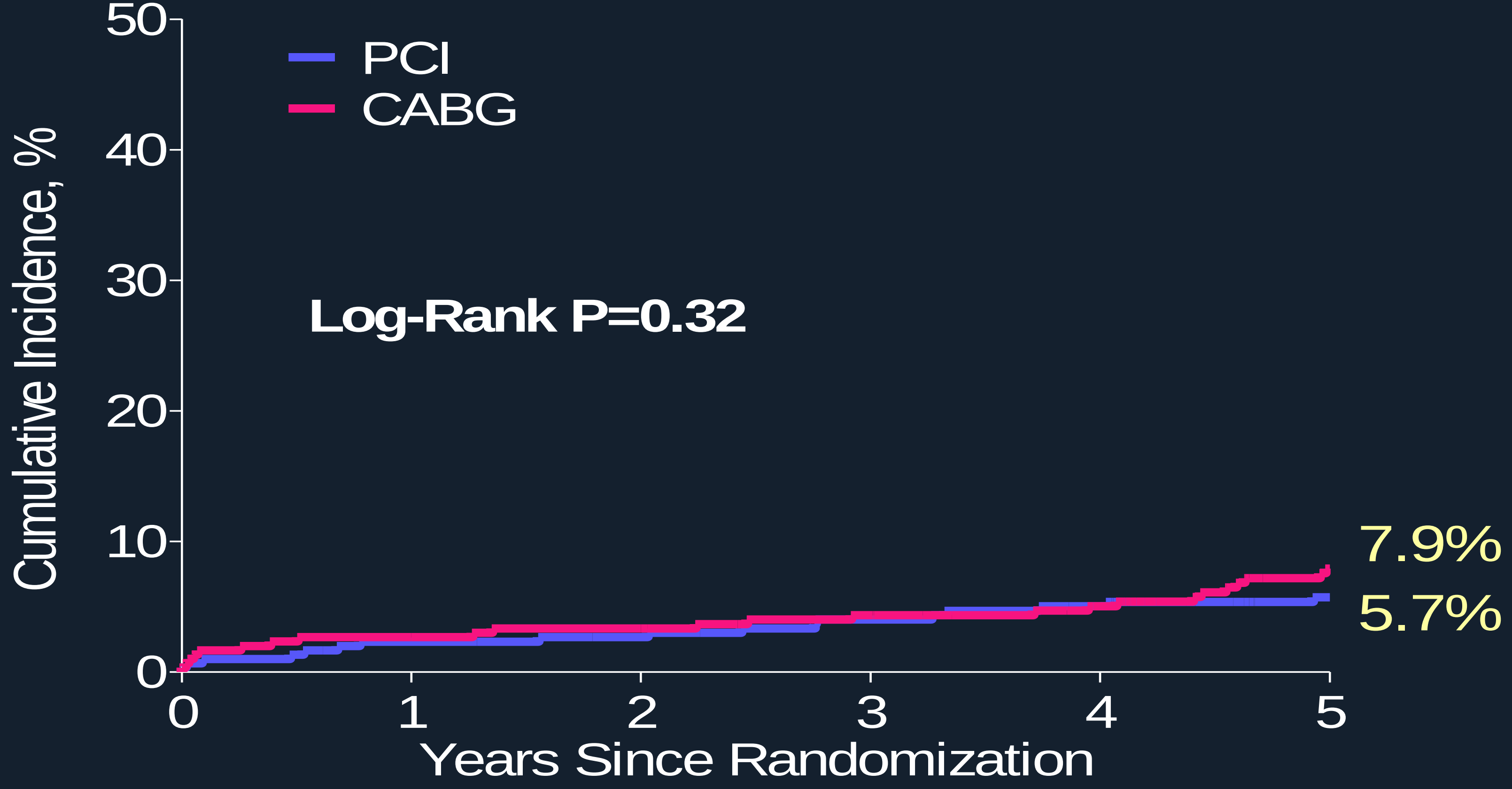


Log-Rank P=0.66

Patient at risk

PCI	300	288	284	277	270	256
CABG	300	287	284	277	268	247

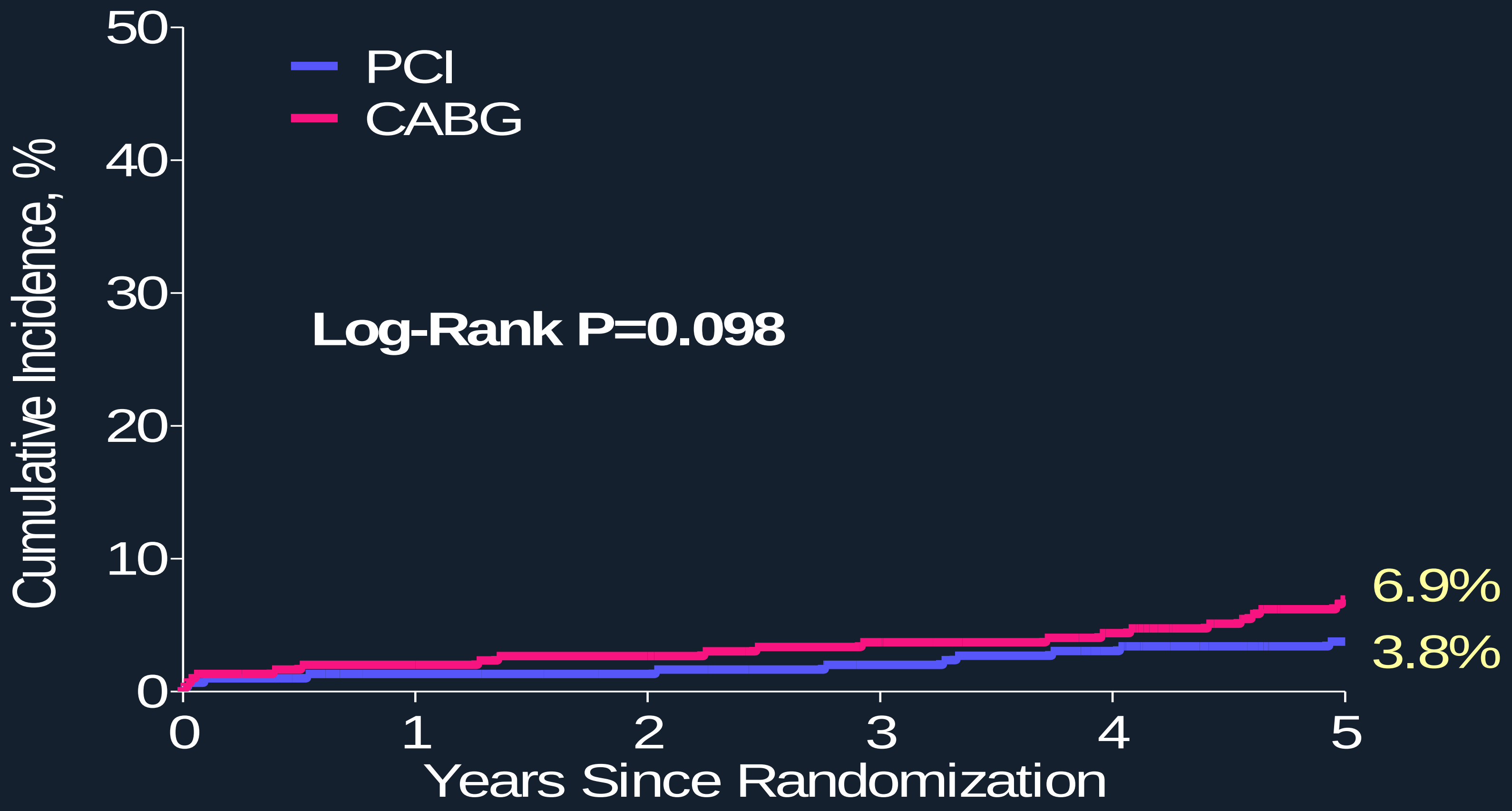
Death from Any Cause



Patient at risk

PCI	300	292	289	283	277	262
CABG	300	291	288	281	273	252

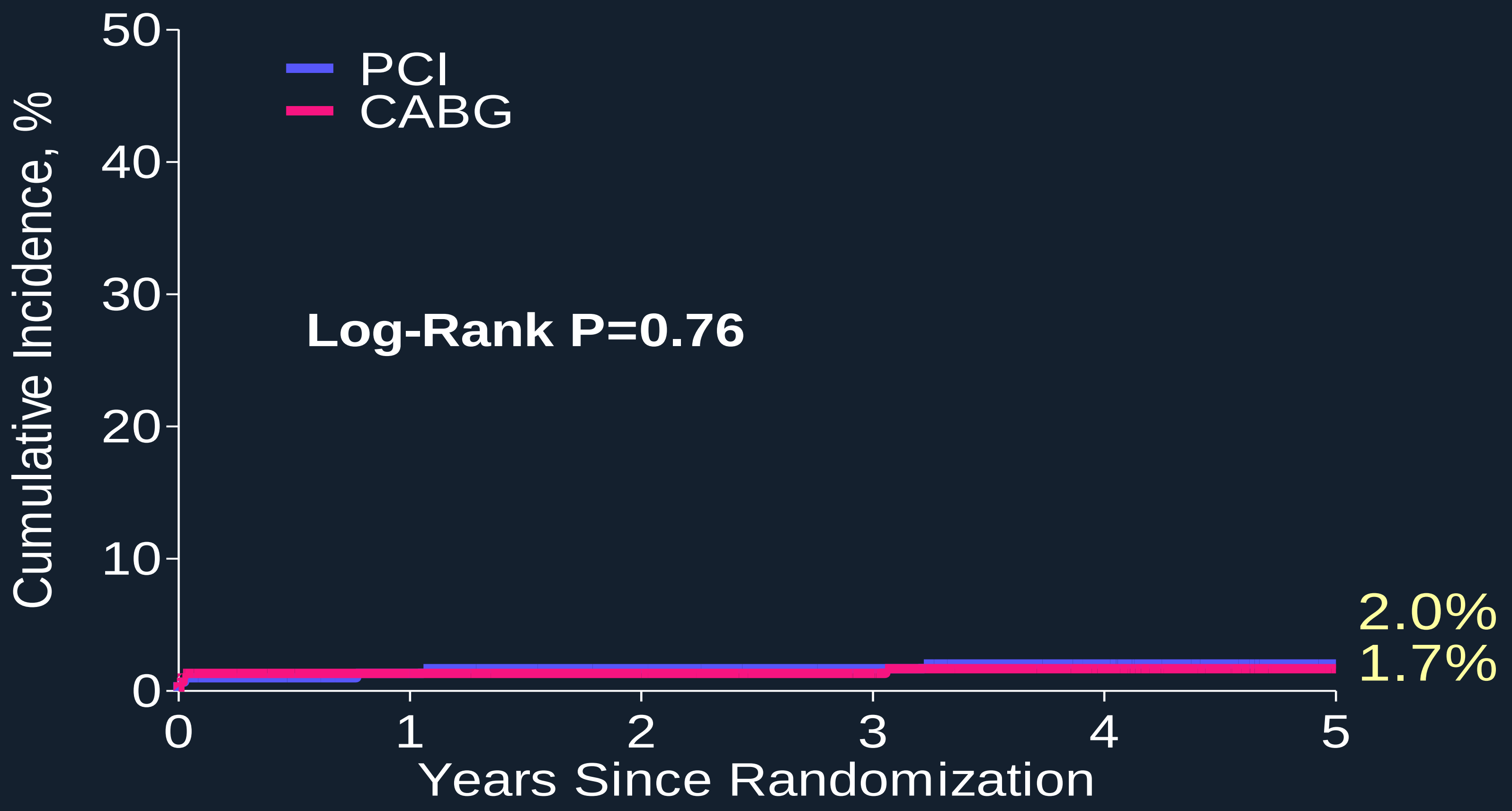
Cardiac Death



Patient at risk

PCI	300	292	289	283	277	262
CABG	300	291	288	281	273	252

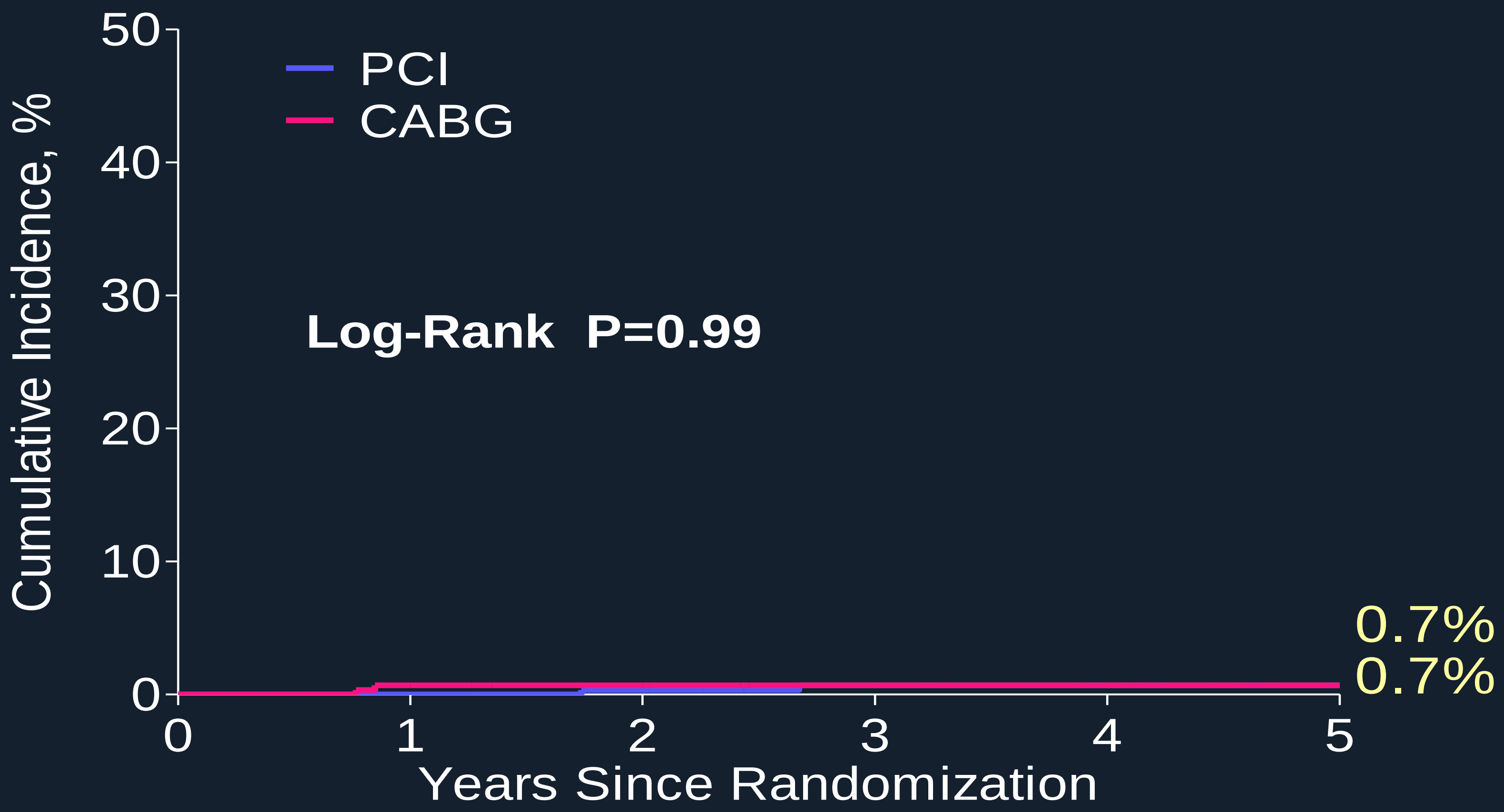
Myocardial Infarction



Patient at risk

PCI	300	288	284	278	271	257
CABG	300	289	286	279	270	249

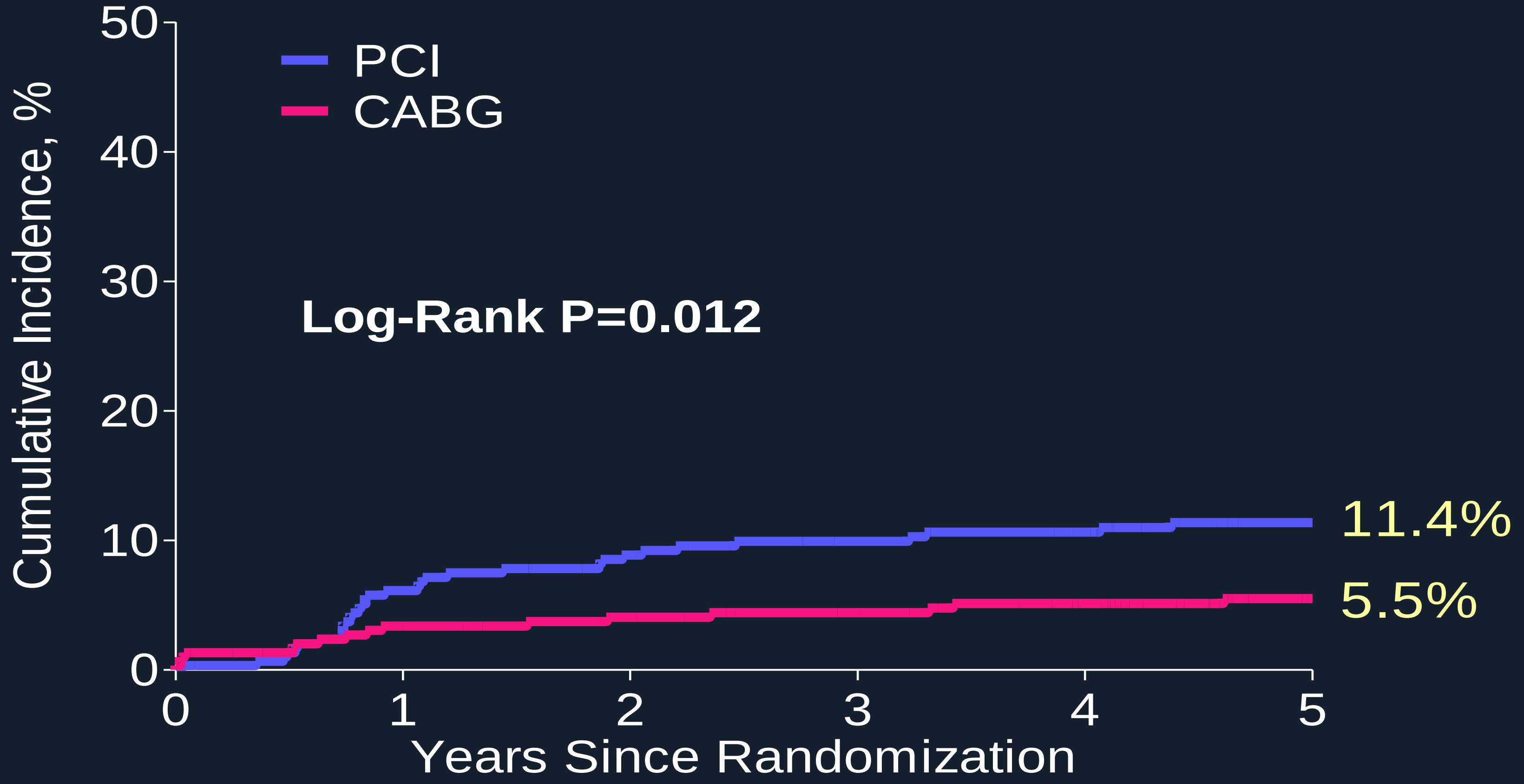
Stroke



Patient at risk

PCI	300	292	289	282	276	261
CABG	300	289	286	279	271	250

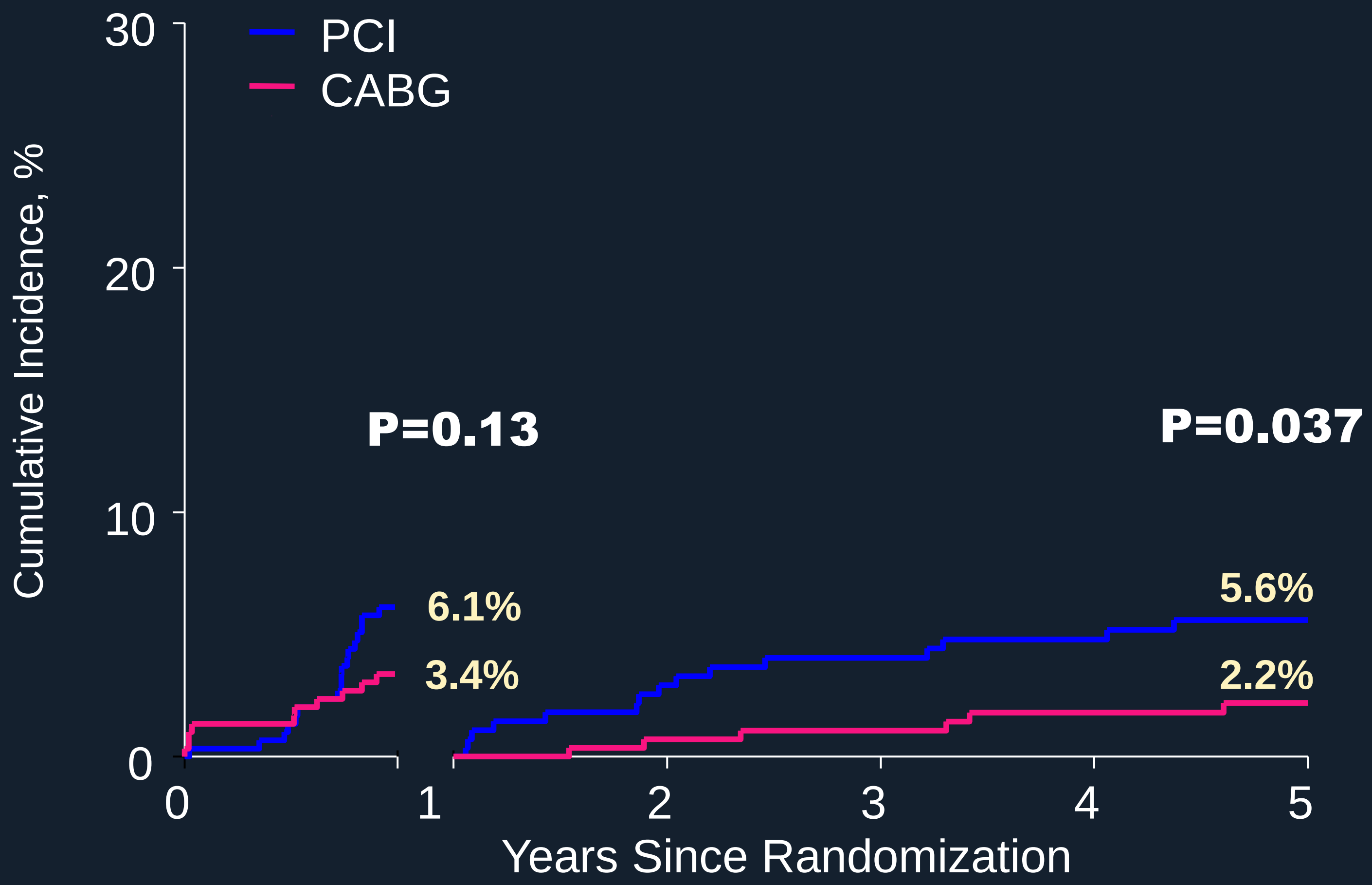
Ischemia-Driven TVR



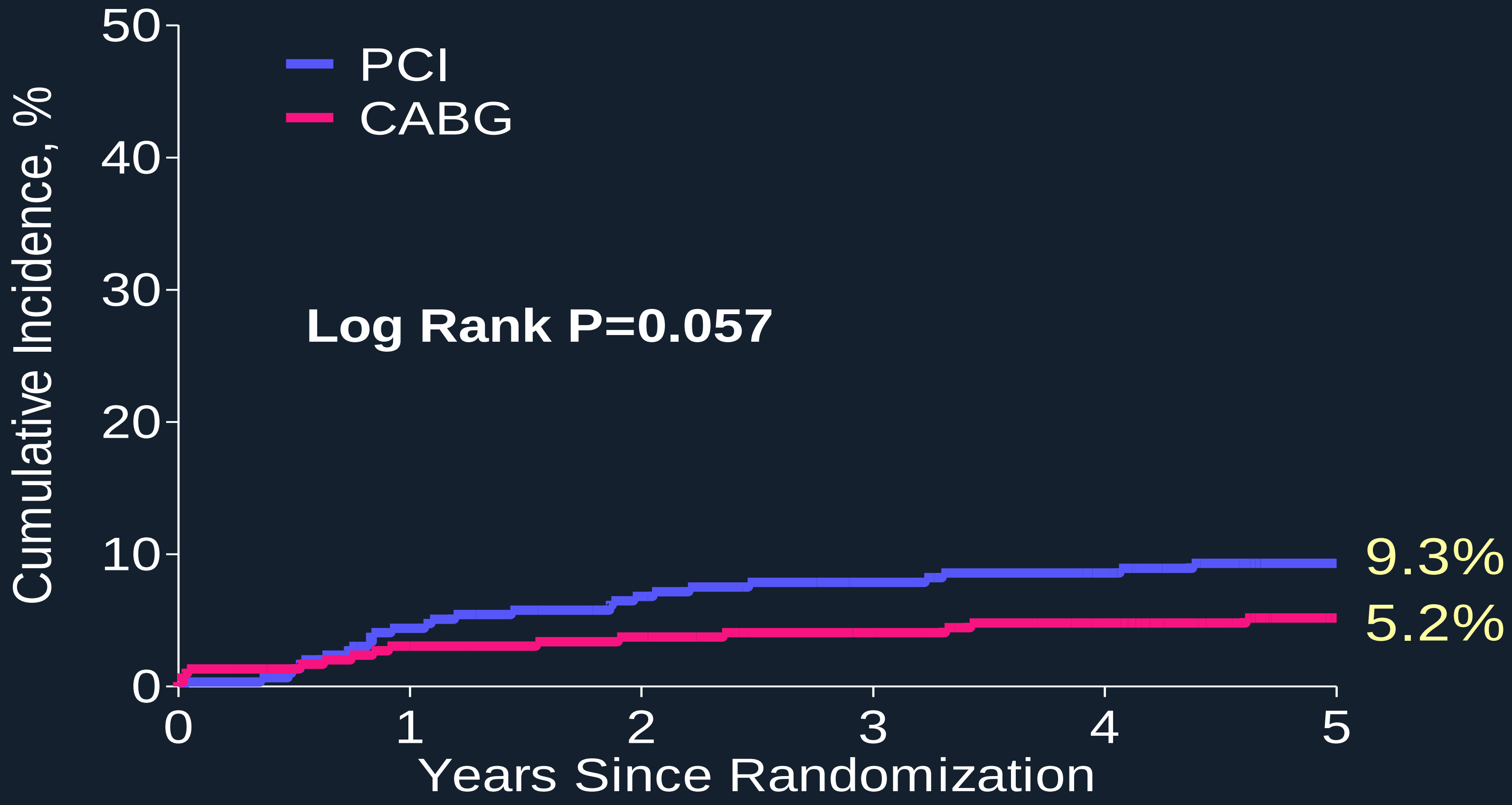
Patient at risk

PCI	300	274	263	254	248	232
CABG	300	283	278	271	261	240

Land Mark Analysis
Ischemia-Driven TVR



Clinical-Driven TVR

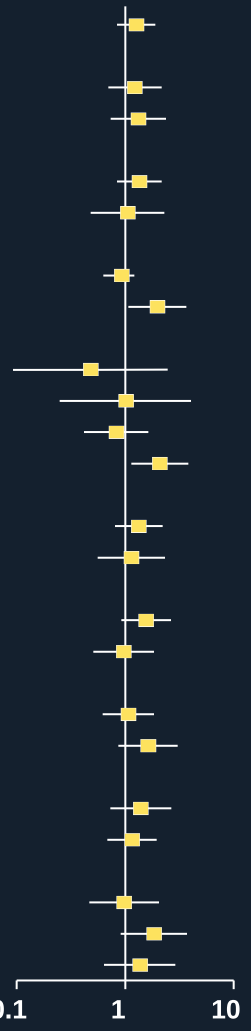


Patient at risk

PCI	300	279	269	260	253	237
CABG	300	284	279	272	262	240

Subgroup Analysis

Subgroup	MACCE PCI *n / total n (%)*	 CABG	Hazard Ratio (95% CI)	Pvalue	Pvalue for Interaction
Overall	52/300 (17.5)	42/300 (14.3)	1.27 (0.84-1.90)	0.26	-
Age					0.86
≥ 65 yr	24/129 (18.8)	23/149 (15.8)	1.23 (0.70-2.18)	0.47	
<65 yr	28/171 (16.5)	19/151 (12.8)	1.33 (0.74-2.38)	0.33	
Sex					0.60
Male	39/228 (17.3)	30/231 (13.3)	1.35 (0.84-2.17)	0.21	
Female	13/72 (18.1)	12/69 (17.5)	1.06 (0.48-2.31)	0.89	
Left main coronary artery stenosis					0.043
>70 %	20/140 (14.4)	27/159 (17.4)	0.83 (0.47-1.48)	0.53	
50-70 %	32/160 (20.2)	15/141 (10.9)	1.98 (1.07-3.65)	0.027	
Coronary artery disease distribution					0.14
Left main only	2/27 (7.4)	5/34 (14.8)	0.48 (0.09-2.47)	0.37	
LM with 1VD	4/50 (8.0)	4/53 (7.7)	1.02 (0.25-4.07)	0.98	
LM with 2VD	16/101 (16.0)	17/90 (19.2)	0.83 (0.42-1.64)	0.59	
LM with 3VD	30/122 (24.8)	16/123 (13.3)	2.09 (1.14-3.84)	0.015	
Bifurcation involvement					0.71
Yes	37/200 (18.7)	26/183 (14.7)	1.34 (0.81-2.22)	0.25	
No	15/99 (15.2)	15/111 (13.6)	1.14 (0.56-2.33)	0.73	
RCA involvement					0.27
Yes	33/149 (22.3)	24/159 (15.5)	1.56 (0.92-2.64)	0.095	
No	19/151 (12.7)	18/141 (13.0)	0.97 (0.51-1.85)	0.93	
Acute coronary syndrome					0.35
Yes	25/140 (17.9)	27/163 (16.8)	1.07 (0.62-1.85)	0.79	
No	27/160 (17.1)	15/137 (11.4)	1.63 (0.87-3.06)	0.13	
Diabetes					0.66
Yes	23/102 (22.7)	15/90 (16.9)	1.39 (0.73-2.67)	0.32	
No	29/198 (14.8)	27/210 (13.2)	1.16 (0.69-1.96)	0.58	
Syntax score					0.49
0-22	16/129 (12.5)	13/104 (13.0)	0.98 (0.47-2.05)	0.97	
23-32	22/102 (21.7)	12/97 (12.6)	1.85 (0.91-3.73)	0.083	
≥ 33	14/58 (24.2)	13/68 (19.2)	1.37 (0.64-2.91)	0.41	

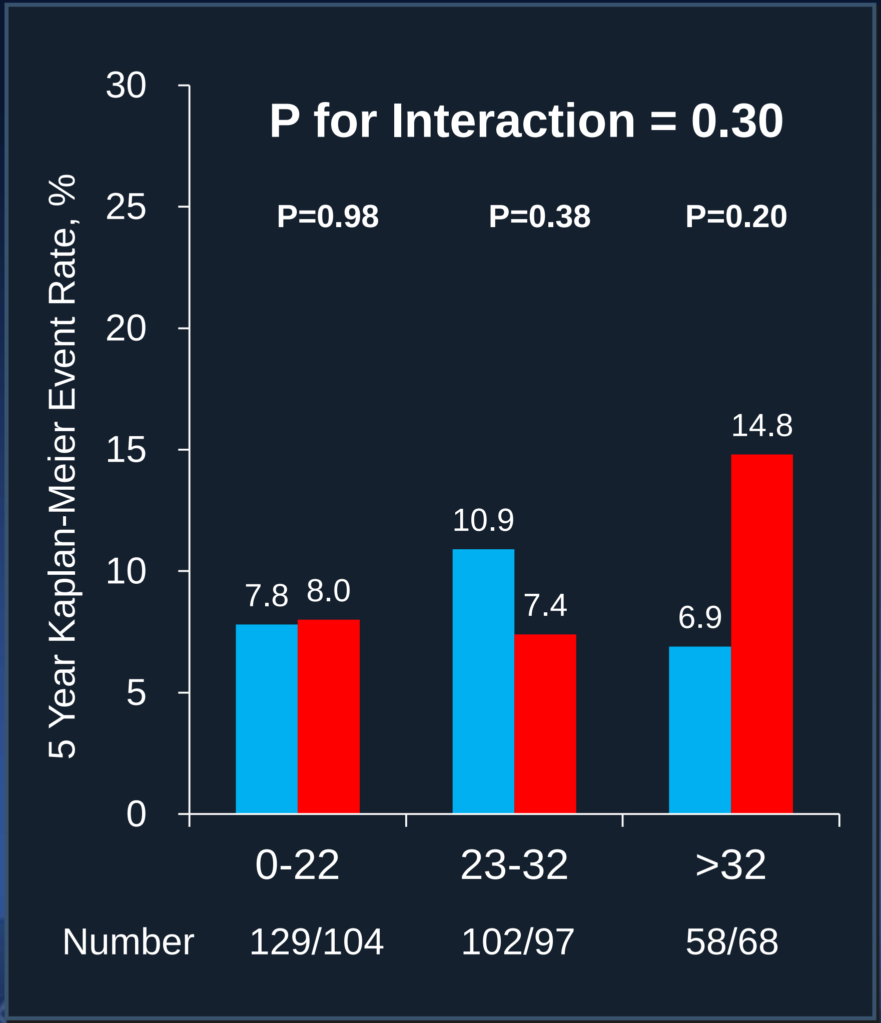


PCI better CABG better

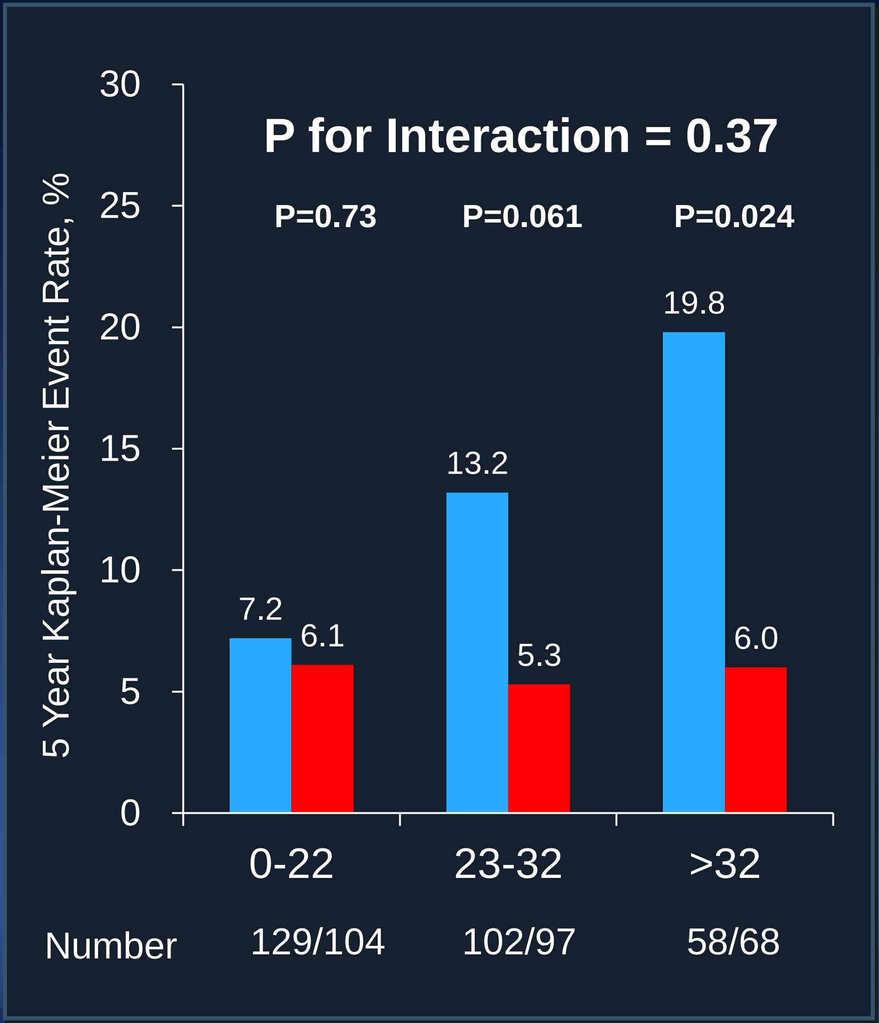
SYNTAX Score

🟦 PCI
🟥 CABG

Death, MI, or Stroke



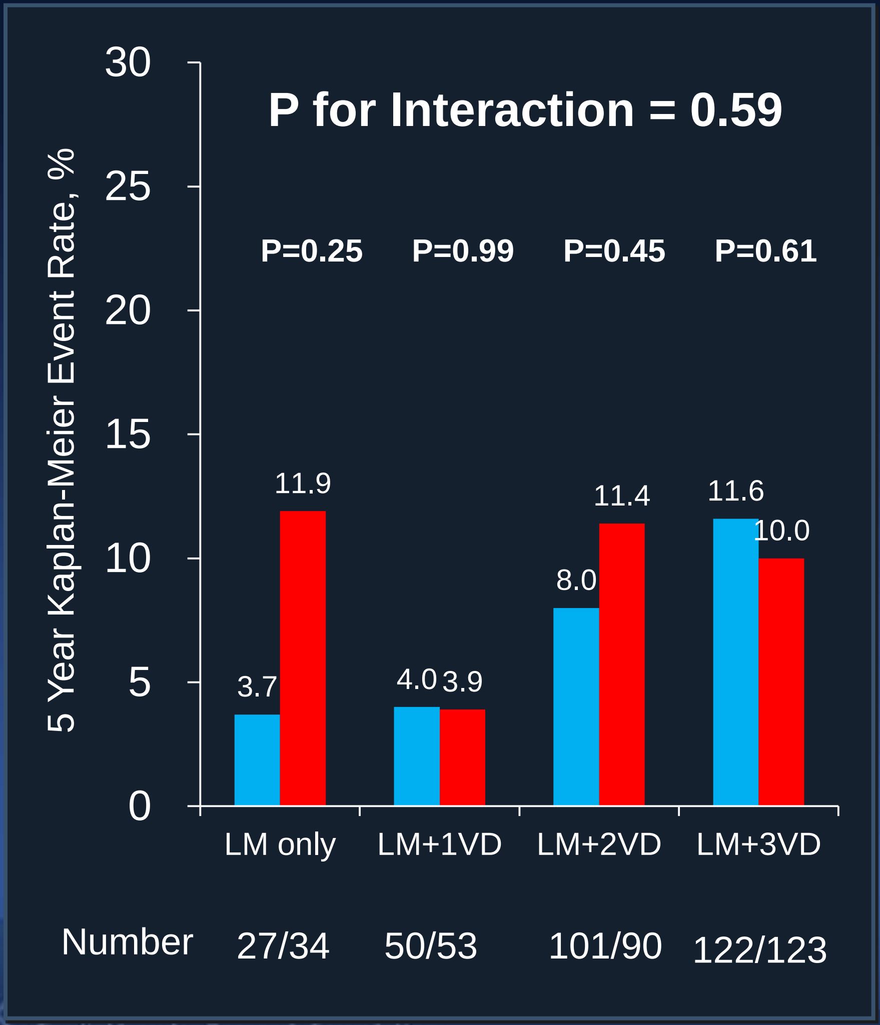
iTVR



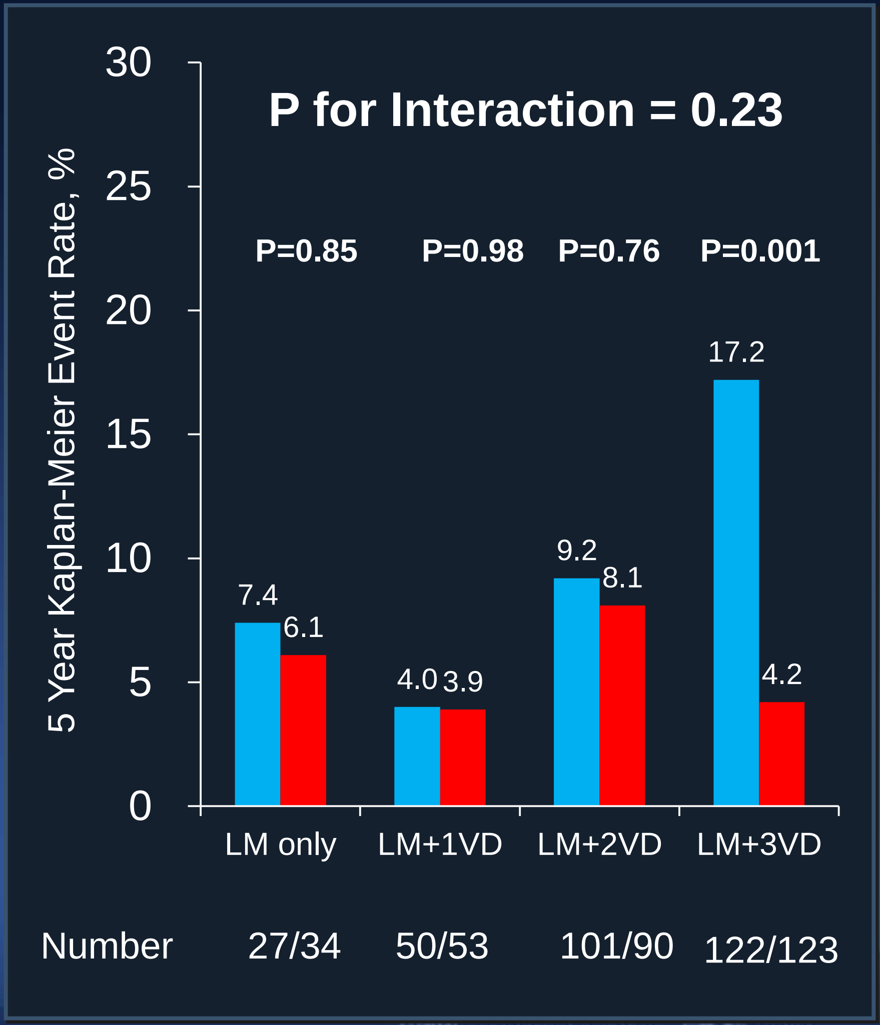
Disease Distribution

🟦 PCI
🟥 CABG

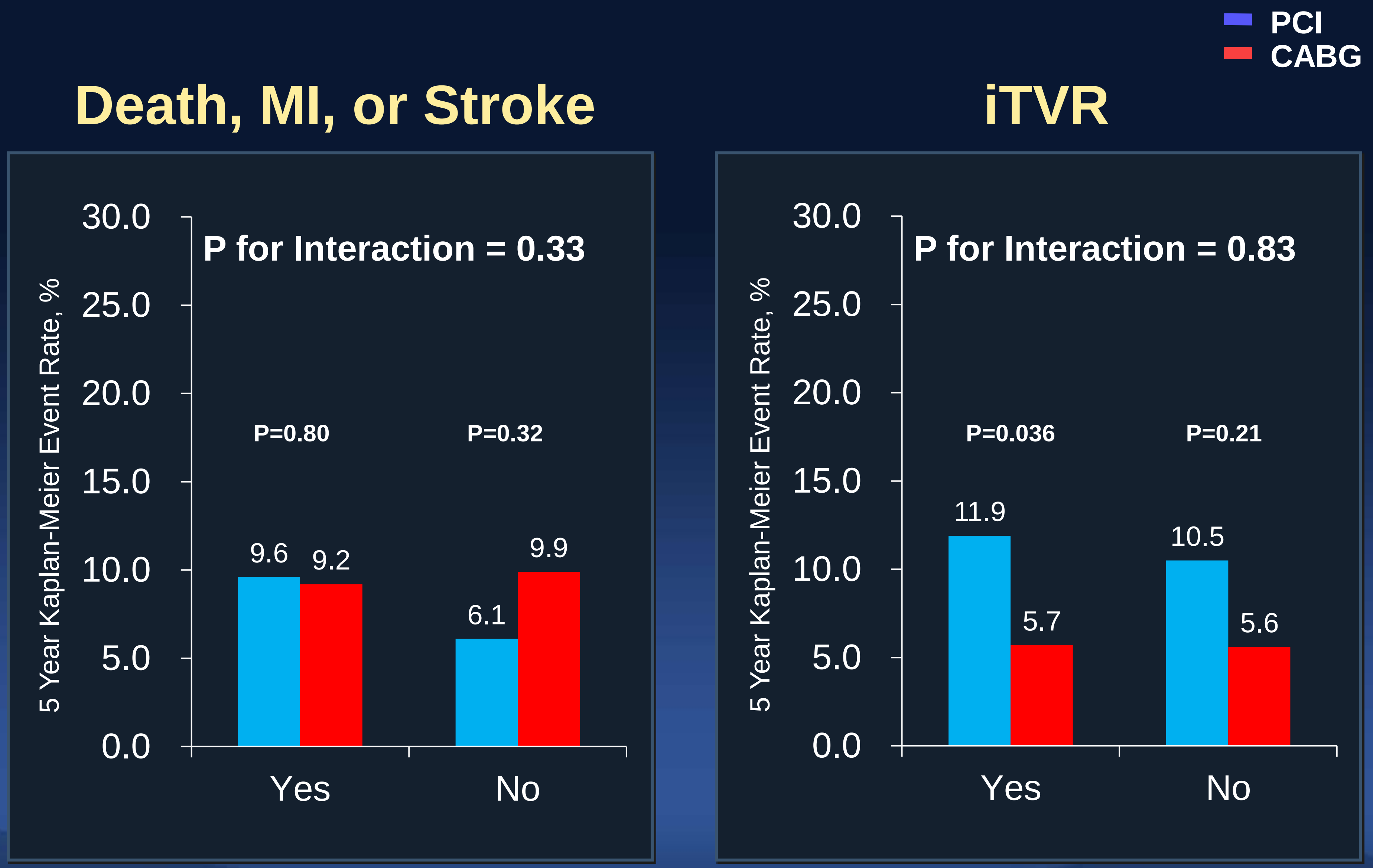
Death, MI, or Stroke



iTVR



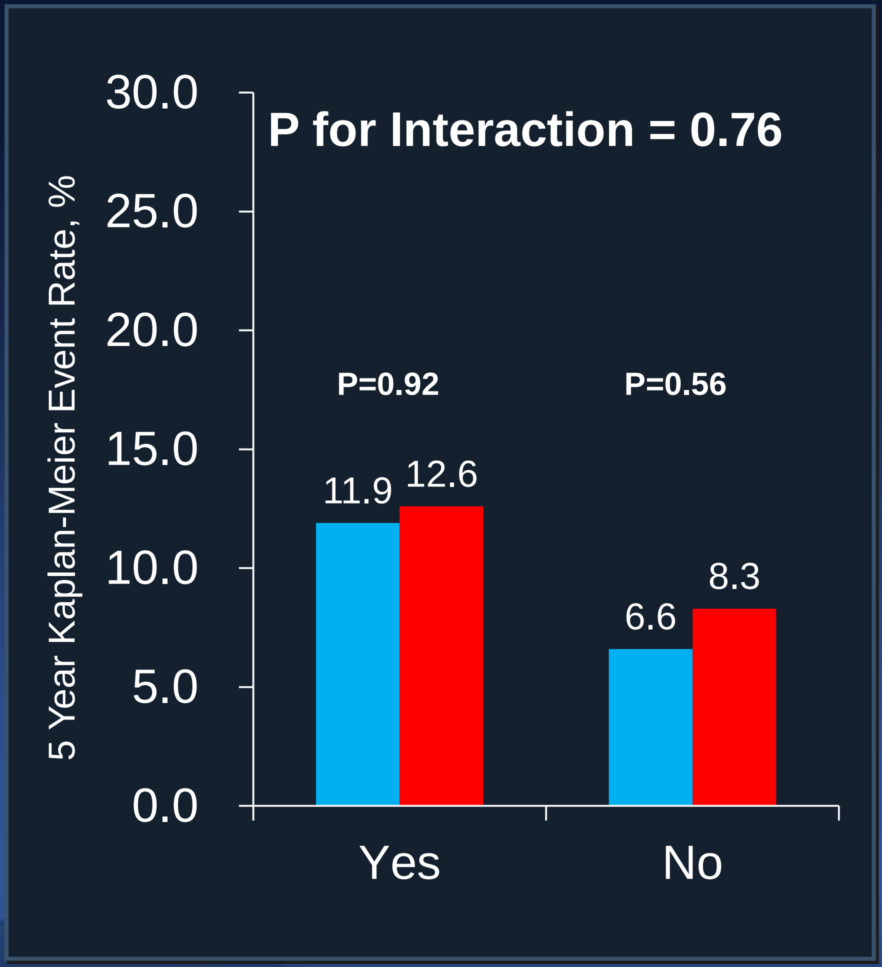
Bifurcation



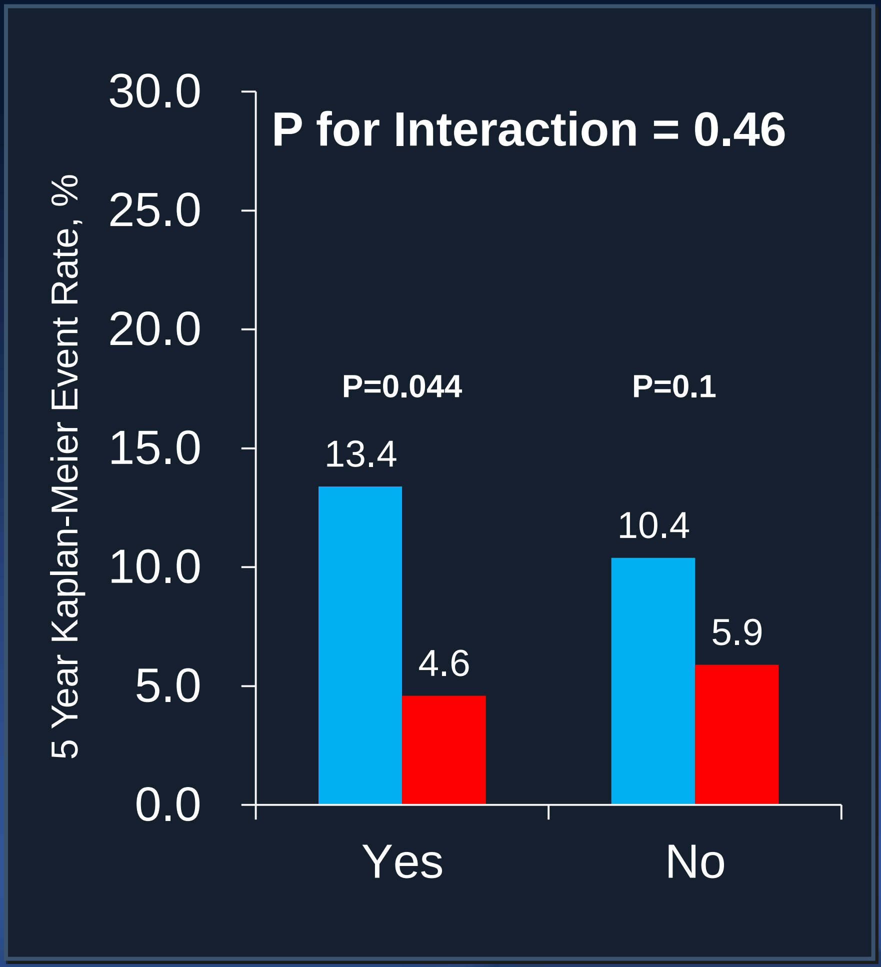
Diabetes

🟦 PCI
🟥 CABG

Death, MI, or Stroke



iTVR



Conclusion

- At 5 years, the rate of MACCE as well as the rate of death, MI, or stroke was not significantly different between patients assigned to PCI with sirolimus-eluting stents and those who underwent CABG.

- Our findings supported current guidelines stating that left main stenting is a feasible revascularization strategy for patients with suitable coronary anatomy.