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

Seung-Jung Park, MD, PhD

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





Disclosure Statement of Financial Interest

- I, (Seung-Jung Park,MD) DO NOT have a financial interest/ arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
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MAIN-COMPARE Registry

Wave 1 (BMS era)

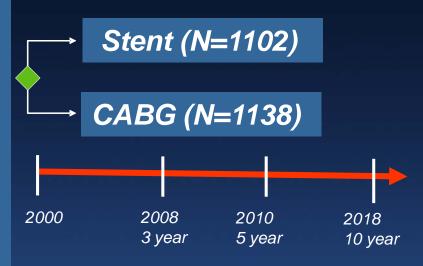
LM disease treated with BMS (n=318) and concurrent CABG (n=448) btw 2000~2003

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



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





Enrollment Criteria

Inclusion Criteria

Patients with unprotected left main disease (defined as stenosis of more than 50%) who underwent stenting or isolated CABG ("Unprotected" is defined as no coronary artery bypass grafts to the LAD or the LCX artery)

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

- All comparative analyses were performed in the overall cohort, wave 1 (BMS era), and wave 2 (DES era) cohort.
- To adjust baseline characteristics between PCI and CABG, propensity analyses using (1) the inverse-probability-oftreatment 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 Seoul National University Bundang Hospital

Kangnam St Mary's Hospital Samsung Medical Center

Yoido St Mary's Hospital Ajou University Hospital

Kyungpook National University Hospital Yonsei University Medical Center

Gachon University Gil Medical Center Chonnam National University Hospital

Seoul National University Hospital Chung-Nam University Hospital

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

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

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





RESULTS

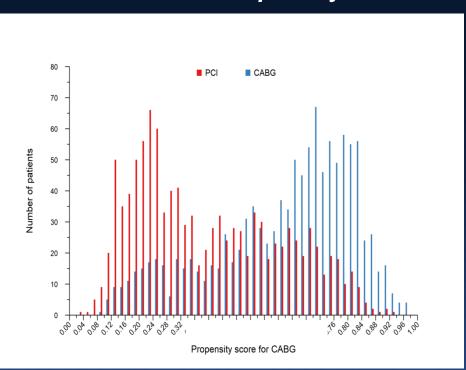




Baseline Characteristics

	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	CABG		PCI	CABG		PCI	CABG
	(N = 1102)	(N = 1138)	P Value	(N = 1102)	(N = 1138)	P Value	(N=659)	(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 Group	CABG (n = 1138)	PCI (n = 1102)
Off-pump surgery (%)	42	_
At least one arterial conduit (%)	98	
IMA to LAD Graft (%) in patients with arterial conduits	98	
Grafts / Patients (Mean \pm 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 <i>±</i> 0.5
Total length of stents at LMCA (mm)		28±21
Average stent diameter at LM site	<u>-</u>	3.5±0.4
Number of stents per patients	1	1.9±1.1



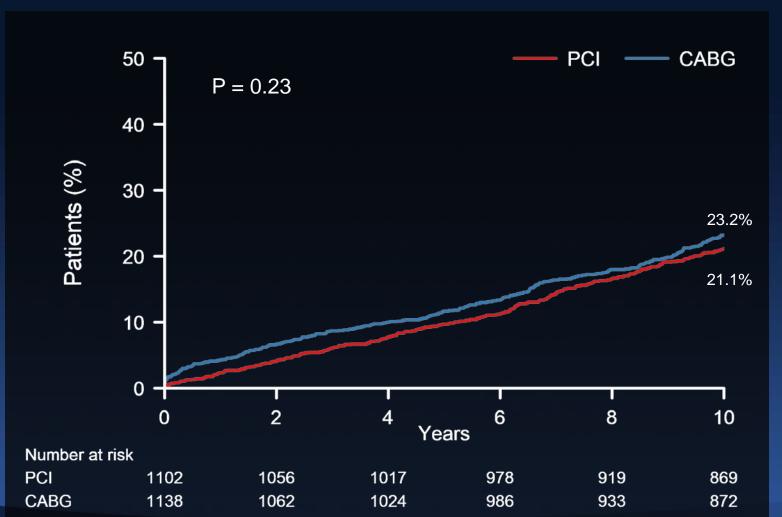


Unadjusted Kaplan-Meier Curves

- 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



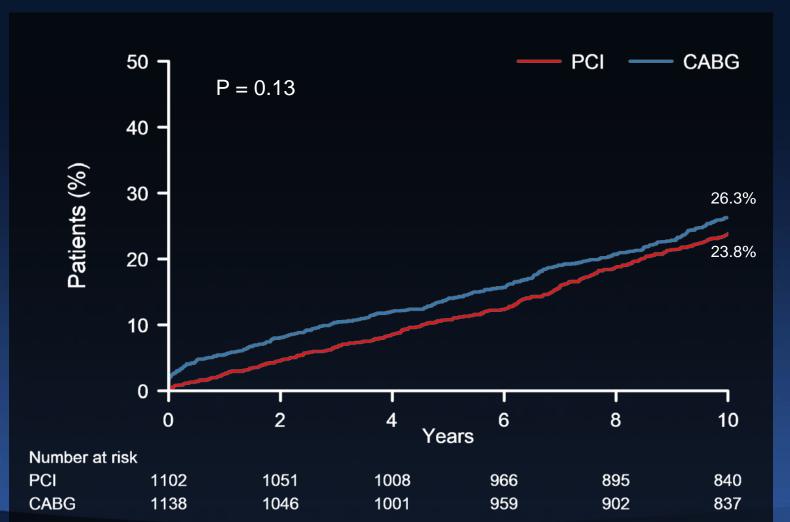
Overall Cohort Death







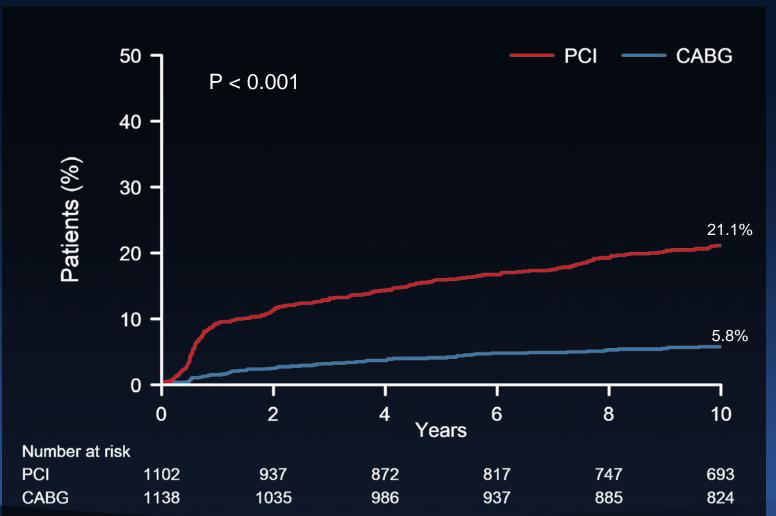
Overall Cohort Death, Q-MI, or Stroke







Overall Cohort TVR







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



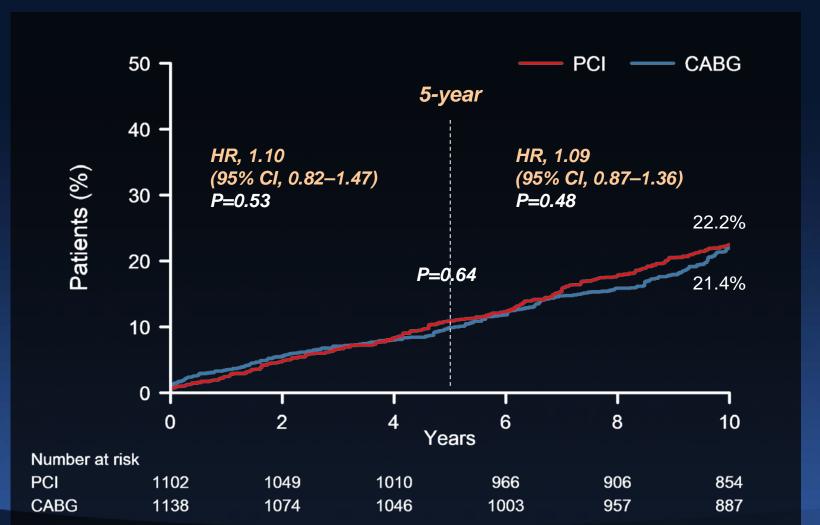


Adjusted Curves with the Use of IPTW Method





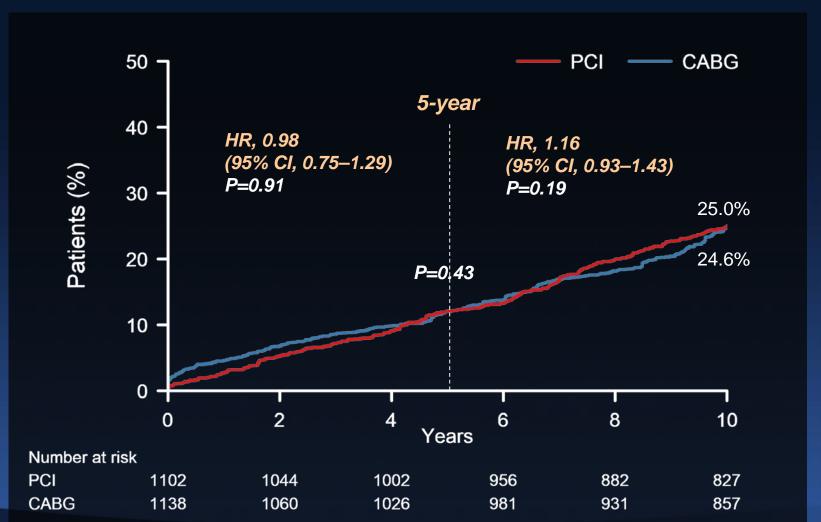
Overall Cohort Death







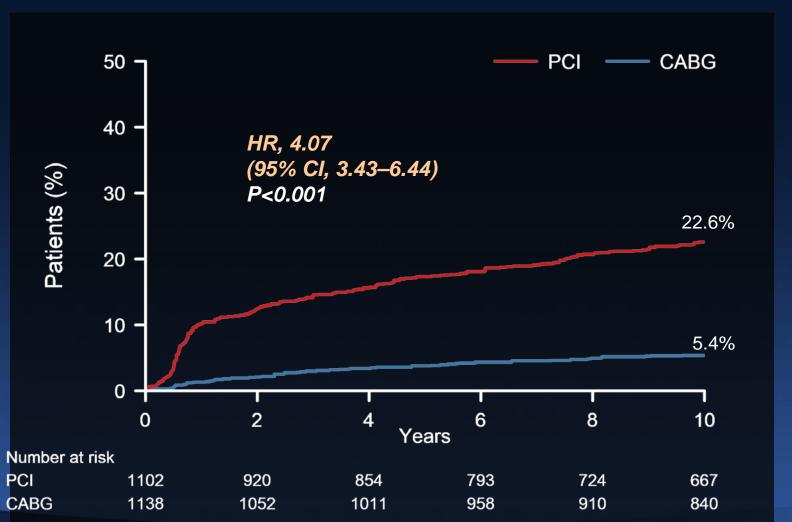
Overall Cohort Death, Q-MI, or Stroke







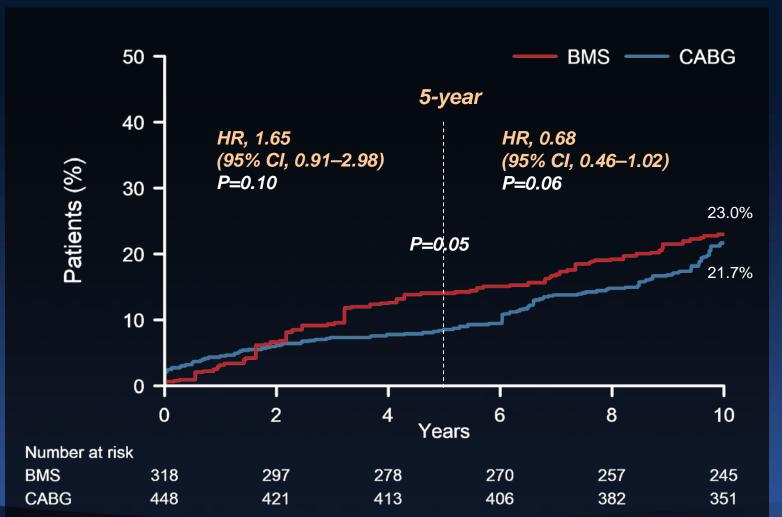
Overall Cohort TVR







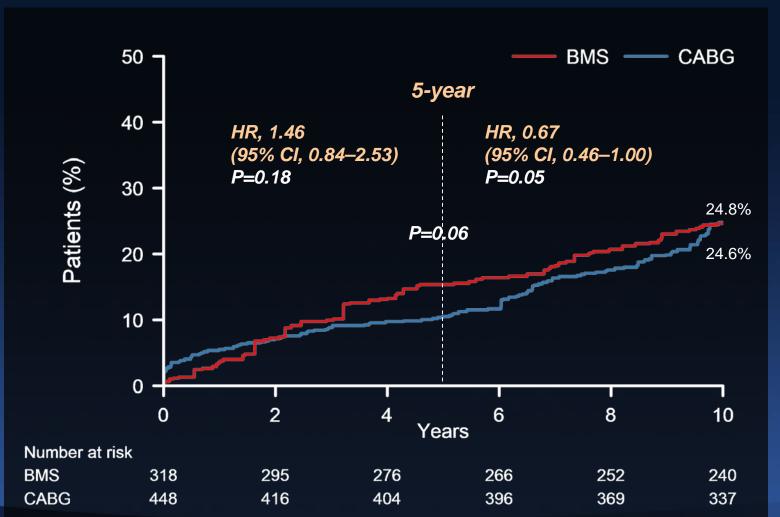
Wave 1 (BMS vs. CABG) Death







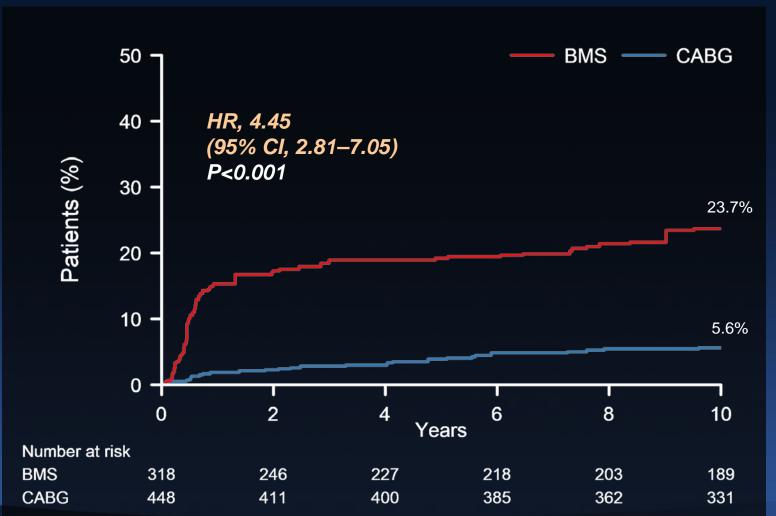
Wave 1 (BMS vs. CABG) Death, Q-MI, or Stroke







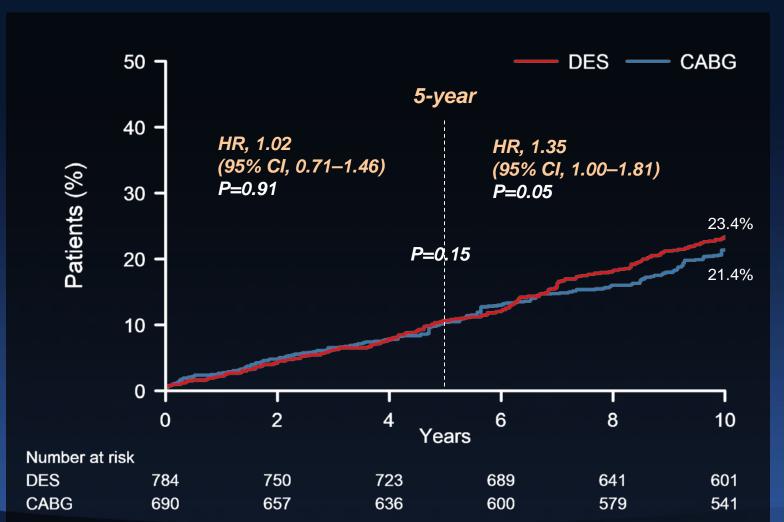
Wave 1 (BMS vs. CABG) TVR







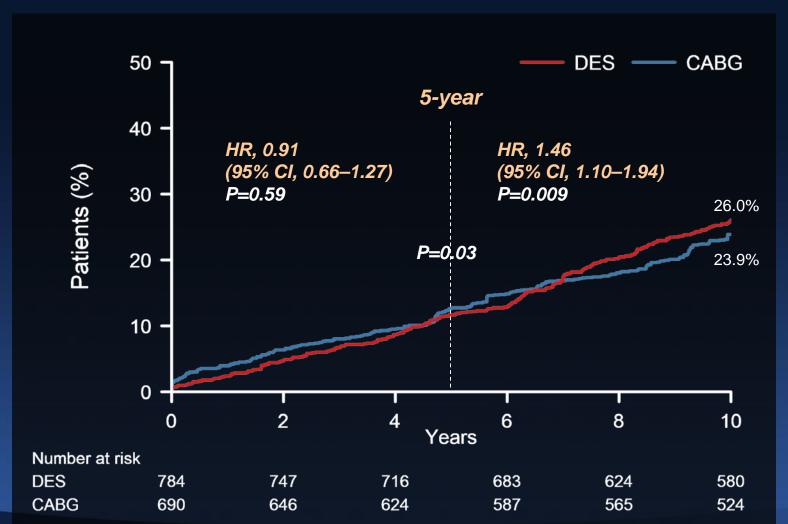
Wave 2 (DES vs, CABG) Death







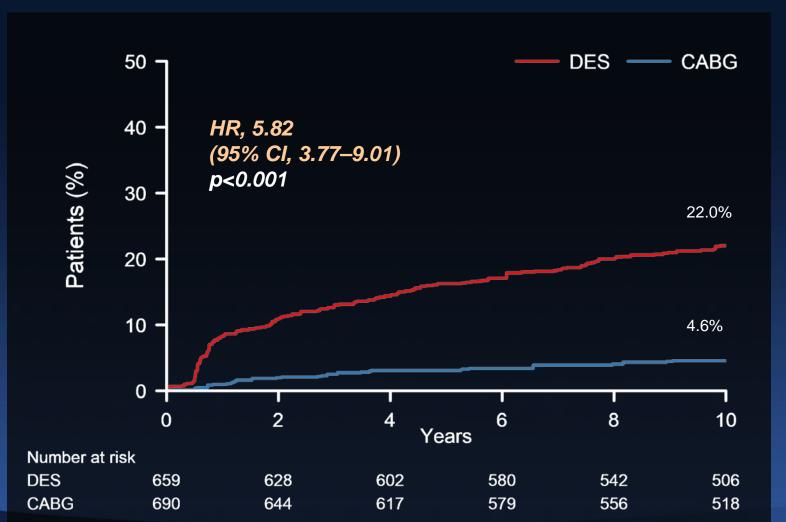
Wave 2 (DES vs. CABG) Death, Q-MI, or Stroke







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 IDTM	N = 2240 patients		N = 766 patients		N = 1474 patients	
Analyses with IPTW	(PCI 1102, CABG 1138)		(BMS 318, CABG 448)		(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		0.42		0.00		0.02
(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	N = 1318 patients		N = 386 patients		N = 864 patients	
Propensity-score Matching	(PCI 659, CABG 659)		(BMS 193, CABG 193)		(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		0.00		0.47		0.00
(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.
- The rate of target-vessel failure was consistently higher in the PCI group.



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).
- We evaluated the first-generation of DES. However, previous our reports did not find any meaningful difference in outcomes among several types of first- and secondgeneration DES for LMCA disease.





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