

**Ten-Year Outcomes of Stents vs.
Coronary-Artery Bypass Grafting for
Left Main Coronary Artery Disease
From the MAIN-COMPARE Registry**

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BACKGROUND

- Although CABG is the standard choice of revascularization for significant left main coronary artery (LMCA) disease, PCI for LM disease has been widely expanded with marked advancements of stents, antithrombotic drugs, periprocedural management, and experienced expertise.

BACKGROUND

- Recently, 2 large-sized RCTs (i.e., EXCEL and NOBLE) showed conflicting results with regards to the effects of PCI with DES and CABG on clinical outcomes.
- Moreover, both trials reported a trend toward late catch-up or crossover in the rates the composite end point favoring CABG over PCI during the late period of follow-up. Therefore, longer-term follow-up is necessary to examine additional differences between PCI and CABG over time.

OBJECTIVE

- The MAIN-COMPARE registry was designed to compare outcomes of PCI and CABG for unprotected LMCA disease in multiple centers of Korea.
- To obtain a more reliable very long-term treatment effect of stenting or CABG, we have now extended the follow-up duration for the all study patients, for whom follow-up data were available for at least 10 years.

METHODS

MAIN-COMPARE Registry

Wave 1 (BMS era)

LM disease treated with BMS (n=318) and concurrent CABG (n=448) btw 2000~2003

Wave 2 (DES era)

LM disease treated with DES (n=784) and concurrent CABG (n=690) btw 2003~2006

From January 2000 through June 2006

Total
2240

Stent (N=1102)

CABG (N=1138)



Clinical follow-up every 12 months
Death, Composite of Death/MI/Stroke, TVR

Enrollment Criteria

Inclusion Criteria

Patients with unprotected left main disease (defined as stenosis of more than 50%) who underwent stenting or isolated CABG

Exclusion Criteria

- Prior CABG
- Concomitant valvular or aortic surgery
- ST-elevation MI
- Cardiogenic shock at presentation

Revascularization Procedures

- The choice of revascularization strategy was at the discretion of the treating physicians and/or patients after consideration of several clinical and anatomic factors or surgical risk for CABG.
- PCI was performed exclusively with bare-metal stents (BMS) between January 2000 and May 2003 and exclusively with DES between May 2003 and June 2006.

Primary Outcome Measures

- Death
- Composite of death, Q-wave MI, or stroke
- Target-vessel revascularization

Outcome Definitions

- Death was defined as death from any cause
- Q-wave myocardial infarction was defined as the documentation of a new pathologic Q-wave after index treatment.
- Stroke, as detected by neurological deficits, was confirmed by a neurologist and imaging modalities.
- Target-vessel revascularization was defined as repeat revascularization of the treated vessel, including *any* segments of the LAD and/or LCX.

Follow-up and National DB Linkage

- Clinical follow-up was recommended at 1 month, 6 months, and 1 year, and then annually up to 10 years.
- In this report, the follow-up period was extended through December 31, 2016, to ensure that all patients had the opportunity for at least 10-year follow-up evaluation.
- For validation of complete follow-up data on mortality, information about vital status was obtained from the National Population Registry of the Korea National Statistical Office with the use of a unique personal identification number up to December, 31, 2016.

Statistical Analysis

- To adjust baseline characteristics between PCI and CABG, propensity analyses using (1) the inverse-probability-of-treatment weighting (IPTW) and (2) propensity-score matching were performed.
- To characterize the time-dependent nature of the relative treatment effects and to compensate for the violation of the proportional-hazards assumption, we performed weighted piecewise Cox regression models with robust standard errors according to a prespecified time point at 5 years after index treatment.

Participating Centers

Investigating centers (12 Major Cardiac Centers in Korea)

Asan Medical Center

Kangnam St Mary's Hospital

Yoido St Mary's Hospital

Kyungpook National University Hospital

Gachon University Gil Medical Center

Seoul National University Hospital

Seoul National University Bundang Hospital

Samsung Medical Center

Ajou University Hospital

Yonsei University Medical Center

Chonnam National University Hospital

Chung-Nam University Hospital

P.I. : Seung-Jung Park, MD, Duk-Woo Park, MD, Asan Medical Center

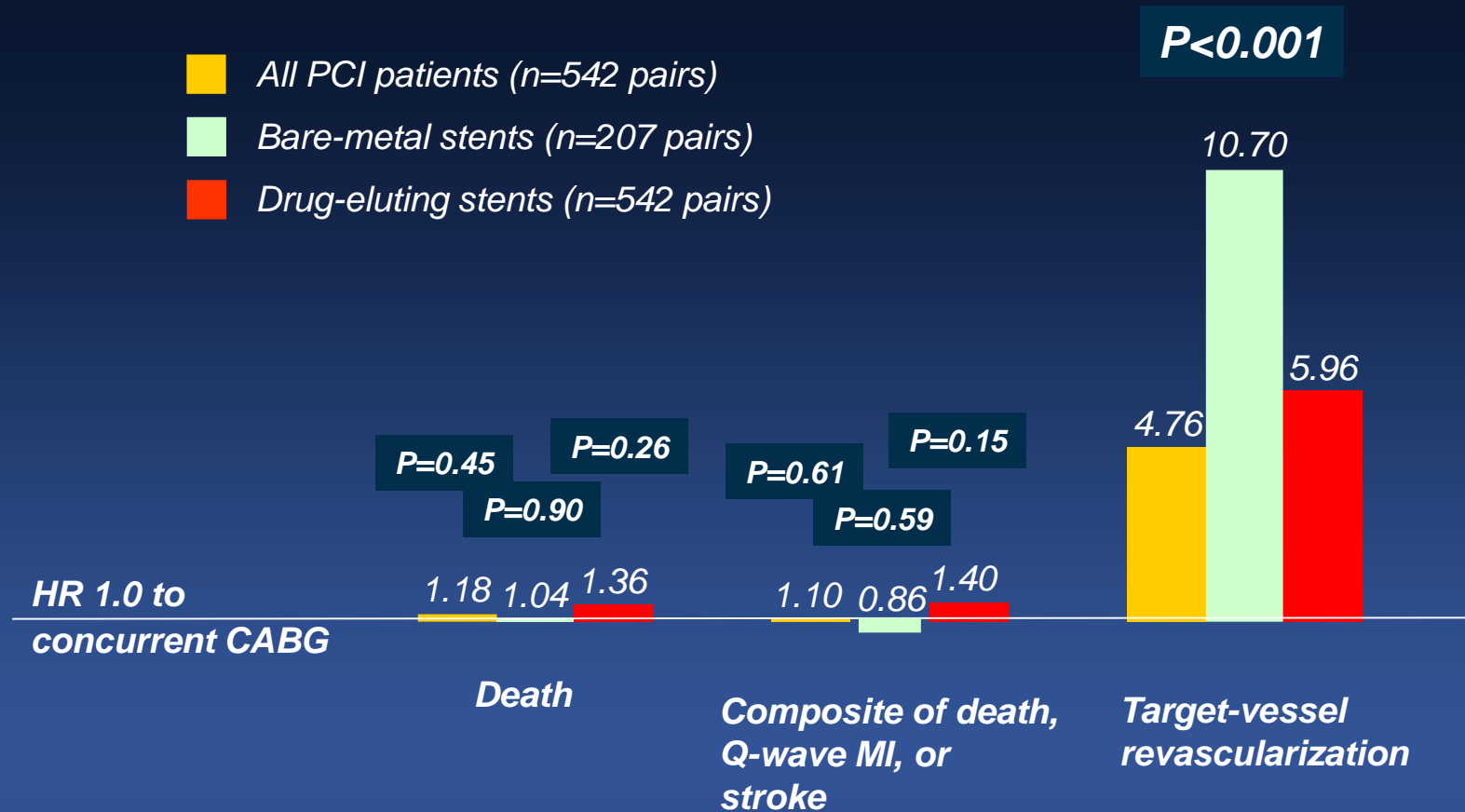
Sponsors: CardioVascular Research Foundation (CVRF)

Data analysis and management: Clinical Research Center in CVRF, AMC.

Local independent event committee: Clinical Research Center in CVRF, AMC.

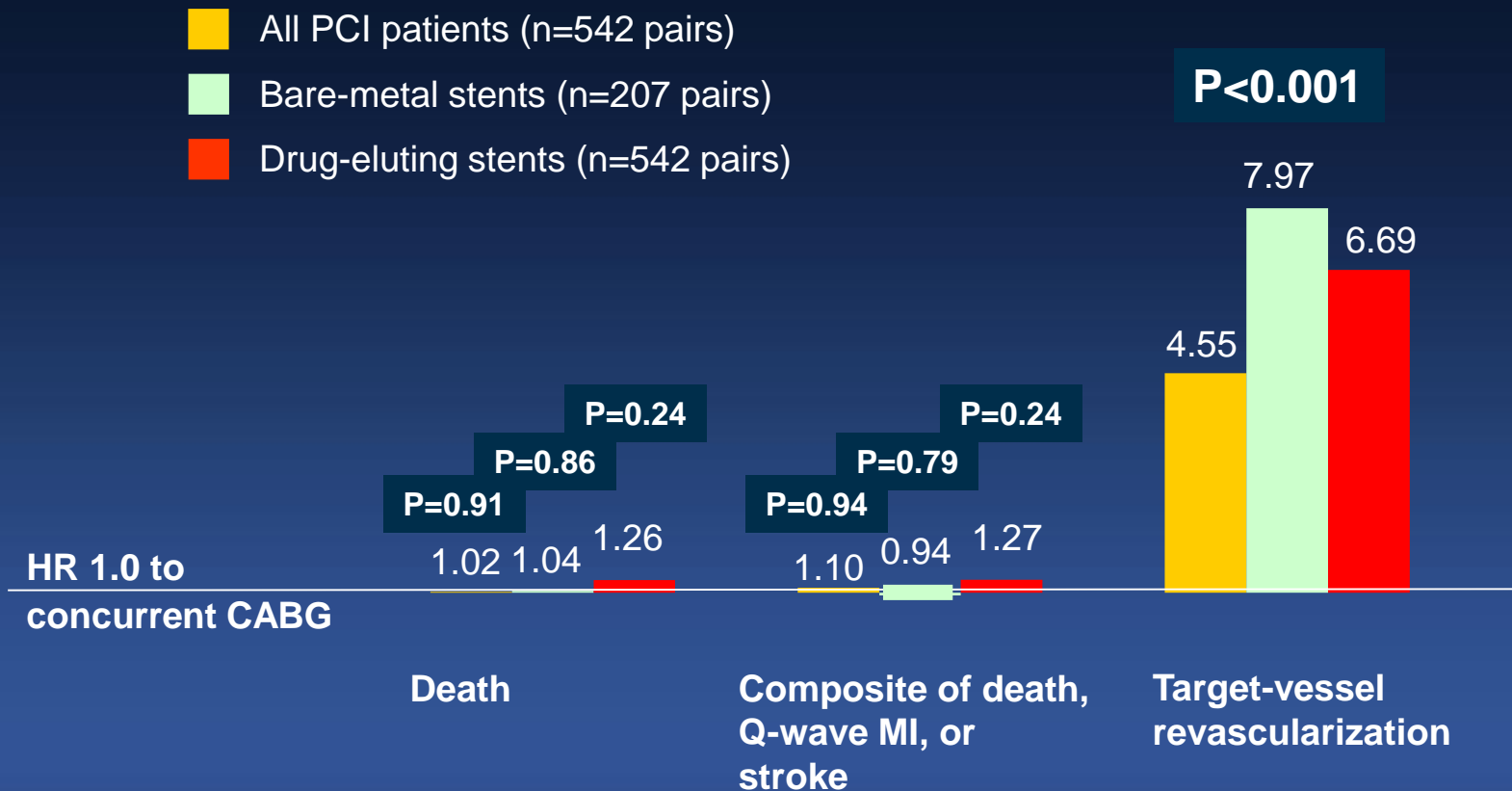
MAIN COMPARE Registry, 3-Year

Adjusted HR by Use of PS Matching



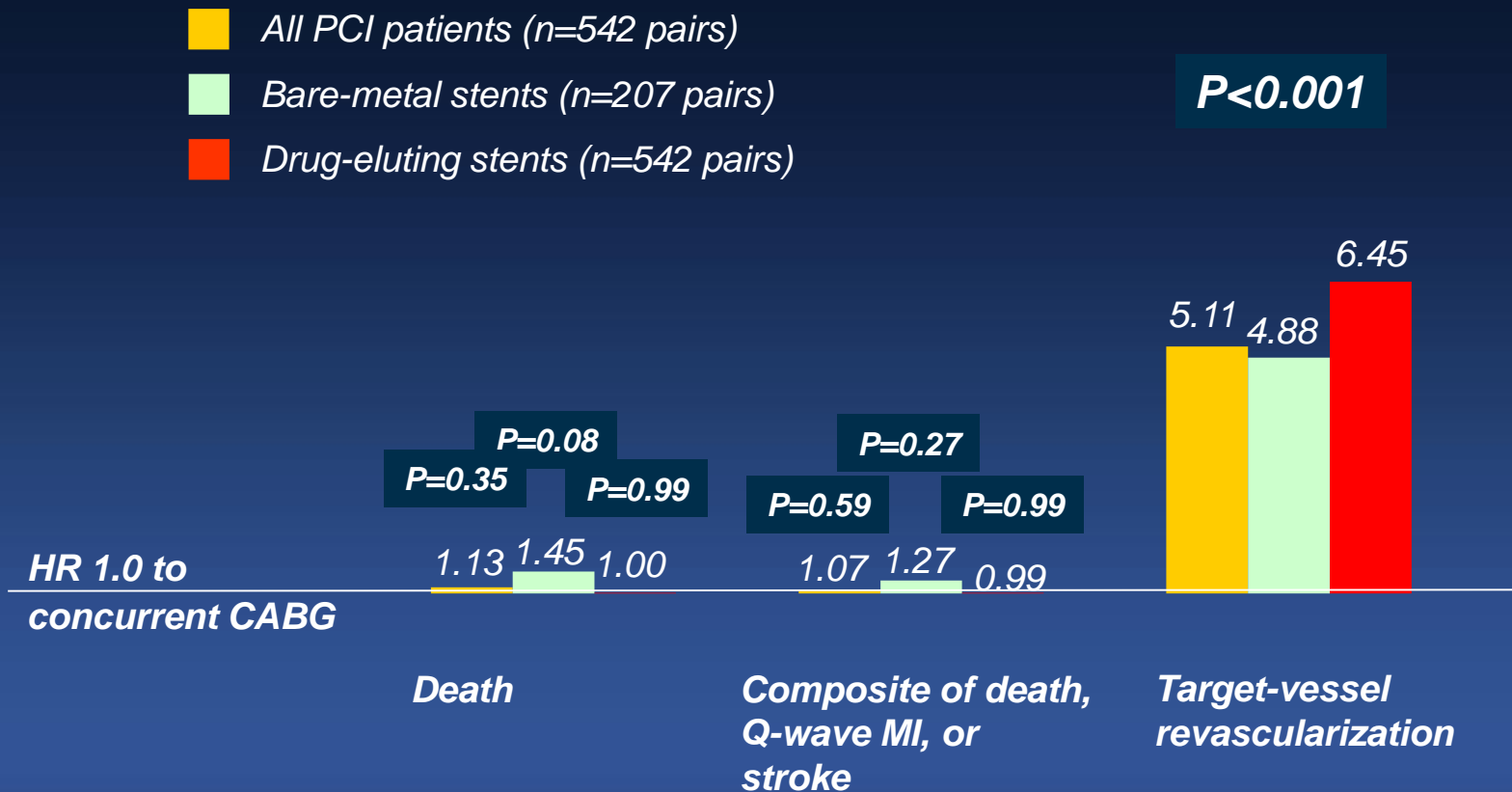
MAIN COMPARE Registry, 5-Year

Adjusted HR by Use of PS Matching



MAIN COMPARE Registry, 5-Year

Adjusted HR by Use of IPTW Method

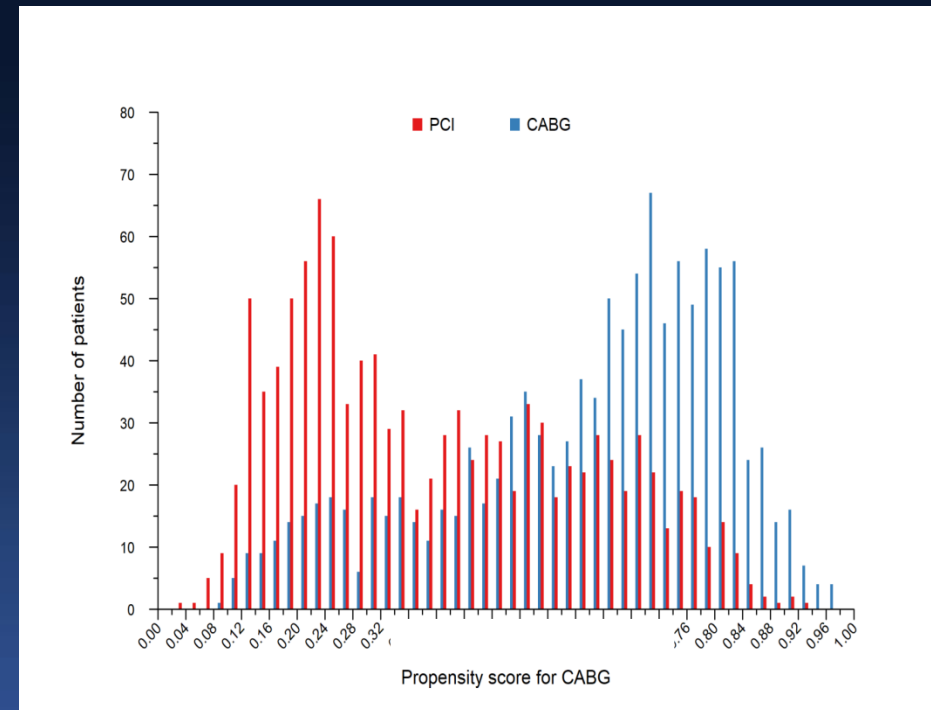


RESULTS

Baseline Characteristics

	Unadjusted Data		
	PCI (N = 1102)	CABG (N = 1138)	P Value
Age (yr)	61.3±11.7	62.9±9.4	<0.001
Male gender	779 (70.7)	830 (72.9)	0.24
Diabetes mellitus			
Any diabetes	327 (29.7)	395 (34.7)	0.01
Requiring insulin	75 (6.8)	93 (8.2)	0.22
Hypertension	546 (49.5)	562 (49.4)	0.94
Hyperlipidemia	315 (28.6)	371 (32.6)	0.04
Current smoker	282 (25.6)	339 (29.8)	0.03
Previous PCI	200 (18.1)	125 (11.0)	<0.001
Previous MI	89 (8.1)	132 (11.6)	0.005
Previous CHF	27 (2.5)	38 (3.3)	0.21
Chronic lung disease	22 (2.0)	23 (2.0)	0.97
Cerebrovascular disease	78 (7.1)	83 (7.3)	0.84
PVD	16 (1.5)	62 (5.4)	<0.001
Renal failure	30 (2.7)	34 (3.0)	0.71
Ejection fraction (%)	60.6±10.8	57.2±11.9	<0.001

Distribution of Propensity-Score



Baseline Characteristics

	Unadjusted Data			Data Adjusted with IPTW			After Propensity Matching	
	PCI (N = 1102)	CABG (N = 1138)	P Value	PCI (N = 1102)	CABG (N = 1138)	P Value	PCI (N=659)	CABG (N=659)
Age (yr)	61.3±11.7	62.9±9.4	<0.001	62.1±11.0	62.1±10.1	0.89	62.6±11.2	63.2±9.7
Male gender	779 (70.7)	830 (72.9)	0.24	797 (72.3)	820 (72.1)	0.90	472 (71.6)	457 (69.4)
Diabetes mellitus								
Any diabetes	327 (29.7)	395 (34.7)	0.01	338 (30.6)	356 (31.3)	0.73	338 (30.6)	197 (29.9)
Requiring insulin	75 (6.8)	93 (8.2)	0.22	84 (7.6)	89 (7.9)	0.82	84 (7.6)	44 (6.7)
Hypertension	546 (49.5)	562 (49.4)	0.94	525 (47.7)	551 (48.4)	0.71	525 (47.7)	335 (50.8)
Hyperlipidemia	315 (28.6)	371 (32.6)	0.04	340 (30.8)	339 (29.8)	0.60	340 (30.8)	201 (30.5)
Current smoker	282 (25.6)	339 (29.8)	0.03	313 (28.4)	330 (29.0)	0.76	313 (28.4)	188 (28.5)
Previous PCI	200 (18.1)	125 (11.0)	<0.001	165 (15.0)	172 (15.1)	0.93	165 (15.0)	99 (15.0)
Previous MI	89 (8.1)	132 (11.6)	0.005	99 (9.0)	111 (9.8)	0.54	99 (9.0)	67 (10.2)
Previous CHF	27 (2.5)	38 (3.3)	0.21	32 (2.9)	33 (2.9)	0.95	32 (2.9)	17 (2.6)
Chronic lung disease	22 (2.0)	23 (2.0)	0.97	25 (2.3)	20 (1.7)	0.36	8 (1.2)	10 (1.5)
Cerebrovascular disease	78 (7.1)	83 (7.3)	0.84	71 (6.5)	74 (6.5)	0.96	48 (7.3)	48 (7.3)
PVD	16 (1.5)	62 (5.4)	<0.001	46 (4.2)	43 (3.9)	0.66	15 (2.3)	10 (1.5)
Renal failure	30 (2.7)	34 (3.0)	0.71	34 (3.1)	35 (3.1)	0.98	16 (2.4)	21 (3.2)
Ejection fraction (%)	60.6±10.8	57.2±11.9	<0.001	59.8±11.0	59.0±11.2	0.12	59.7±11.1	59.4±11.5

Baseline Characteristics

	Unadjusted Data			Data Adjusted with IPTW			After Propensity Matching	
	PCI (N = 1102)	CABG (N = 1138)	P Value	PCI (N = 1102)	CABG (N = 1138)	P Value	PCI (N=659)	CABG (N=659)
ECG findings			0.53			0.92		
Sinus rhythm	1078 (97.8)	1105 (97.1)		1076 (97.7)	1109 (97.4)		644 (97.7)	641 (92.3)
Atrial fibrillation	22 (2.0)	31 (2.7)		24 (2.2)	28 (2.5)		15 (2.3)	17 (2.6)
Other	2 (0.2)	2 (0.2)		1 (0.1)	1 (0.1)		0 (0.0)	1 (0.2)
Clinical indication			<0.001			0.96		
Silent ischemia	33 (3.0)	25 (2.2)		30 (2.7)	32 (2.8)		23 (3.5)	19 (2.9)
Chronic stable angina	353 (32.0)	226 (19.9)		289 (26.1)	296 (26.0)		166 (25.2)	173 (26.3)
Unstable angina	608 (55.2)	775 (68.1)		677 (61.4)	692 (60.1)		401 (60.9)	402 (61.0)
NSTEMI	108 (9.8)	112 (9.8)		107 (9.7)	118 (10.4)		69 (10.5)	65 (9.9)
LM disease location			0.04			0.87		
Ostium or shaft	557 (50.6)	526 (46.2)		522 (47.3)	543 (47.7)		316 (48.0)	321 (48.7)
Distal bifurcation	545 (49.5)	612 (53.8)		580 (52.7)	595 (52.3)		343 (52.0)	338 (51.3)
Extent of disease			<0.001			0.98		
LM only	278 (25.2)	71 (6.2)		175 (15.9)	186 (16.4)		81 (12.3)	71 (10.8)
LM plus 1-VD	264 (24.0)	119 (10.5)		192 (17.4)	201 (17.6)		114 (17.3)	112 (17.0)
LM plus 2-VD	287 (26.0)	299 (26.3)		288 (26.1)	291 (25.6)		212 (32.2)	223 (33.8)
LM plus 3-VD	273 (24.8)	649 (57.0)		448 (40.1)	460 (40.4)		252 (38.2)	253 (38.4)
RCA disease	396 (35.9)	804 (70.7)	<0.001	584 (53.0)	597 (52.5)	0.81	350 (53.1)	353 (53.6)
Restenotic lesion	32 (2.9)	14 (1.2)	0.005	22 (2.0)	22 (1.9)	0.88	17 (2.6)	12 (1.8)

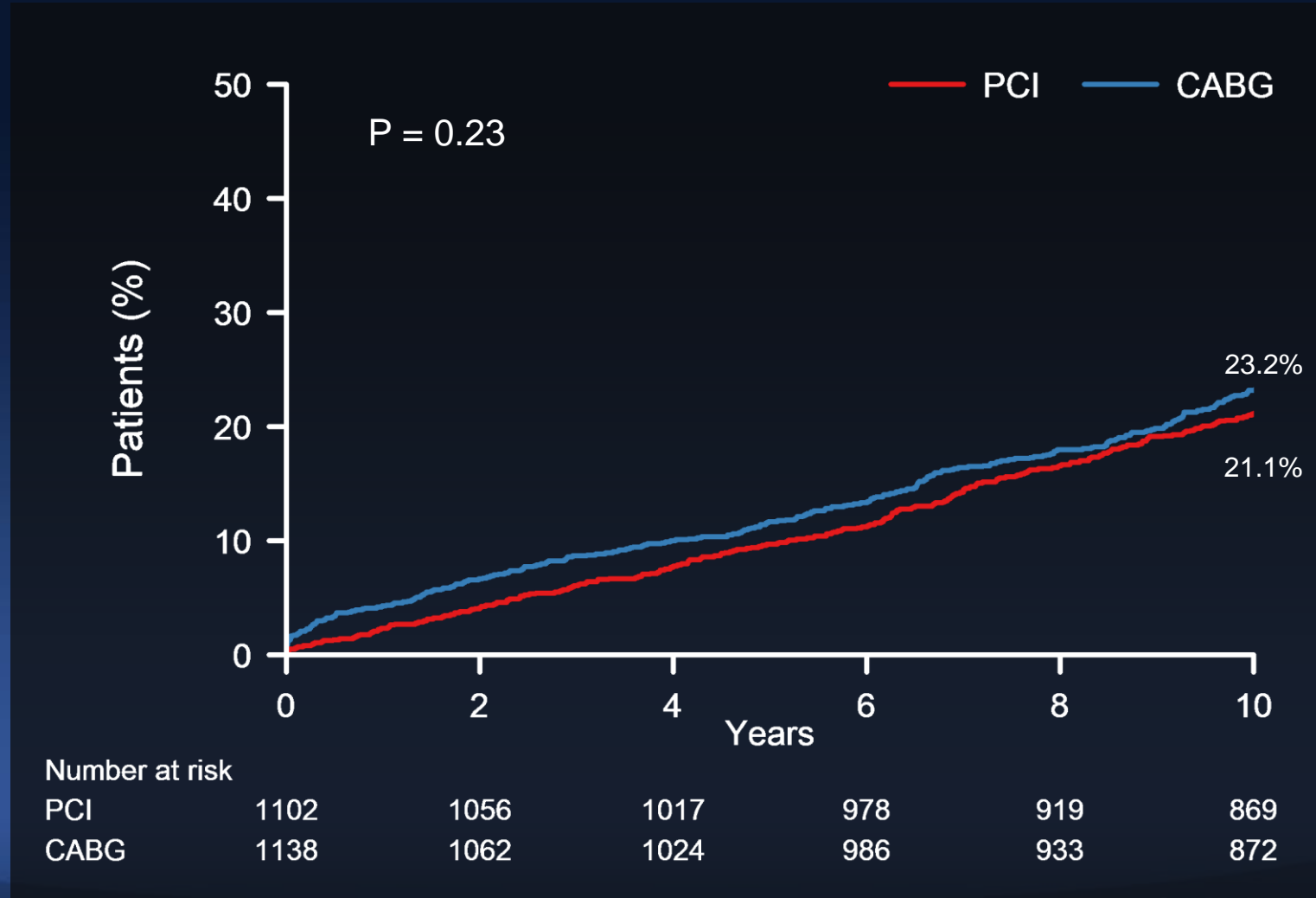
Procedural Characteristics

	CABG (n = 1138)	PCI (n = 1102)
CABG Group		
Off-pump surgery (%)	42	-
At least one arterial conduit (%)	98	-
IMA to LAD Graft (%) in patients with arterial conduits	98	-
✓ Grafts / Patients (Mean ± SD)	2.9±1.0	-
PCI Group		
Bare-metal stents(%)	-	29
Drug-eluting stents (%)	-	71
Sirolimus stents of DES (%)	-	77
Paclitaxel stents of DES (%)	-	23
Number of stents at LMCA lesions	-	1.2±0.5
Total length of stents at LMCA (mm)	-	28±21
Average stent diameter at LM site	-	3.5±0.4
✓ Number of stents per patients	-	1.9±1.1

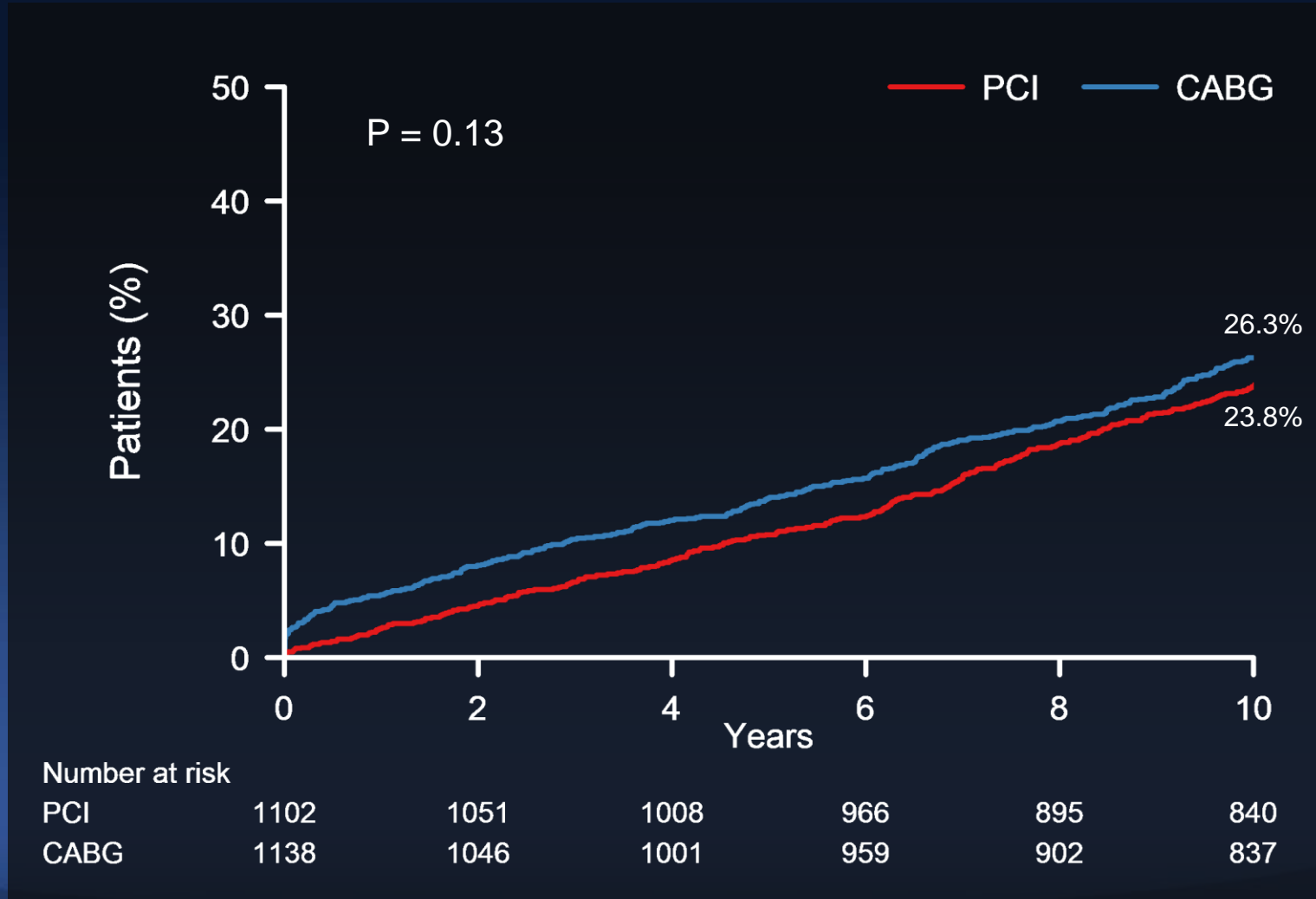
Unadjusted Kaplan-Meier Curves

- The median duration of follow-up among all patients was 12.0 years (IQR, 10.7 to 13.5); the maximum follow-up was 17.6 years.
- The follow-up status for major clinical events was ascertained for 2,211 patients (98.7%) of the overall population

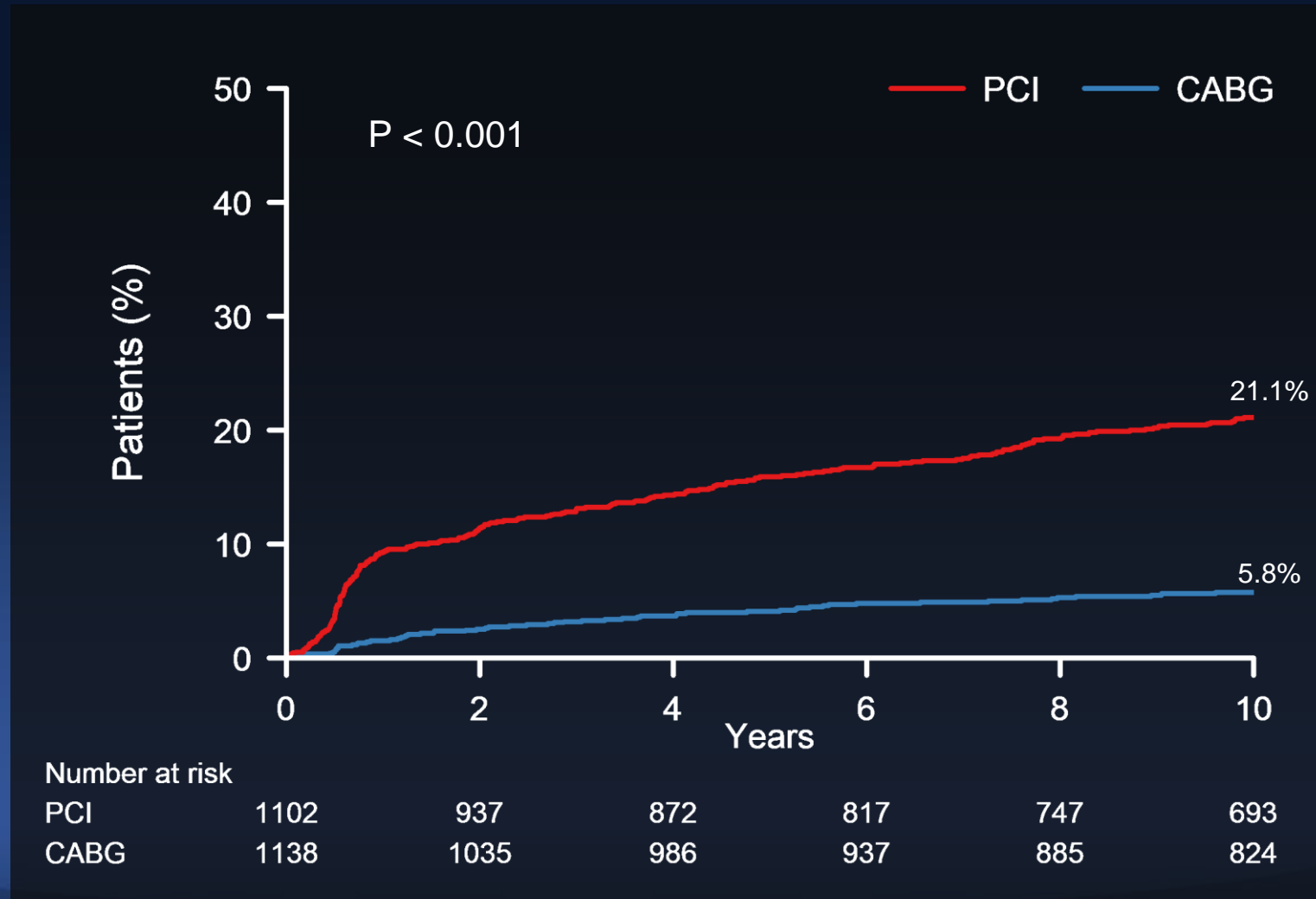
Overall Cohort Death



Overall Cohort Death, Q-MI, or Stroke

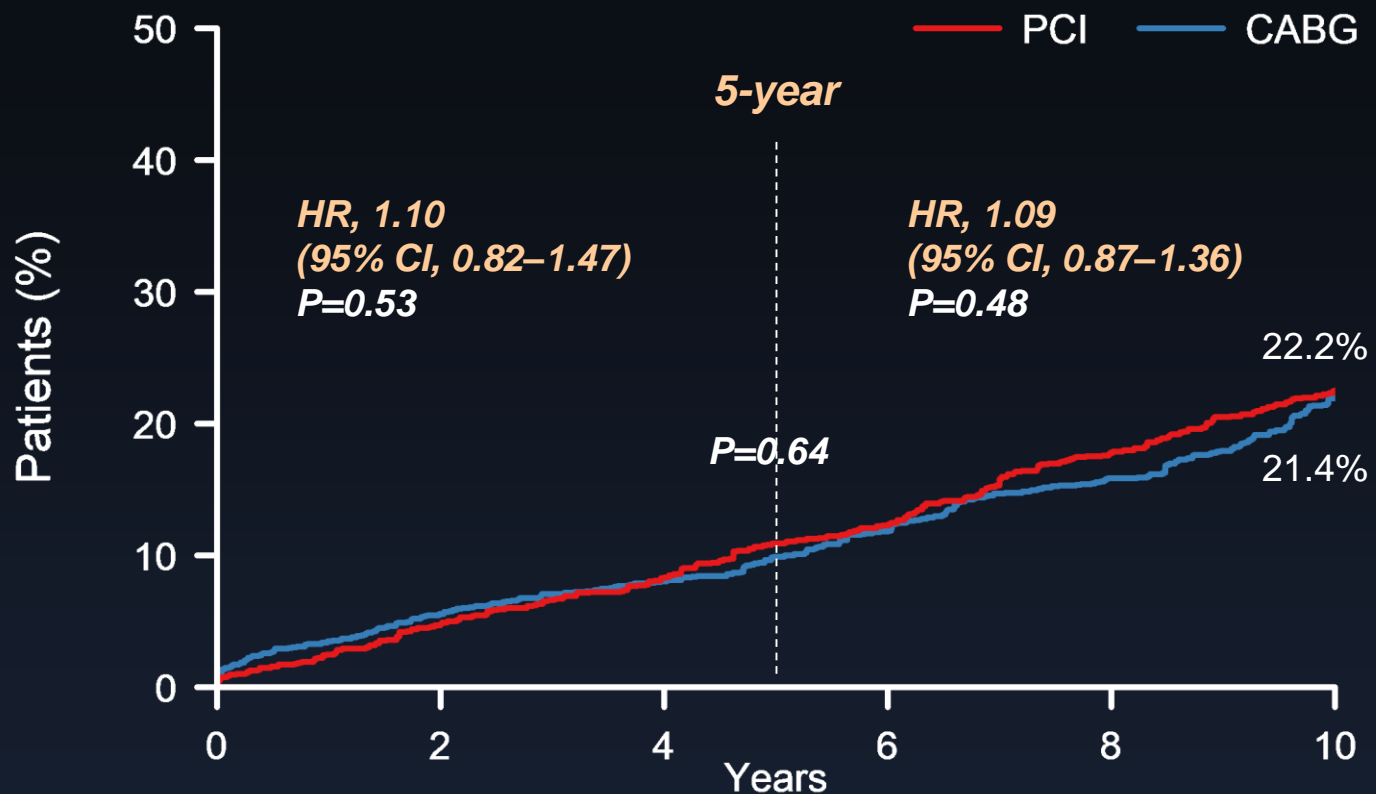


Overall Cohort TVR



Adjusted Curves with the Use of IPTW Method

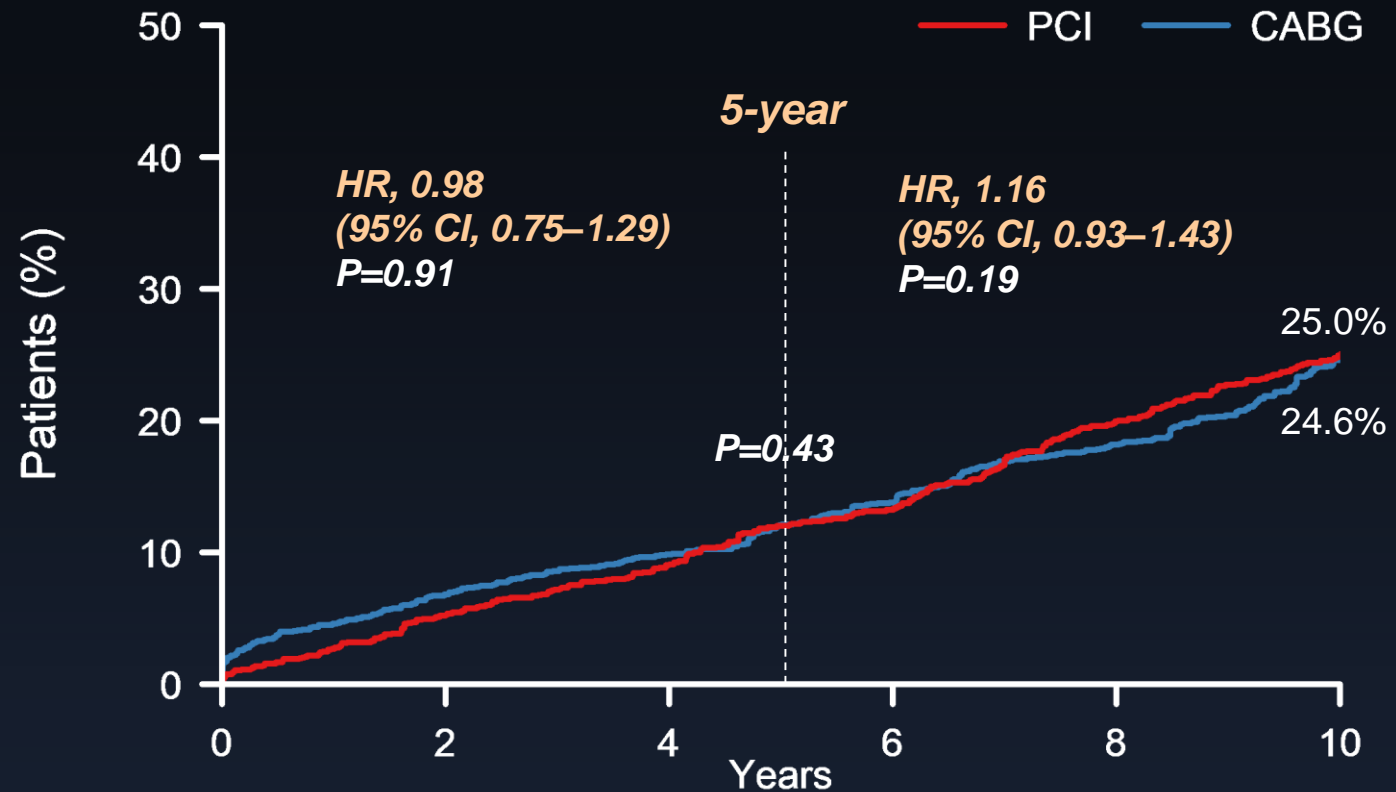
Overall Cohort Death



Number at risk

PCI	1102	1049	1010	966	906	854
CABG	1138	1074	1046	1003	957	887

Overall Cohort Death, Q-MI, or Stroke



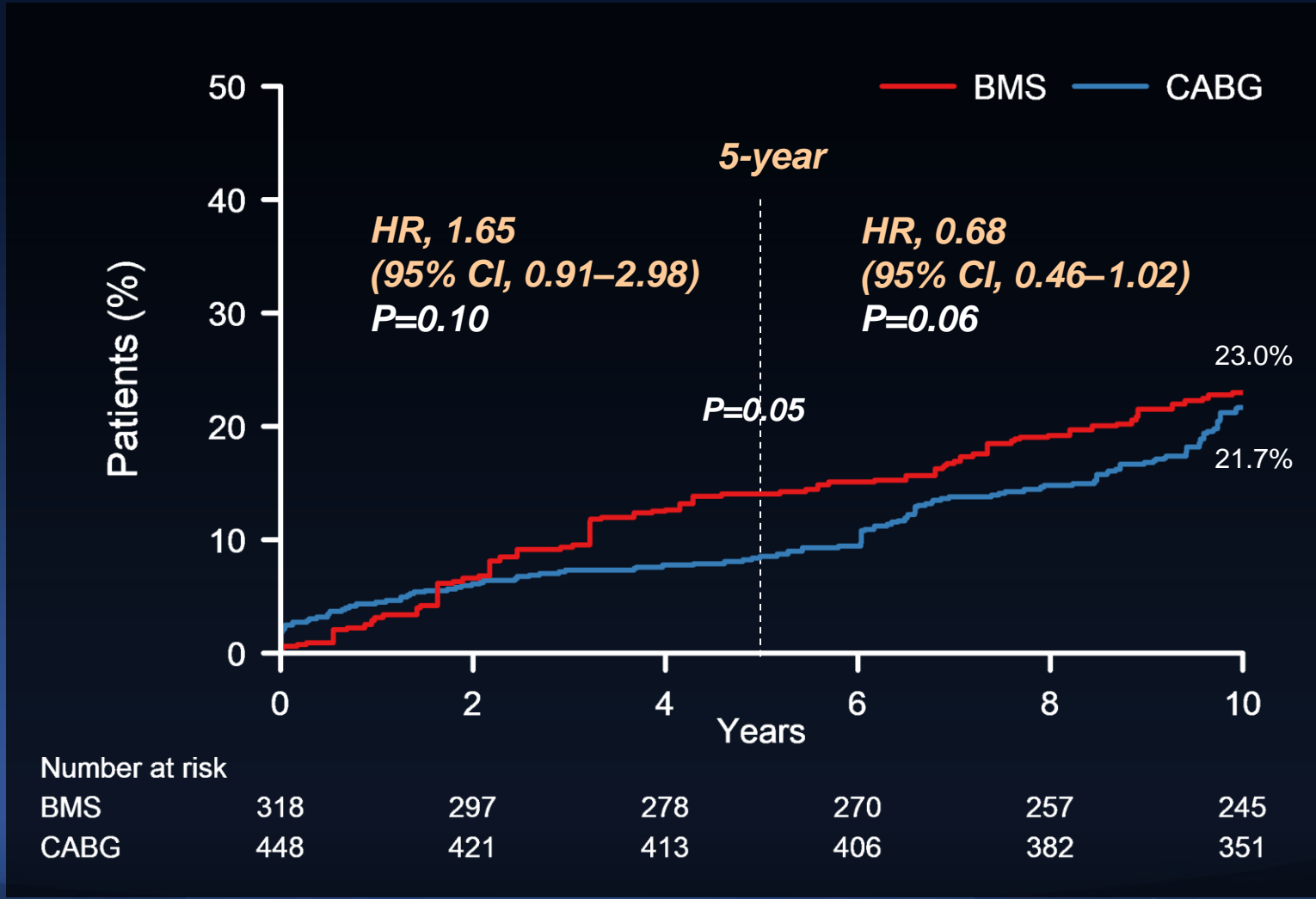
Number at risk

PCI	1102	1044	1002	956	882	827
CABG	1138	1060	1026	981	931	857

Overall Cohort TVR

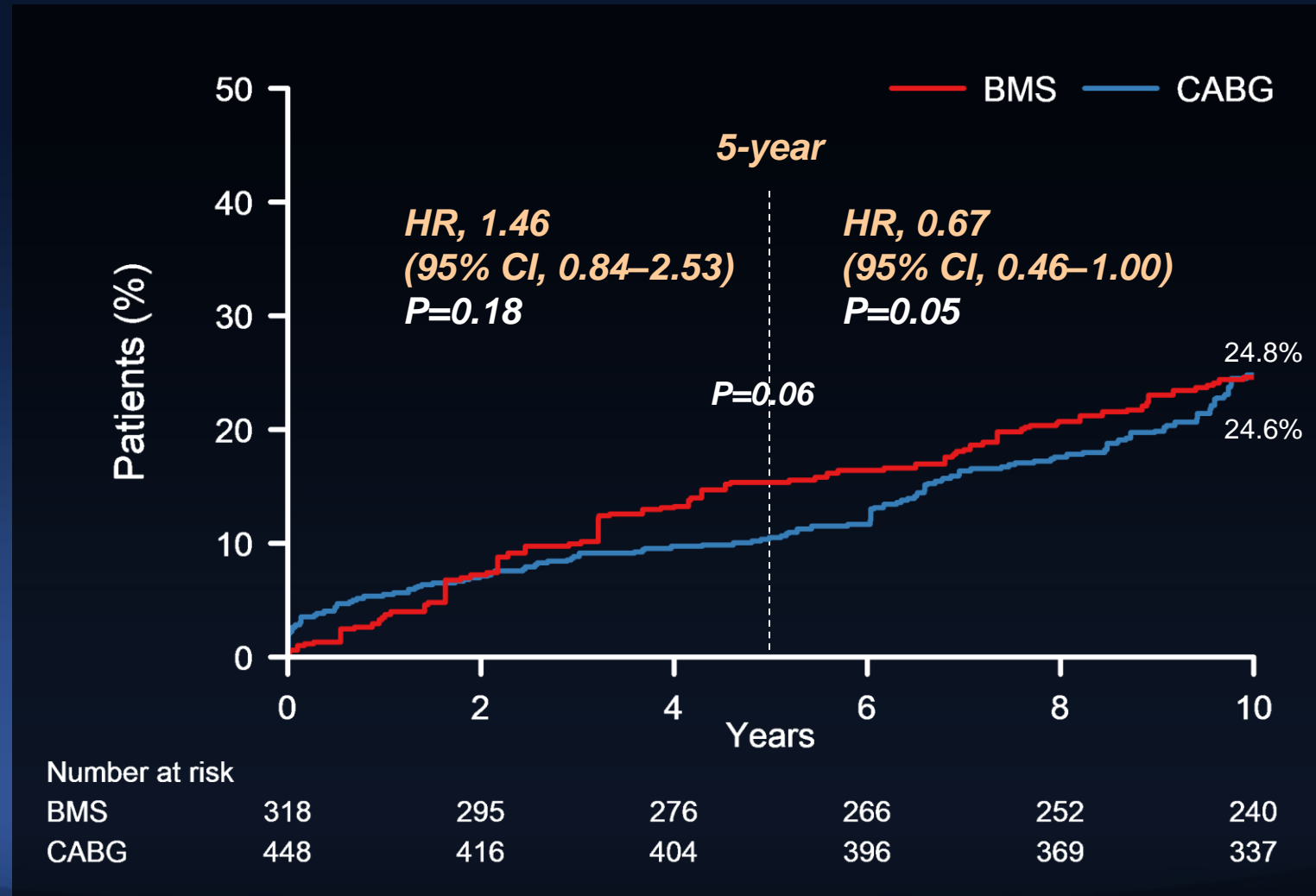


Wave 1 (BMS vs. CABG) Death

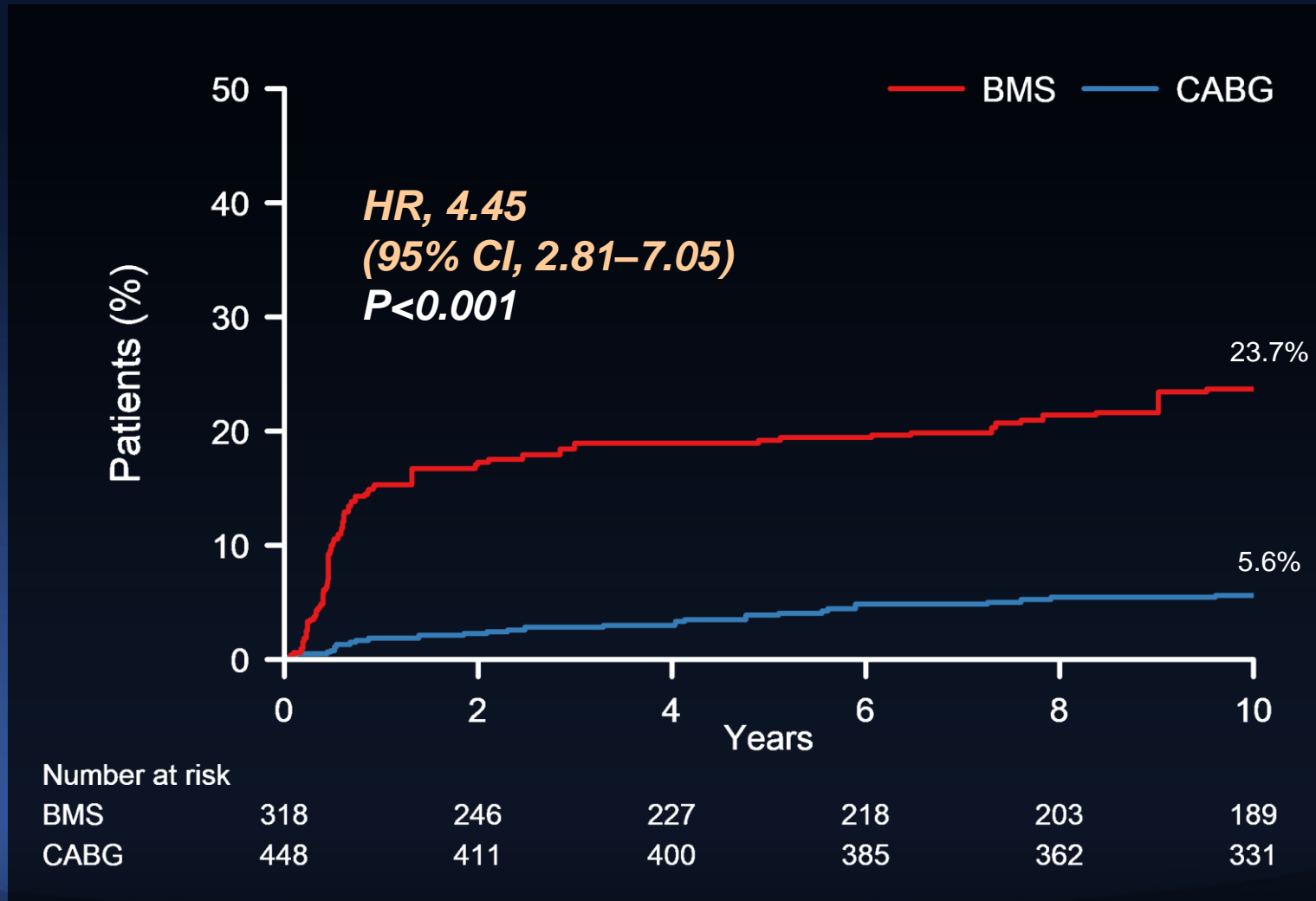


Wave 1 (BMS vs. CABG)

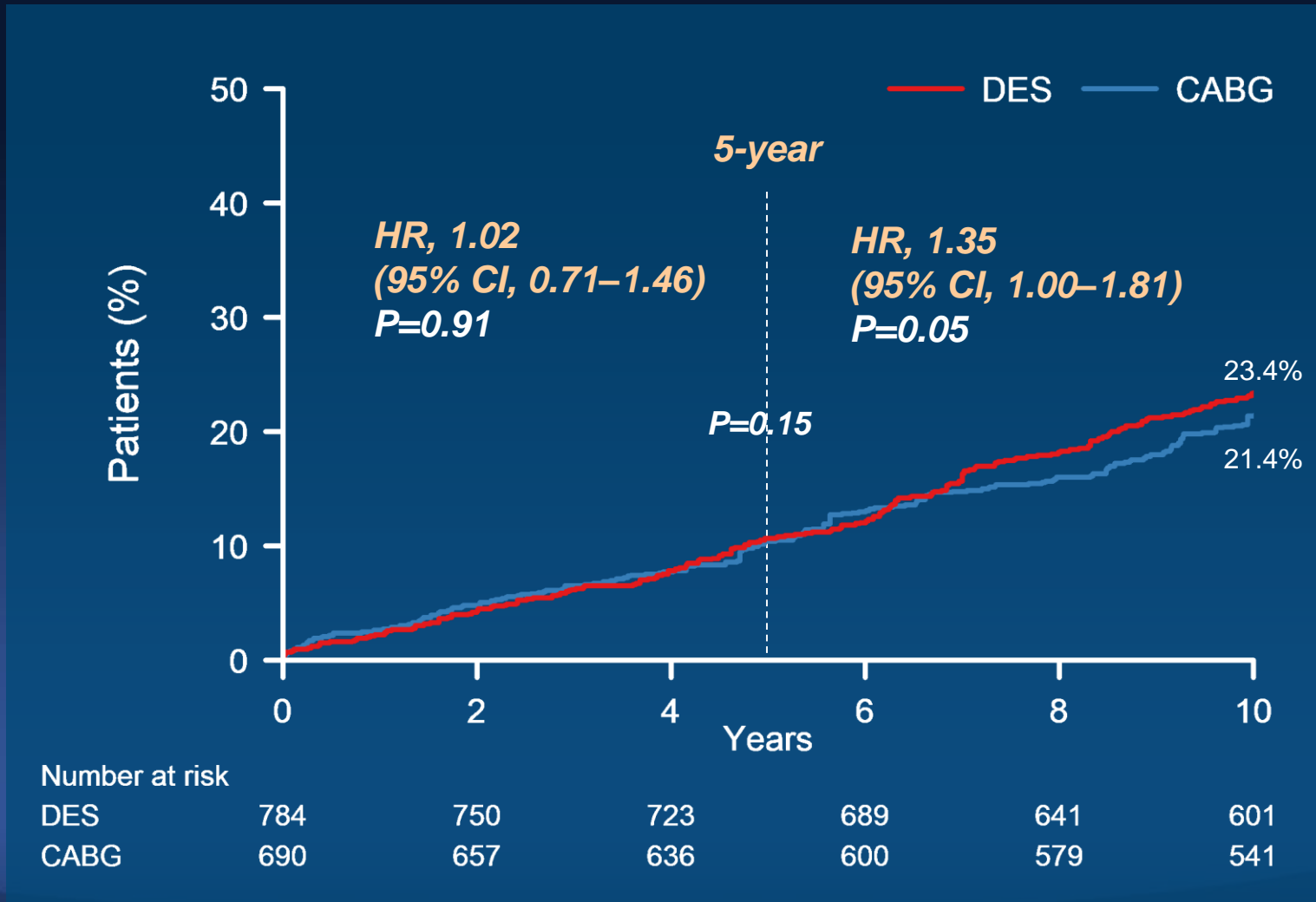
Death, Q-MI, or Stroke



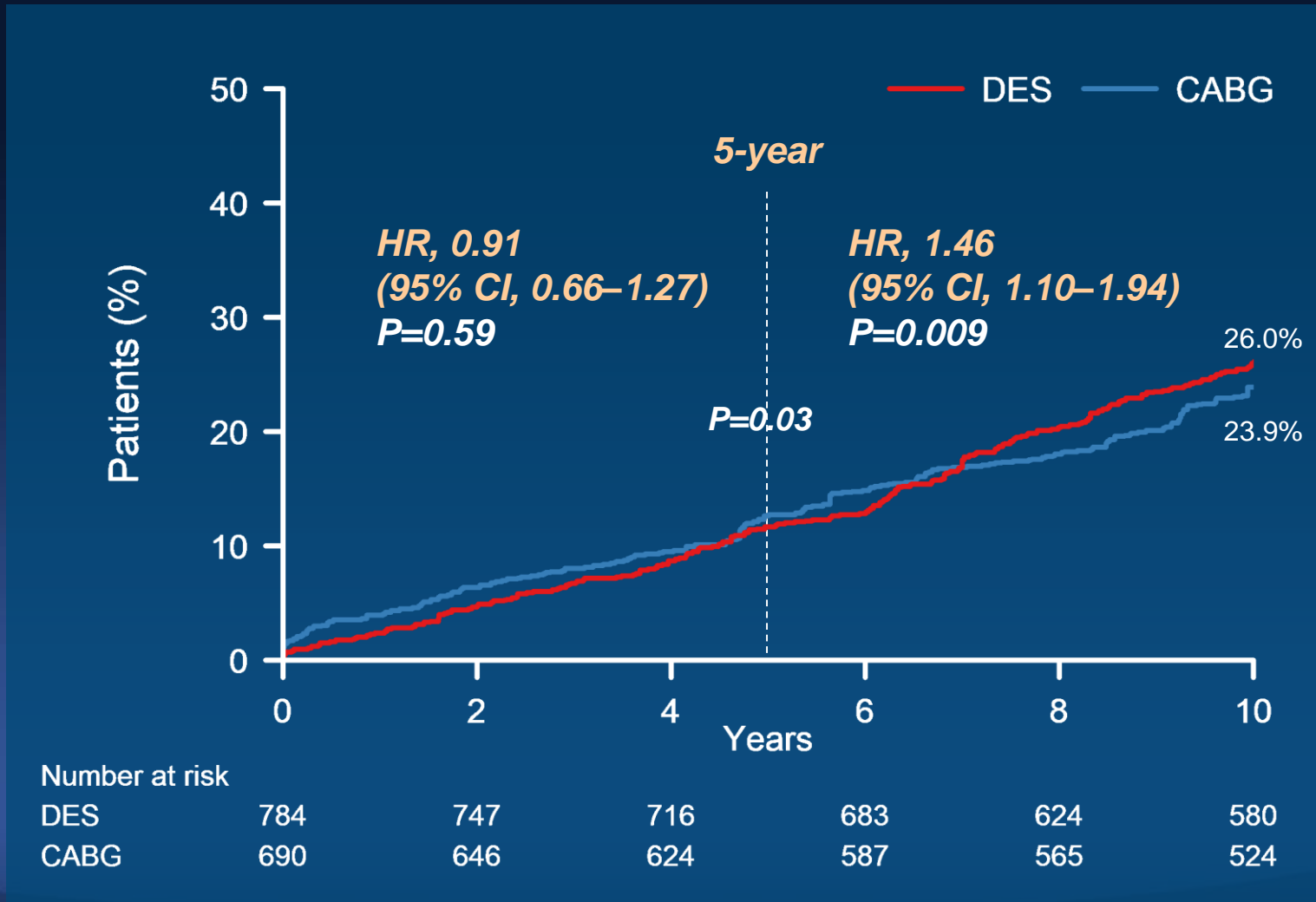
Wave 1 (BMS vs. CABG) TVR



Wave 2 (DES vs, CABG) Death



Wave 2 (DES vs, CABG) Death, Q-MI, or Stroke



Wave 2 (DES vs. CABG) TVR



Hazard Ratios for Clinical Outcomes Before and After 5-Year of Follow-up

Outcome	Overall Cohort		Wave 1* (BMS)		Wave 2* (DES)	
	Hazard Ratio [†] (95% CI)	P value	Hazard Ratio [†] (95% CI)	P value	Hazard Ratio [†] (95% CI)	P value
Analyses with IPTW	N = 2240 patients (PCI 1102, CABG 1138)		N = 766 patients (BMS 318, CABG 448)		N = 1474 patients (DES 784, CABG 690)	
Death		0.64		0.05		0.15
0~5 years	1.10 (0.82–1.47)	0.53	1.65 (0.91–2.98)	0.10	1.02 (0.71–1.46)	0.91
>5 years	1.09 (0.87–1.36)	0.48	0.68 (0.46–1.02)	0.06	1.35 (1.00–1.81)	0.05
Composite outcome (death, Q-wave MI or stroke)		0.43		0.06		0.03
0~5 years	0.98 (0.75–1.29)	0.91	1.46 (0.84–2.53)	0.18	0.91 (0.66–1.27)	0.59
>5 years	1.16 (0.93–1.43)	0.19	0.67 (0.46–1.00)	0.05	1.46 (1.10–1.94)	0.009
TVR, All period	4.07 (3.43–6.44)	<0.001	4.45 (2.81–7.05)	<0.001	5.82 (3.77–9.01)	<0.001
Analyses with Propensity-score Matching	N = 1318 patients (PCI 659, CABG 659)		N = 386 patients (BMS 193, CABG 193)		N = 864 patients (DES 432, CABG 432)	
Death		0.27		0.29		0.25
0~5 years	0.91 (0.66–1.24)	0.55	1.29 (0.67–2.46)	0.45	1.04 (0.70–1.54)	0.86
>5 years	1.21 (0.94–1.55)	0.14	0.74 (0.48–1.14)	0.17	1.30 (0.95–1.78)	0.09
Composite outcome (death, Q-wave MI or stroke)		0.03		0.17		0.03
0~5 years	0.85 (0.63–1.14)	0.27	1.18 (0.65–2.12)	0.59	0.92 (0.63–1.34)	0.66
>5 years	1.34 (1.06–1.70)	0.02	0.67 (0.44–1.04)	0.07	1.48 (1.10–2.00)	0.01
TVR, All period	4.70 (3.26–6.76)	<0.001	6.05 (3.12–11.8)	<0.001	5.07 (3.11–8.27)	<0.001

Conclusions

- In this large-scale, multi-center cohort of patients with LMCA disease, there was no significant difference in the rates of death and a composite end point of death, Q-wave MI, or stroke between the PCI and the CABG groups up to 10 years.
- However, in the cohort comparing DES and concurrent CABG, DES was associated with higher risks of death and serious composite outcomes compared to CABG after 5 years: the treatment benefit of CABG has diverged over time during continued follow-up.

Study Limitations

- This was a nonrandomized, observational study and thus potential selection and ascertainment bias should be acknowledged. Although rigorous adjustment was performed, hidden bias may remain due to the influence of unmeasured confounders (i.e., frailty or detailed information of concomitant atherosclerotic burden).
- Although previous our reports did not find any meaningful difference in outcomes among several types of first- and second-generation DES for LMCA disease. We evaluated the first-generation of DES.

10-Year Outcomes of Stents Versus Coronary Artery Bypass Grafting for Left Main Coronary Artery Disease

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