Long-Term Outcomes After Stenting Versus Coronary Artery Bypass Grafting for Unprotected Left Main Coronary Artery Disease: 10-Year Results of Bare-Metal Stents and 5-Year Results of Drug-Eluting Stents From the ASAN–MAIN (ASAN Medical Center–Left MAIN Revascularization) Registry

#### Duk-Woo Park, MD, PhD

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





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**Interventional Cardiology** 

#### Long-Term Outcomes After Stenting Versus Coronary Artery Bypass Grafting for Unprotected Left Main Coronary Artery Disease

10-Year Results of Bare-Metal Stents and 5-Year Results of Drug-Eluting Stents From the ASAN-MAIN (ASAN Medical Center-Left MAIN Revascularization) Registry

Duk-Woo Park, MD,\* Young-Hak Kim, MD,\* Sung-Cheol Yun, PHD,‡ Jong-Young Lee, MD,\* Won-Jang Kim, MD,\* Soo-Jin Kang, MD,\* Seung-Whan Lee, MD,\* Cheol-Whan Lee, MD,\* Jae-Joong Kim, MD,\* Suk-Jung Choo, MD,† Cheol-Hyun Chung, MD,† Jae-Won Lee, MD,† Seong-Wook Park, MD,\* Seung-Jung Park, MD\*

Seoul, Korea



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### Background

- Current guidelines and appropriateness criteria for coronary revascularization recommend CABG as the standard treatment for patients with left main coronary artery (LMCA) disease.
- However, improvements in interventional techniques and adjunctive pharmacologic therapy have led to a reevaluation of the role of PCI as an optional treatment for LMCA disease, and several studies have shown the feasibility and the favorable midterm outcomes of PCI with stenting.





### Background

- Recently, several reports have shown the successful use of coronary stenting compared with CABG in patients with unprotected LMCA disease.
- Whether or not the results achieved with coronary stents will be stable for 5 to 10 years remains to be determined in unprotected LMCA disease.





### Objective

 We therefore compared the long-term (beyond 5 years up to 10 years) safety and effectiveness of coronary stenting and CABG among patients with unprotected LMCA disease.







### **Study Population**

- Complete 10-year follow-up cohort; consecutive patients with unprotected LMCA disease (defined as stenosis of more than 50%) who underwent BMS or isolated CABG between January 1, 1995 and April 30, 1999.
- Complete 5-year follow-up cohort: LMCA patients who underwent DES or concurrent CABG between January 1, 2003, and May 31, 2004.
- The follow-up extended through June, 2009, to ensure that all patients had an opportunity for at least 10 years for BMS and 5 year for DES patients.



### **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
- STEMI
- Cardiogenic shock at presentation





### **Revascularization Procedures**

- Patients underwent PCI, instead of CABG, because of either the patient's or physician's preference or the high surgical risk.
- PCI patients were prescribed aspirin plus thienopyridine (ticlopidine or clopidogrel) before or during the procedure. After PCI, aspirin was prescribed indefinitely and thienopyridine for at least 1 month in BMS and at least 6 months in DES patients.
- Surgical revascularization was performed using standard techniques. IMA was preferentially utilized for revascularization of the LAD artery.





### **Study Outcome**

#### **Primary Safety Outcomes**

- Death
- Composite of death, Q-wave MI, or stroke

#### **Primary Efficacy Outcome**

Target-vessel revascularization (TVR)







### **Outcome Definitions**

- Death from any cause was considered and also classified as cardiac or noncardiac.
- The diagnosis of MI was assessed by the universal definition of MI. Q-wave MI was defined as documentation of a new pathologic Q wave after the index treatment.
- Stroke, as indicated by neurologic deficits, was confirmed by a neurologist on the basis of imaging studies.
- TVR was defined as repeat revascularization of the treated vessel, including any segments of the LAD and the LCX.





### **Data Collection and Follow-up**

- Clinical follow-up was recommended at 1 month, 6 months, and 1 year, and then annually thereafter.
- Routine angiographic follow-up for all patients treated with PCI, but not with CABG, was recommended 6 to 10 months after the procedure
- Information about vital status was obtained (through June 31, 2009) from the Korea National Statistical Office using a unique personal identification number.





### **Statistical Analysis**

- Survival curves were constructed using Kaplan-Meier estimates and compared with the log-rank test.
- To reduce treatment selection biases and potential confounding, we performed adjustment for significant differences in the baseline characteristics using propensity score analysis (covariate adjustment and quartile-methods).



# Results





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#### Patients and Follow-Up Completeness Janua **Complete 10-Year Follow-Up Cohort (N=350)** : BMS (N=100) vs. CABG (N=250) **10-year complete follow-up available in 96.9%** BMS CABG Second quarter, 2003 **Complete 5-Year Follow-Up Cohort (N=395)** : DES (N=176) vs. CABG (N=219) 5-year complete follow-up available in 97.2% LIVICA disease DES CABG **Current time** NIVERSITY OF ULSAN CardioVascular Research Foundation

### **Procedural Characteristics**

Procedural characteristics	10-year cohort	5-year cohort
CABG patients	250 patients	219 patients
On-pump surgery	243 (97.2)	178 (81.3)
Grafts per patients	4.3±1.2	3.3±1.0
Arterial grafts per patient	1.1±0.7	2.5±0.9
Venous grafts per patient	3.2±1.4	0.9±0.7
Use of IMA-to-LAD graft	225 (90.0)	209 (95.4)
PCI patients	100 BMS	176 DES
Total number of stents in LM	1.3±0.6	1.3±0.6
Total length of stents in LM	16.2±9.2	35.2±27.0
Maximal balloon size	4.4±0.6	3.9±0.5
Use of IABP	5 (5.0)	12 (6.8)
IVUS guidance	67 (67.0)	157 (89.2)
Use of reopro	5 (5.0)	11 (6.3)
Distal bifurcation treatment	30 patients	119 patients
Single stenting	15 (50.0)	71 (59.7)
Complex 2 stenting	15 (50.0)	48 (40.3)
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### **Baseline Characteristics**

	10-year follow-up cohort			5-year follow-up cohort			
Variable	BMS (n=100)	CABG (n=250)	Р	DES (n=176)	CABG (n=219)	Р	
Demographics							
Age (years)	55±10	61±9	<0.001	61±12	62±8	0.20	
Male gender	60%	74%	0.008	71%	74%	0.51	
BMI (kg/m²)	25±3	26±3	0.86	25±3	25±3	0.58	
Risk factors							
Diabetes mellitus							
Any diabetes	21%	33%	0.03	30%	37%	0.12	
Insulin-requiring	4%	7%	0.27	5%	6%	0.67	
Hypertension	23%	50%	<0.001	47%	55%	0.11	
Hyperlipidemia	34%	46%	0.04	35%	55%	<0.001	
Current smoker	36%	27%	0.10	18%	20%	0.61	





### **Baseline Characteristics**

	10-year	follow-up	cohort	5-year follow-up cohort			
Variable	BMS (n=100)	CABG (n=250)	Р	DES (n=176)	CABG (n=219)	Р	
Previous MI	14%	16%	0.64	9%	11%	0.42	
Previous PCI	12%	10%	0.66	23%	14%	0.02	
Previous CHF	0	3%	0.11	1%	5%	0.01	
COPD	0	2%	0.33	2%	4%	0.43	
CVA	4%	16%	0.002	9%	12%	0.28	
PVD	4%	9%	0.12	2%	12%	<0.001	
Renal failure	4%	5%	0.79	6%	7%	0.64	
Ejection fraction (%)	60±9	57±12	0.004	60±8	57±11	<0.001	





### **Baseline Characteristics**

	10-year	follow-up	cohort	5-year follow-up cohort			
Variable	BMS (n=100)	CABG (n=250)	Р	DES (n=176)	CABG (n=219)	Р	
euroSCORE value	3.3±2.1	4.4±2.2	<0.001	3.3±2.7	4.5±2.6	<0.001	
Parsonnet score	3.0±4.0	5.0±4.8	<0.001	5.4±4.7	5.8±6.6	<0.001	
Clinical indication			<0.001			<0.001	
SA	29%	11%		55%	16%		
UA	68%	86%		35%	78%		
NSTEMI	3%	3%		10%	6%		







### **Angiographic Characteristics**

	10-year follow-up cohort			5-year follow-up cohort			
Variable	BMS (n=100)	CABG (n=250)	Р	DES (n=176)	CABG (n=219)	Р	
Involved location			<0.001			0.78	
Ostium/midshaft	70%	41%		32%	31%		
Distal bifurcation	30%	59%		68%	69%		
Extent of diseased vessel			<0.001			<0.001	
Left main only	55%	10%		23%	5%		
Left main plus 1VD	21%	14%		26%	6%		
Left main plus 2VD	16%	22%		27%	26%		
Left main plus 3VD	8%	53%		24%	64%		
RCA disease	18%	67%	<0.001	42%	80%	<0.001	
Total occlusion $\geq 1$	13%	32%	<0.001	NA	NA	NA	
Restenotic lesion	NA	NA	NA	9 (5.1)	5 (2.3)	0.13	

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\*Mean  $\pm$  SD or N (%)





#### **Observed In-hospital Outcomes**

	10-year follow-up cohort			5-year follow-up cohort			
Clinical events, n (%)	BMS (n=100)	CABG (n=250)	P <sup>†</sup>	DES (n=176)	CABG (n=219)	P <sup>†</sup>	
Death	0	6 (2.4)	0.19	0	5 (2.3)	0.07	
Cardiac	0	4 (1.6)	0.58	0	5 (2.3)	0.07	
Noncardiac	0	2 (0.8)	>0.99	0	0		
MI	8 (8.0)	21 (8.4)	0.90	19 (10.8)	17 (7.8)	0.30	
Q-wave	2 (2.0)	14 (5.6)	0.26	3 (1.7)	8 (3.7)	0.36	
Non-Q-wave	6 (6.0)	7 (2.8)	0.21	16 (9.1)	9 (4.1)	0.04	
Stroke	0	2 (0.8)	>0.99	1 (0.6)	6 (2.7)	0.14	
Death, Q-wave MI, or stroke	2 (2.0)	19 (7.6)	0.046	4 (2.3)	18 (8.2)	0.01	
Any revascularization	2 (2.0)	1 (0.4)	0.20	1 (0.6)	1 (0.5)	>0.99	
TLR	2 (2.0)	1 (0.4)	0.20	1 (0.6)	1 (0.5)	>0.99	
TVR	2 (2.0)	1 (0.4)	0.20	1 (0.6)	1 (0.5)	>0.99	
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N (%)



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## Long-Term Outcomes





#### **Observed 10-Year Outcomes: BMS cohort**



#### **Observed 5-Year Outcomes: DES cohort**



#### **Observed Long-Term Outcomes**

	10-year follow-up cohort			5-year follow-up cohort			
Clinical events, n (%)	BMS (n=100)	CABG (n=250)	P <sup>†</sup>	DES (n=176)	CABG (n=219)	Pt	
Cumulative outcomes		At 10-year			At 5-year		
Death	15 (15.9)	59 (24.1)	0.02	10 (5.9)	24 (11.2)	0.03	
Cardiac	6 (6.9)	25 (11.0)	0.10	6 (3.7)	13 (6.1)	0.22	
Noncardiac	9 (9.6)	34 (14.8)	0.08	4 (2.3)	11 (5.4)	0.06	
MI	15 (16.0)	29 (12.1)	0.43	27 (15.7)	21 (9.7)	0.12	
Q-wave	7 (7.8)	20 (8.5)	0.72	9 (5.5)	12 (5.6)	0.67	
Non-Q-wave	8 (8.3)	9 (3.6)	0.09	18 (10.2)	9 (4.1)	0.02	
Stroke	5 (5.5)	18 (8.8)	0.22	3 (1.7)	12 (5.9)	0.04	
Death, Q-MI, or stroke	24 (25.2)	78 (32.1)	0.04	17 (10.0)	41 (19.1)	0.004	
Any revascularization	41 (43.1)	15 (6.7)	<0.001	32 (19.7)	10 (5.0)	<0.001	
TLR	24 (24.9)	11 (4.9)	<0.001	21 (13.2)	6 (2.9)	0.001	
TVR	35 (36.7)	11 (4.9)	<0.001	26 (16.2)	6 (2.9)	<0.001	

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#### **Adjusted 10-Year Outcomes: BMS cohort**



#### **Adjusted 5-Year Outcomes: DES cohort**



#### Adjusted HR for 10YR-Outcomes for BMS vs. CABG

	Death		Composite of de Q-wave MI, or st	eath, troke	TVR		
Model	HR (95% CI)	Р	HR (95% CI)	Р	HR (95% CI)	Р	
Crude	0.53 (0.31-0.90)	0.02	0.64 (0.42-0.99)	0.04	8.80 (4.57-16.91)	<0.001	
PS covariates	0.81 (0.44-1.50)	0.50	0.92 (0.55-1.53)	0.74	10.34 (4.61-23.18)	<0.001	
PS stratum							
Quartile 1	2.35 (0.32-17.46)	0.40	1.78 (0.24-13.09)	0.57	<u> </u> †	<u> </u> †	
Quartile 2	0.67 (0.20-2.20)	0.51	0.73 (0.26-2.04)	0.54	5.07 (1.21-21.25)	0.03	
Quartile 3	0.49 (0.14-1.71)	0.26	0.78 (0.33-1.86)	0.58	18.80 (4.23-83.46)	<0.001	
Quartile 4	2.41 (0.52-11.03)	0.26	2.27 (0.65-7.91)	0.20	9.71 (1.30-72.37)	0.03	
Summary <sup>‡</sup>	0.91 (0.49-1.69)	0.76	1.02 (0.61-1.71)	0.93	9.25 (4.17-20.50)	<0.001	
Quartile 3 Quartile 4 Summary <sup>‡</sup>	0.49 (0.14-1.71) 2.41 (0.52-11.03) 0.91 (0.49-1.69)	0.26 0.26 0.76	0.78 (0.33-1.86) 2.27 (0.65-7.91) 1.02 (0.61-1.71)	0.58 0.20 0.93	18.80 (4.23-83.46) 9.71 (1.30-72.37) 9.25 (4.17-20.50)	<0.001 0.03 <0.001	

<sup>†</sup>Could not be estimated.

\*HR are for the stenting group, as compared with CABG group





#### Adjusted HR for 5YR-Outcomes for DES vs. CABG

	Death	Composite of death, th Q-wave MI, or stroke			e of death, I, or stroke TVR		
Model	HR (95% CI)	Р	HR (95% CI)	Р	HR (95% CI)	Р	
Crude	0.46 (0.22-0.94)	0.04	0.45 (0.26-0.78)	0.005	4.64 (2.01-10.68)	<0.001	
PS covariates	0.83 (0.34-2.07)	0.70	0.91 (0.45-1.83)	0.79	6.22 (2.26-17.14)	<0.001	
PS stratum							
Quartile 1	<u></u> †	<u> </u>	0.55 (0.07-4.04)	0.55	15.44 (2.17-110.1)	0.006	
Quartile 2	0.63 (0.07-5.41)	0.68	0.78 (0.22-2.75)	0.69	2.35 (0.53-10.52)	0.26	
Quartile 3	0.56 (0.16-1.94)	0.36	0.69 (0.23-2.04)	0.50	6.00 (0.77-46.89)	0.09	
Quartile 4	<u>_</u> †	<u> </u>	<u>_</u> †	<u> </u> †	<u> </u>	<u>_</u> †	
Summary <sup>‡</sup>	0.58 (0.23-1.46)	0.25	0.79 (0.39-1.59)	0.50	5.31 (1.91-14.71)	0.001	
<sup>†</sup> Could not b	e estimated						

\*HR are for the stenting group, as compared with CABG group





### Conclusion

- In this longest follow-up study of complete 10-year with BMS and complete 5-year with DES for unprotected LMCA disease, the adjusted long-term risks of death and a composite of serious outcomes (death, Q-wave MI, or stroke) were similar in the stenting and the CABG groups.
- In contrast, the rate of TVR was significantly lower in the CABG group than in the stenting group.



#### Important Message from This Featured Study

- To the best of our knowledge, this study is the longest follow-up study to compare coronary stenting, even with BMS or DES, with bypass surgery for treatment of unprotected LMCA stenosis.
- Therefore, our study provides important information about a sufficient long-term effect of stenting as compared with CABG, and it is probably best viewed as an indication to proceed with larger, randomized trials with long-term follow-up.



