EES vs. SES in Unprotected Left Main PCI

Results from the EXCELLENT -Registry

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Disclosure

- I, Kyung Woo Park, have nothing to disclose.

Cardiovascular Center
Seoul National University Hospital

Treatment of Unprotected Left Main Coronary Artery Disease

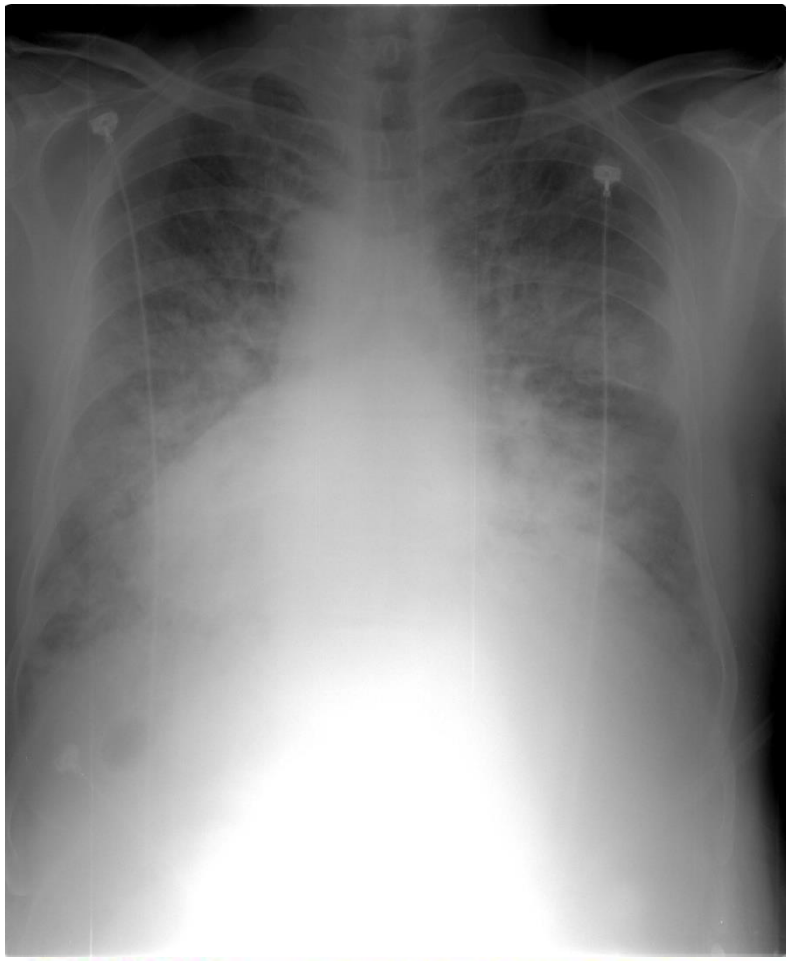
PCI vs. CABG

66/M

Known chronic stable angina

Suffered from watery diarrhea for several days d/t infectious colitis

Showed up for chest pain continuing for 4 hours



V/S: 173/121 – 183 – 20 – 35.7℃

Hb: 17.5 gm/dL

Creatinine: 3.4 mg/dL

CK-MB: 33 ng/mL

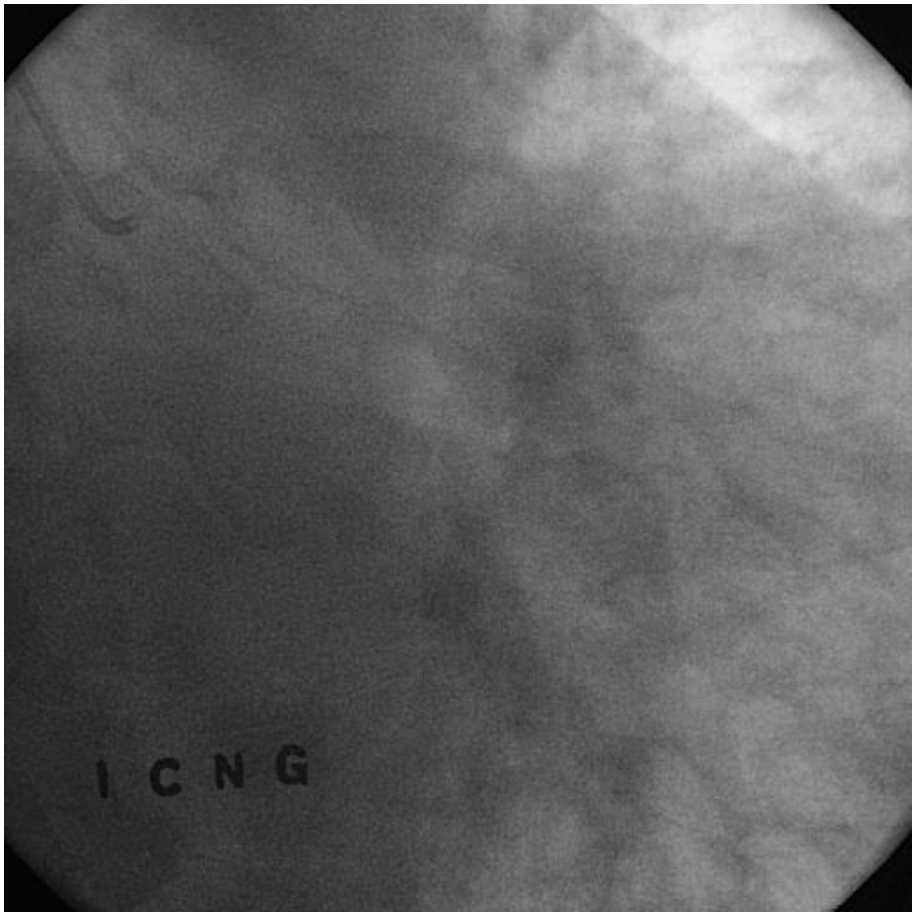
Troponin I: 14.2 ng/mL

Clinical Dx: NSTEMI, Killip class III

66/M

NSTEMI, Killip class III

Left main coronary artery disease



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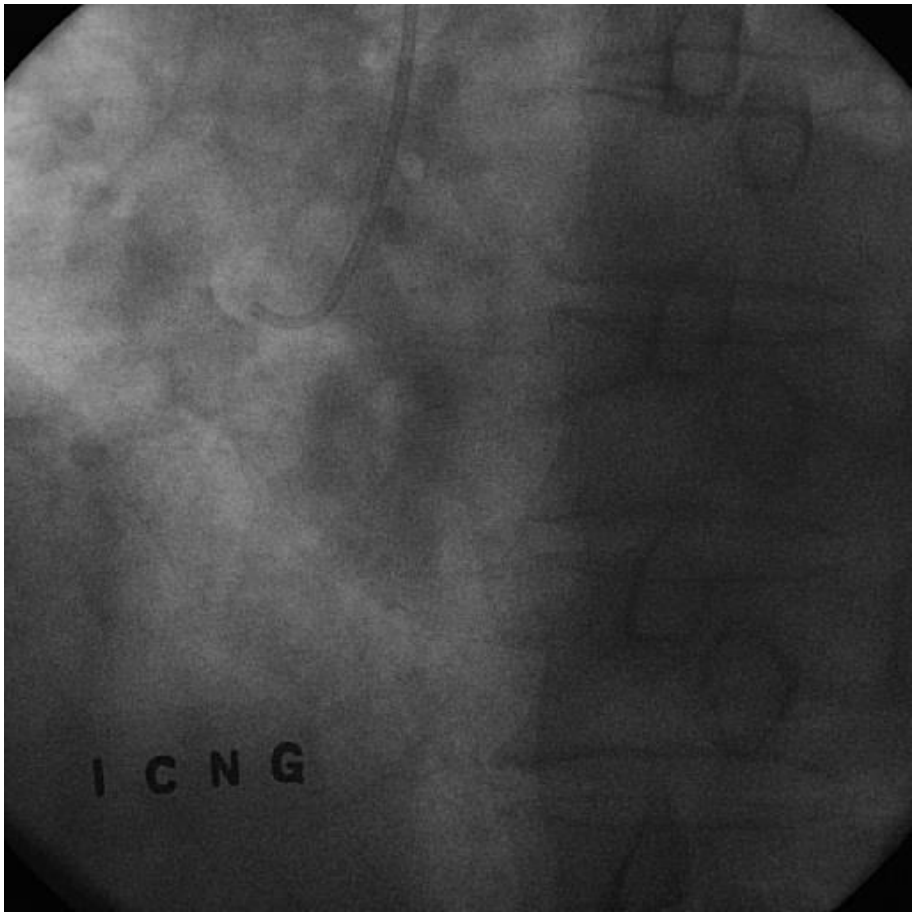
NSTEMI, Killip class III

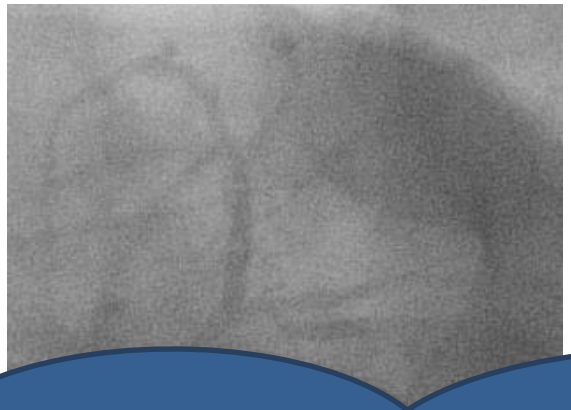
Left main coronary artery disease



CABG? vs. PCI?

Favoring CABG

- **Left main stenosis**



Favoring PCI

- **os to shaft lesion**
- **History of CVA**
- **Old age**

Clinically…

Angiographically…

[Euroscore]

- 66YO = 2
- Serum Cr 3.4 = 2 = 3
- Requiring iv nitrate = 2
- Neurololgic dysfxn+ = 2
- Preoperative ventilation
- Recent MI = 2

➔ Euroscore: 13 ➔ Estimated mortality: 32.2%

[Syntax score]

- Segment 5x2 = 10
- Aortoostial lesion = 1

Sytax score = 11 (low risk)

Changing concept:

PCI could be considered as an alternative of CABG in patients with LMCA.

After thorough discussion…

Successful PCI with Taxus™

However, 4 days later…

CABG vs PCI for LM

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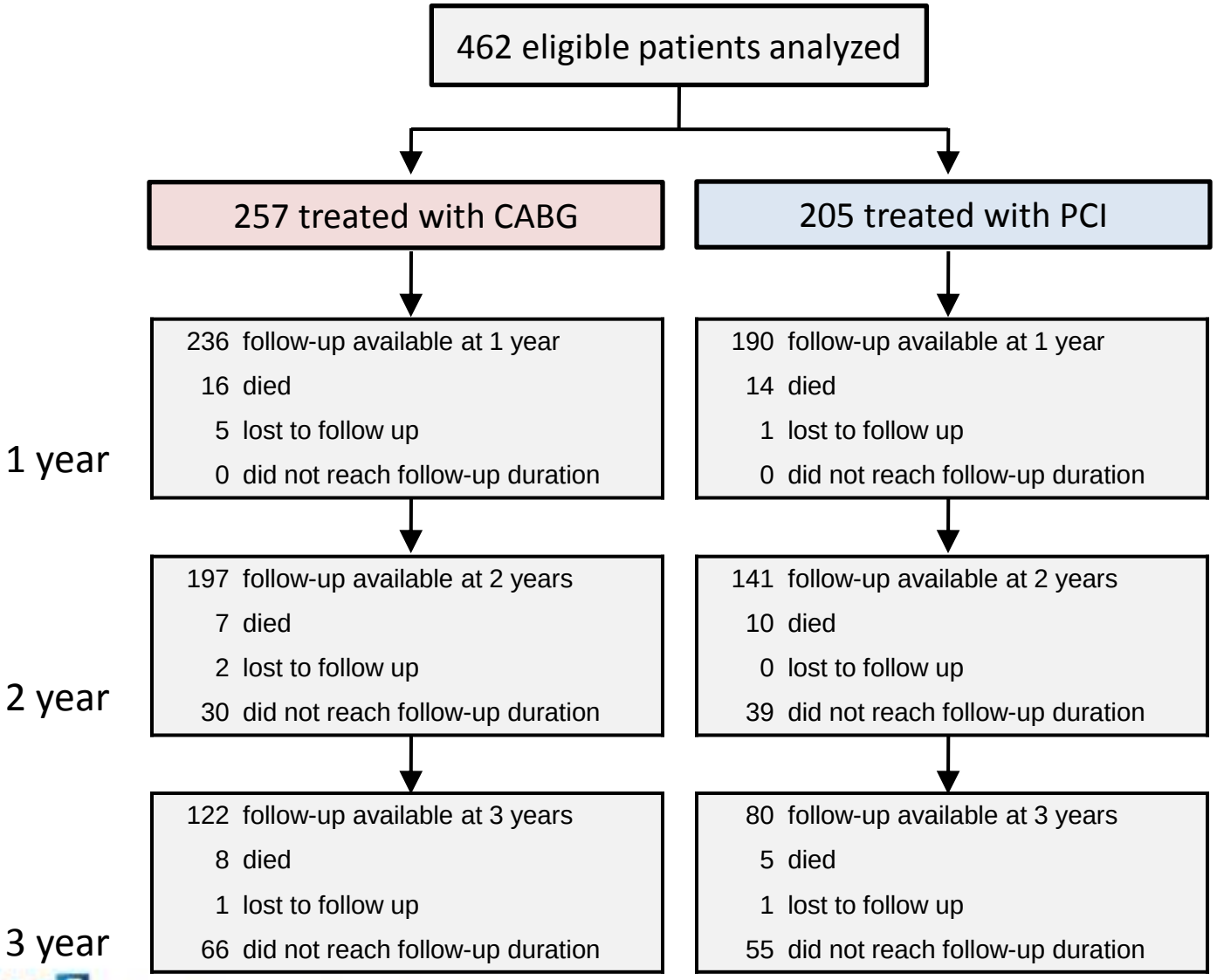

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Kang SH, Park KW, Kim HS et al. Am J Cardiol; 2010

CABG vs PCI for LM

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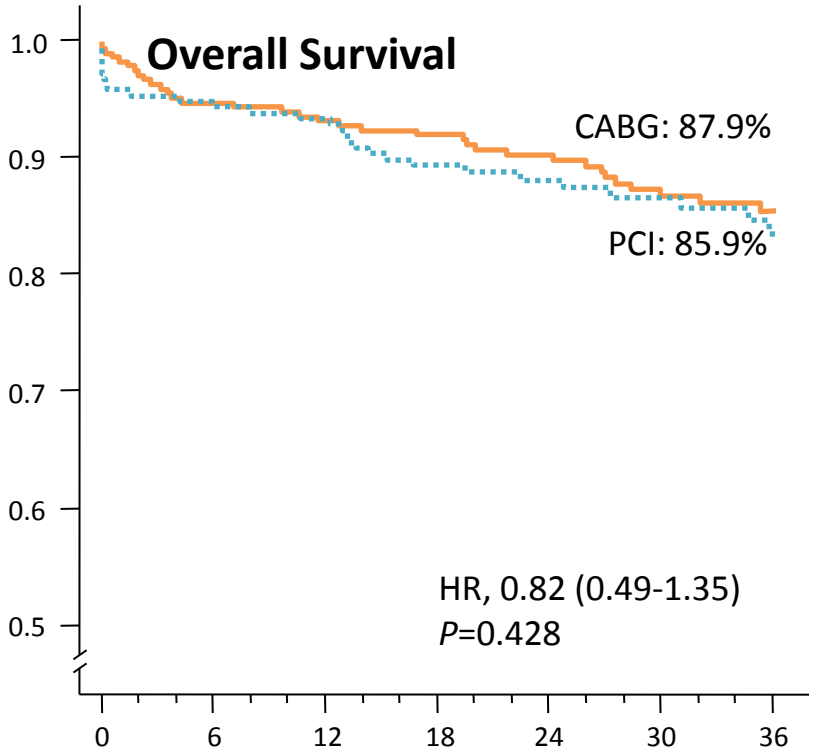
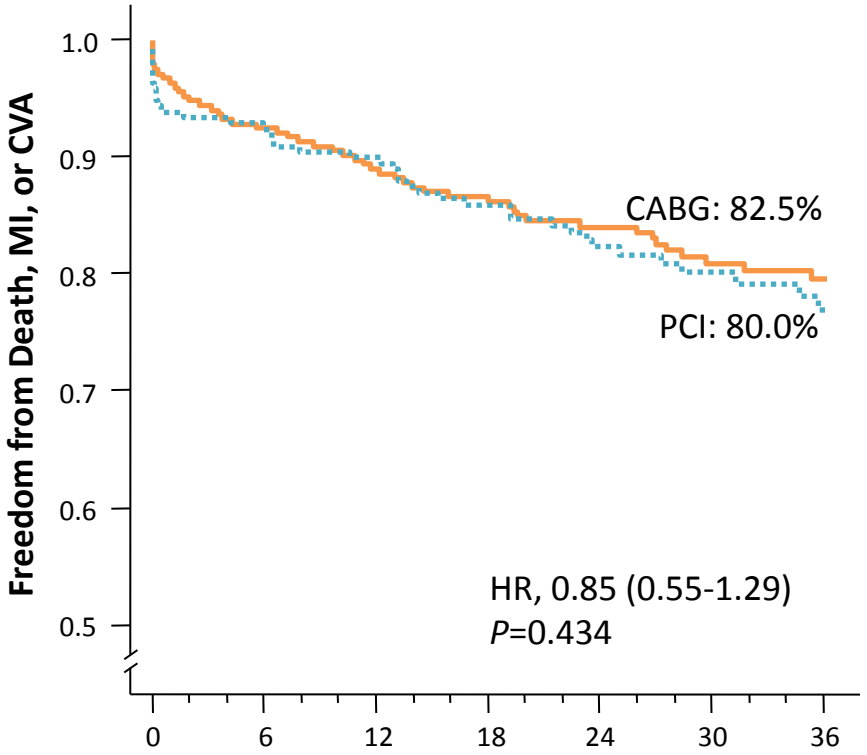
(A) Death from Any Cause



No. at Risk (n)							
CABG	257	242	236	230	197	162	125
PCI	205	193	190	169	142	113	83

(B) Death, MI, or CVA



No. at Risk (n)							
CABG	257	238	227	217	184	151	115
PCI	205	189	183	163	133	104	75

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CABG vs PCI for LM

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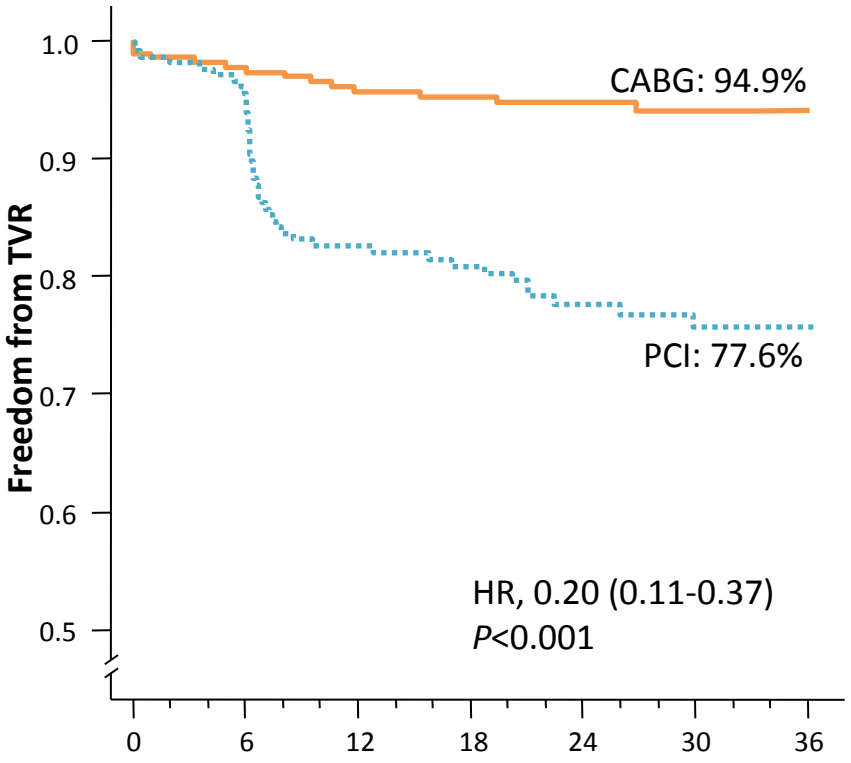
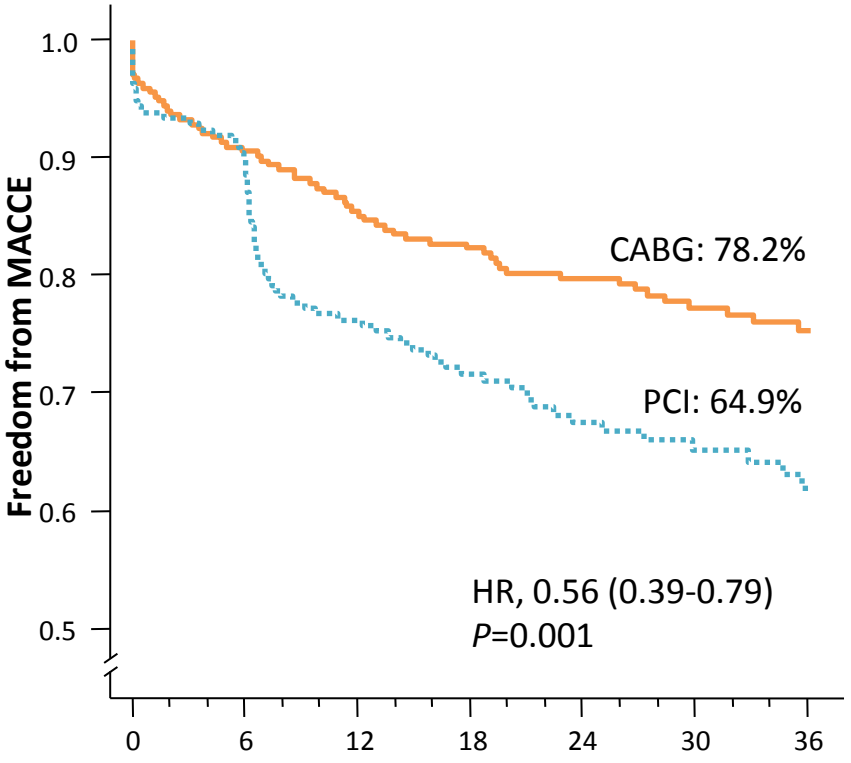
(C) TVR



No. at Risk (n)							
CABG	257	241	233	225	192	158	120
PCI	205	190	185	165	135	105	76

(D) MACCE



No. at Risk (n)							
CABG	257	233	218	207	176	146	109
PCI	205	183	154	135	108	84	60

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CABG vs PCI for LM

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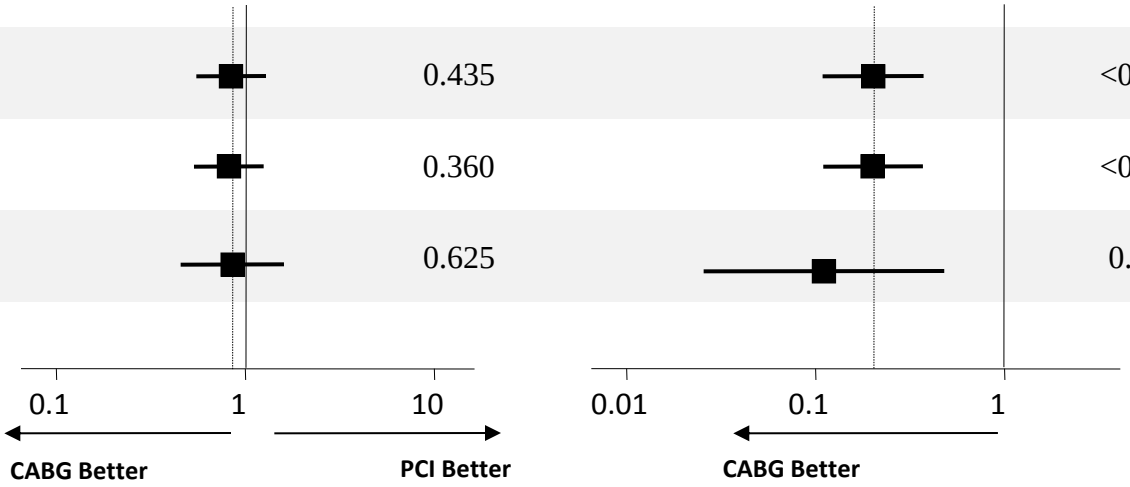
Propensity Score Analysis

Subgroup	Total (CABG/PCI)	Death, MI, or CVA		TVR	
		HR (95% C.I.)	*P*	HR (95% C.I.)	*P*
Crude Population	462 (257/205)		0.435		<0.001
Propensity Score-Adjusted	462 (257/205)		0.360		<0.001
Propensity Score-Matched	208 (104/104)		0.625		0.003



- Scoring propensity to each treatment strategy
- Covariates: sex, age, BMI, indication of revascularization, extent of involved vessel, disease location, type of bifurcation,diabetes, hypertension, current smoking, stroke, peripheral vascular disease, familial history of coronary artery disease, dyslipidemia, chronic kidney diease, serum creatinine, lipid levels (total, LDL, HDL-cholesterol and triglyceride), ejection fraction, use of GP IIb/IIIa inhibitors, emergency procedures, and EuroSCORE

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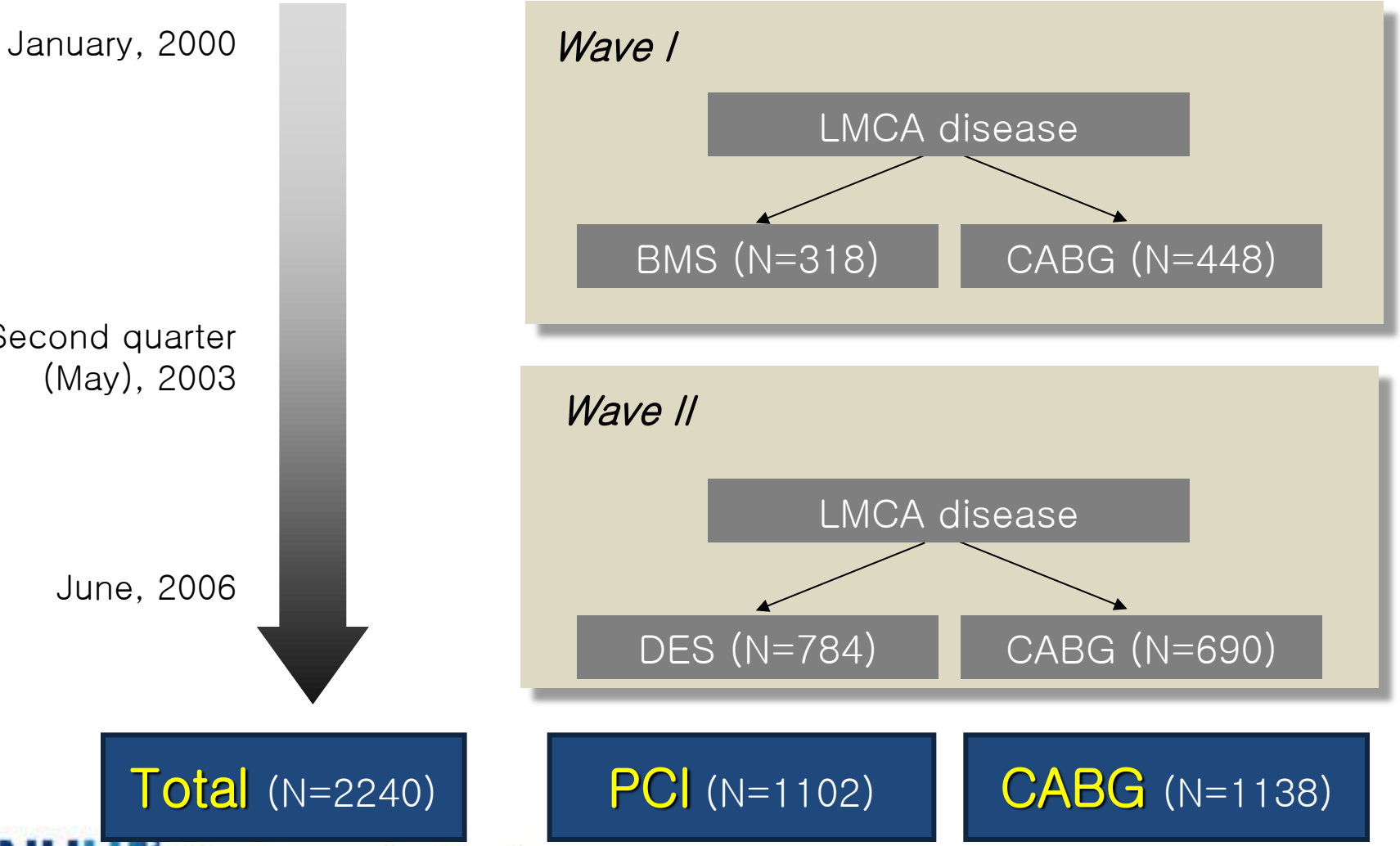
Korean Multicenter MAIN-COMPARE Registry Data

Stenting (BMS or DES) vs. CABG



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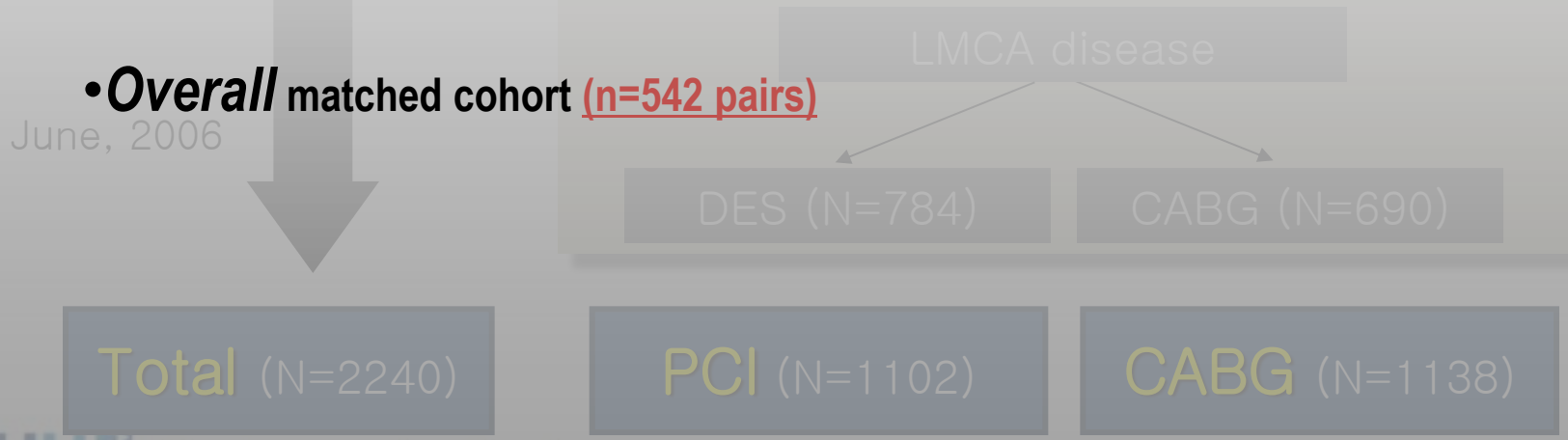
Seung et al. NEJM; 2008

Korean Multicenter MAIN-COMPARE Registry Data

Stenting (BMS or DES) vs. CABG

After Propensity-Matching

- ***Wave 1;*** **BMS vs. contemporary CABG** **(n=207 pairs)**
- ***Wave 2;*** **DES vs. contemporary CABG** **(n=396 pairs)**
- ***Overall*** **matched cohort** **(n=542 pairs)**

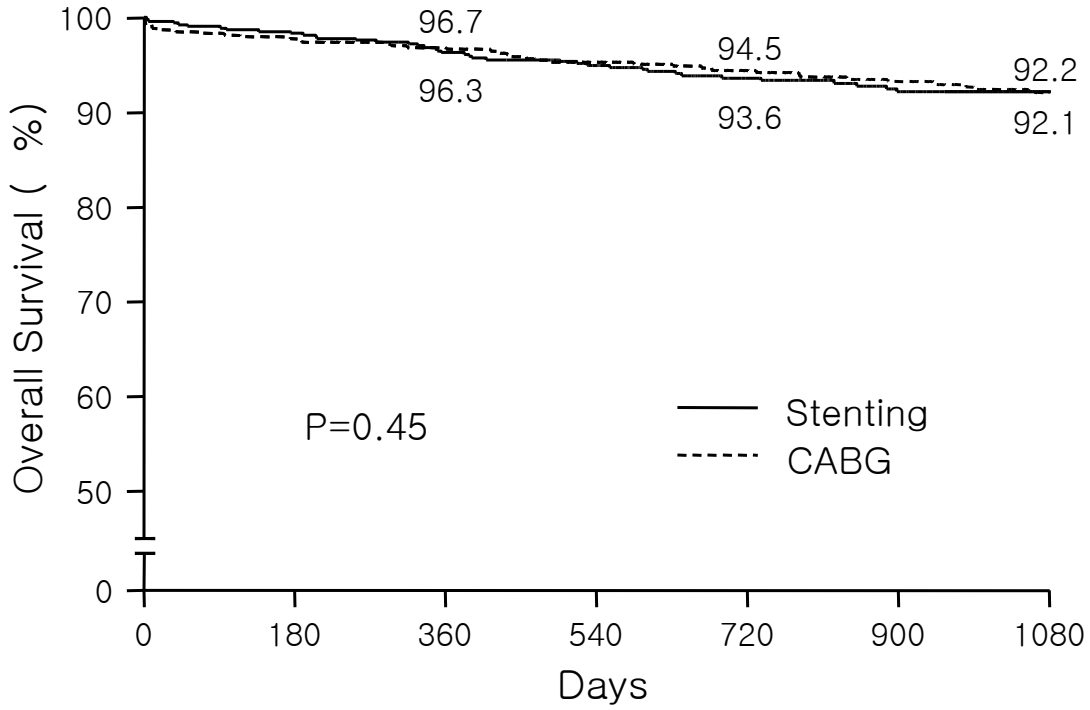


Seung et al. NEJM; 2008

Korean Multicenter MAIN-COMPARE Registry Data

Death

(Overall PCI and CABG matched cohort: 542 pairs)



No. at Risk

Stenting	542	516	372
220			
CABG	542	512	420
317			

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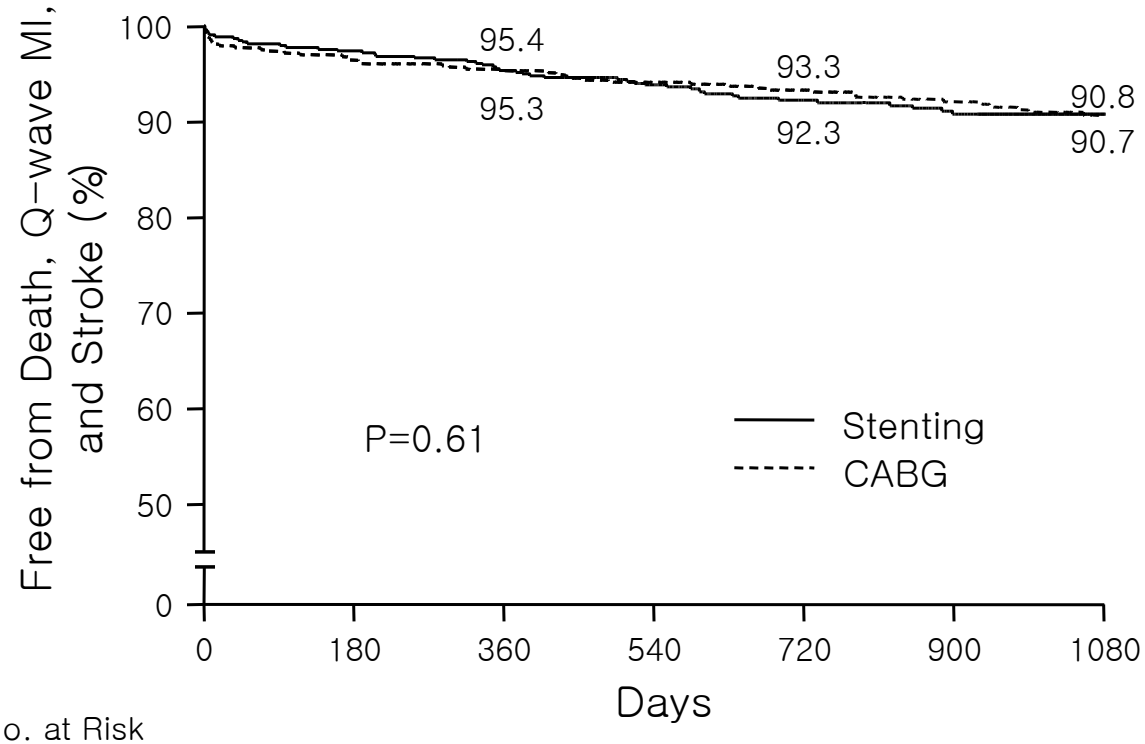
Seung et al. NEJM; 2008

Korean Multicenter MAIN-COMPARE Registry Data

Death, Q-MI, or Stroke

(Overall PCI and CABG matched cohort: 542 pairs)



No. at Risk

Stenting	542	510	366	218
CABG	542	502	412	309

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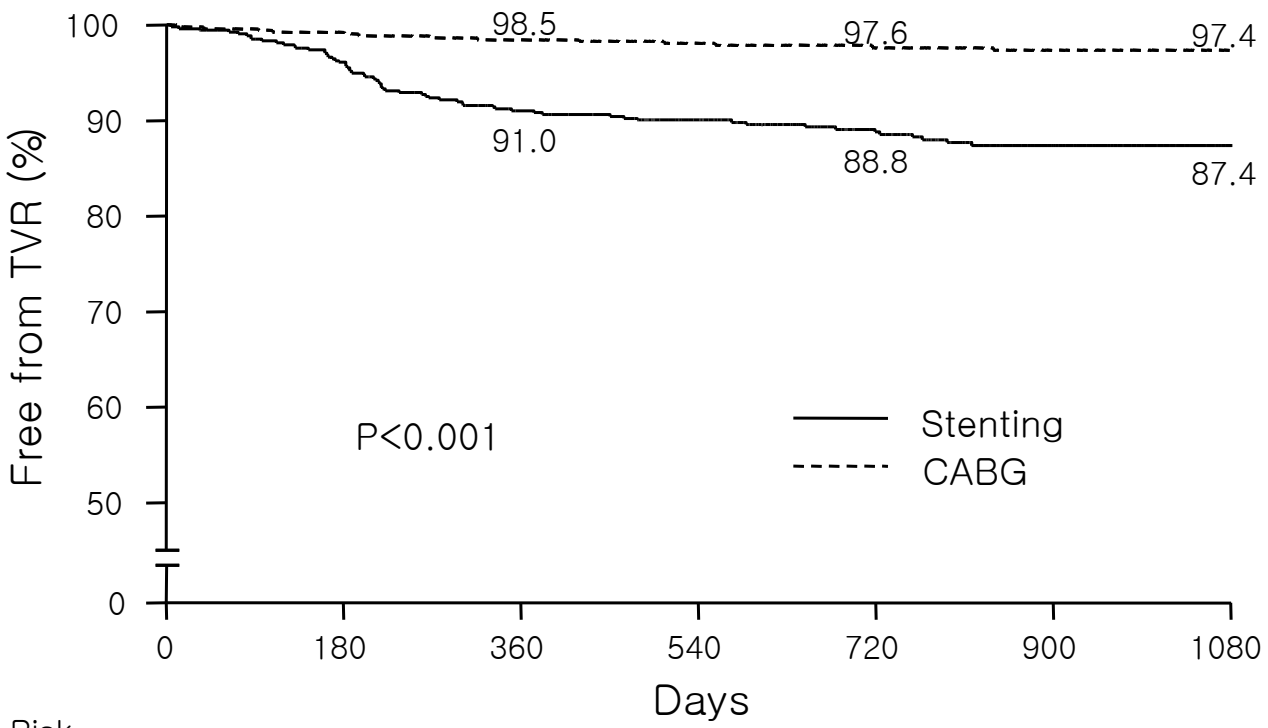
Seung et al. NEJM; 2008

Target-Vessel Revascularization

(Overall PCI and CABG matched cohort: 542 pairs)



No. at Risk

Stenting	542	471	331	193
CABG	542	503	408	305

Seung et al. NEJM; 2008

Hazard Ratios for Clinical Outcomes

(Overall PCI and CABG matched cohort: 542 pairs)

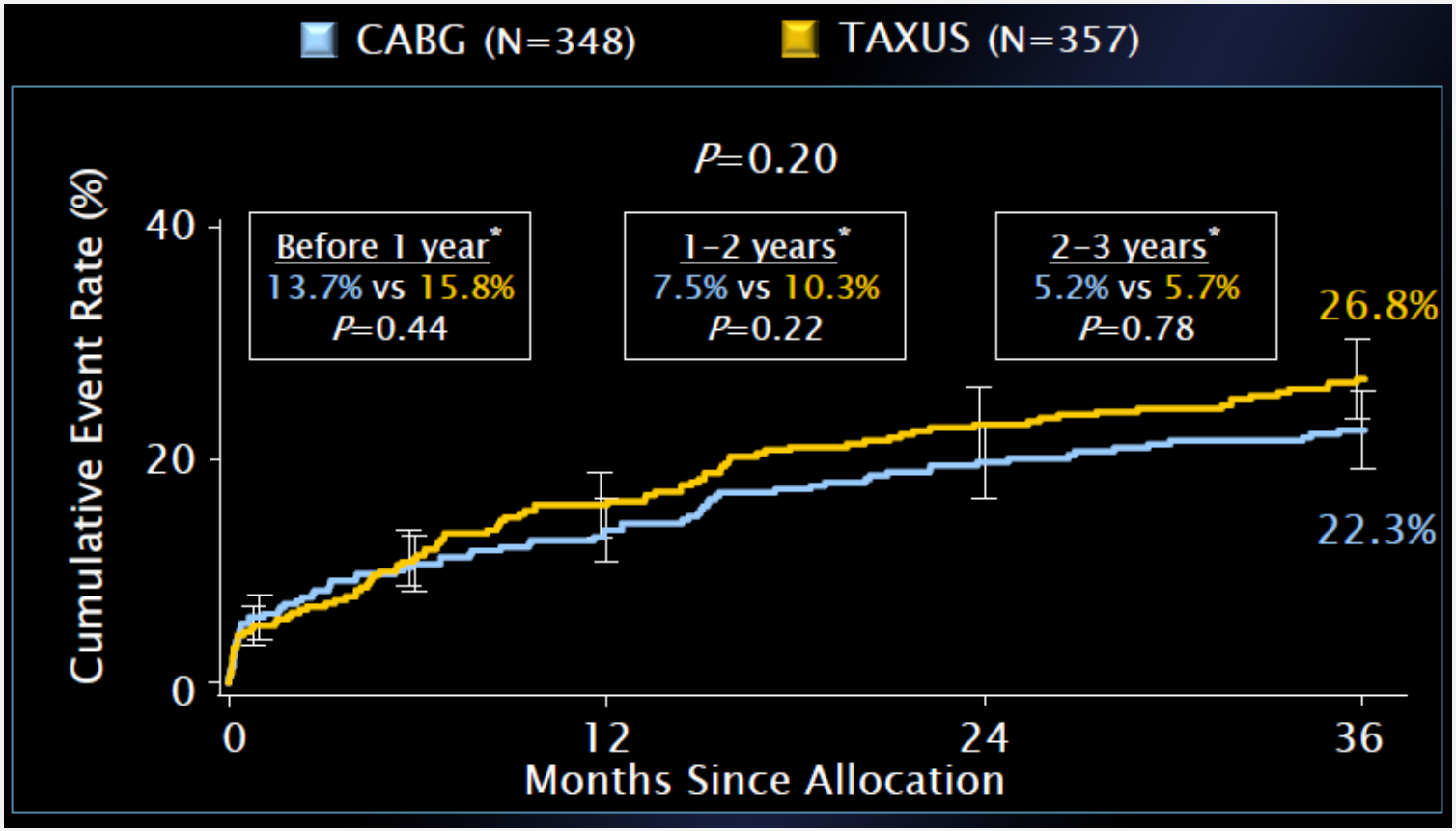
Outcome	Overall Patients (N=542 pairs)	
	HR* (95% CI)	P value
Death	1.18 (0.77-1.80)	0.45
Composite outcome (death, Q-wave myocardial infarction, or stroke)	1.10 (0.75-1.62)	0.61
Target-vessel revascularization	4.76 (2.80-8.11)	<0.001

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

Seung et al. NEJM; 2008

CABG vs. TAXUS

SYNTAX Left Main Subset: MACCE up to 3 years



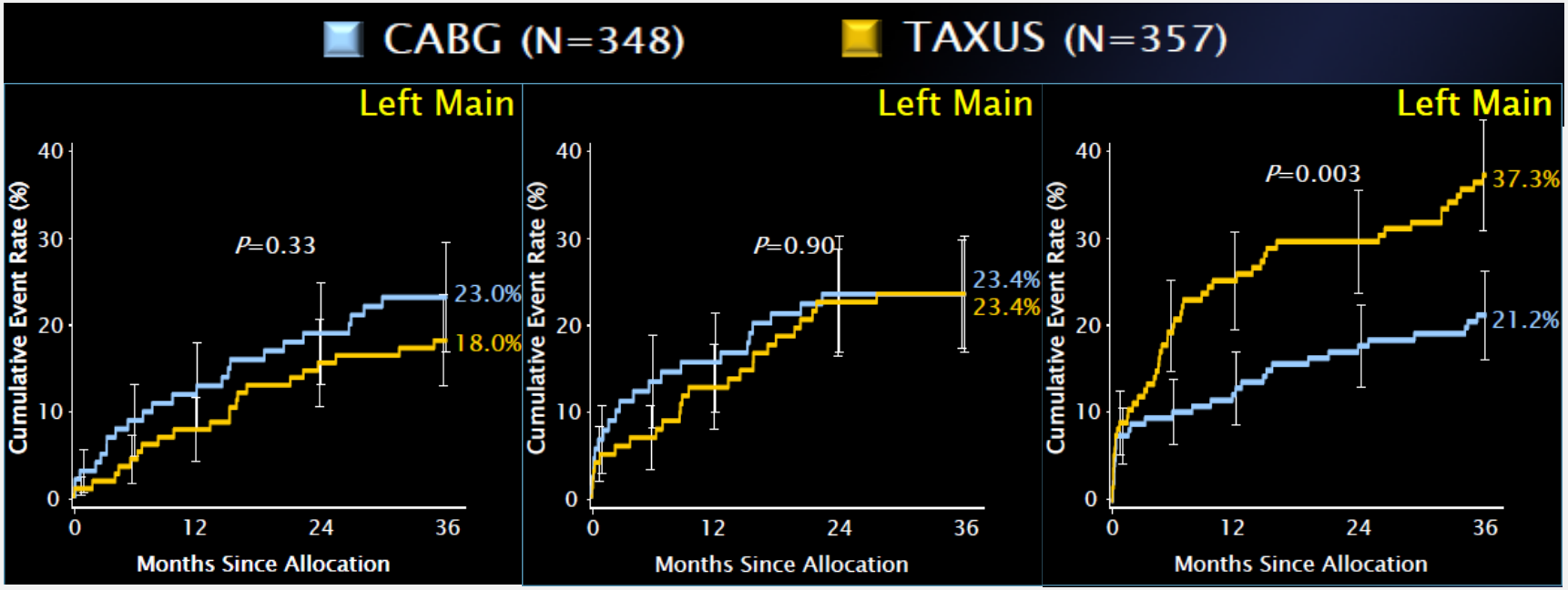
MACCE = death, stroke, MI, or repeat revascularization

- **Revascularization with PCI has comparable safety and efficacy outcomes to CABG**

Serruys. TCT 2010

CABG vs. TAXUS

SYNTAX LM: MACCE according to SYNTAX score



Low SYNTAX score (0 to 22)	Intermediate score (23 to 32)	High SYNTAX score (over 33)

- **PCI is a reasonable alternative to CABG in patient with low and intermediate SYNTAX score.**

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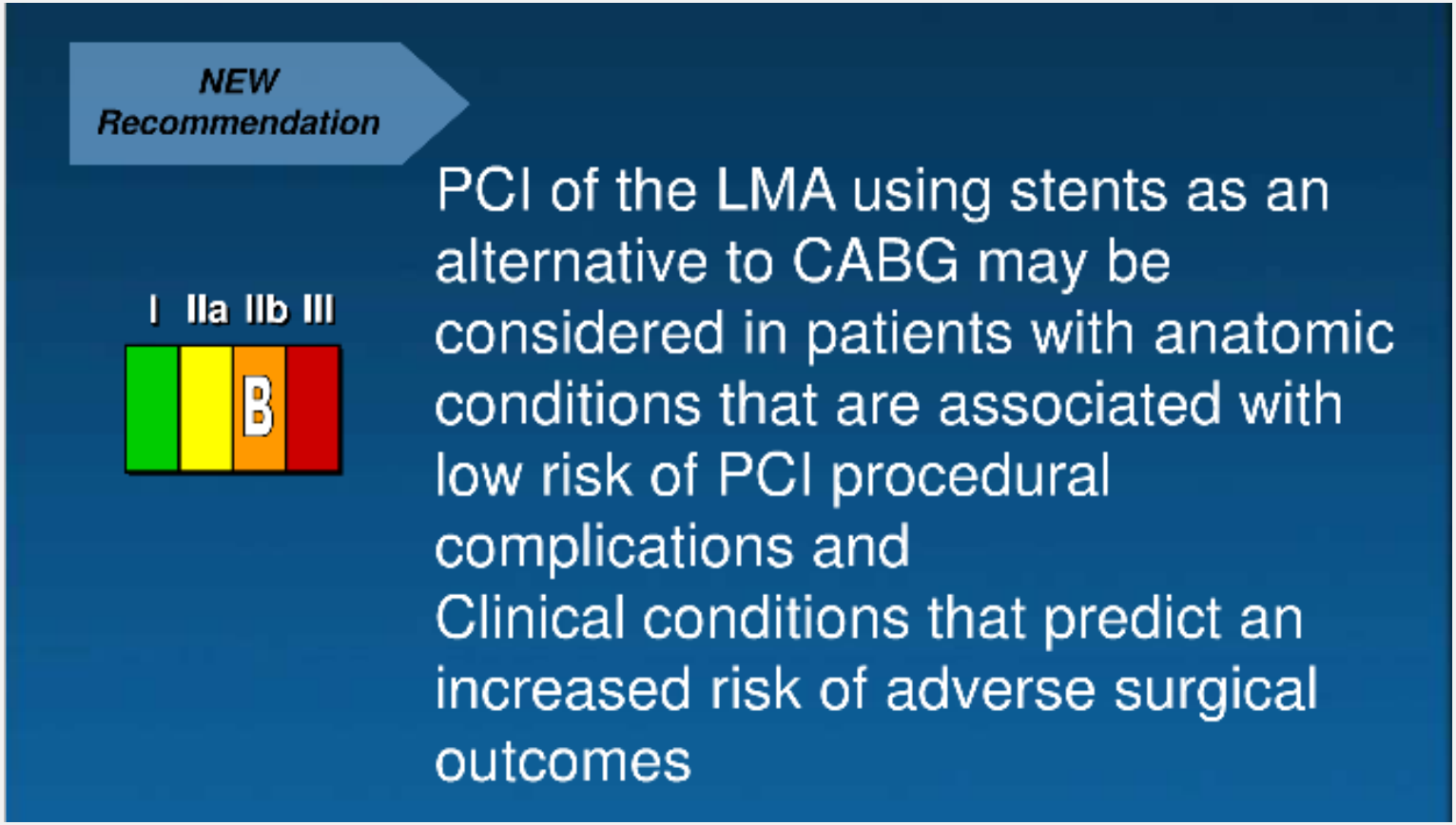
Serruys. TCT 2010 presentation

PCI for unprotected Left Main



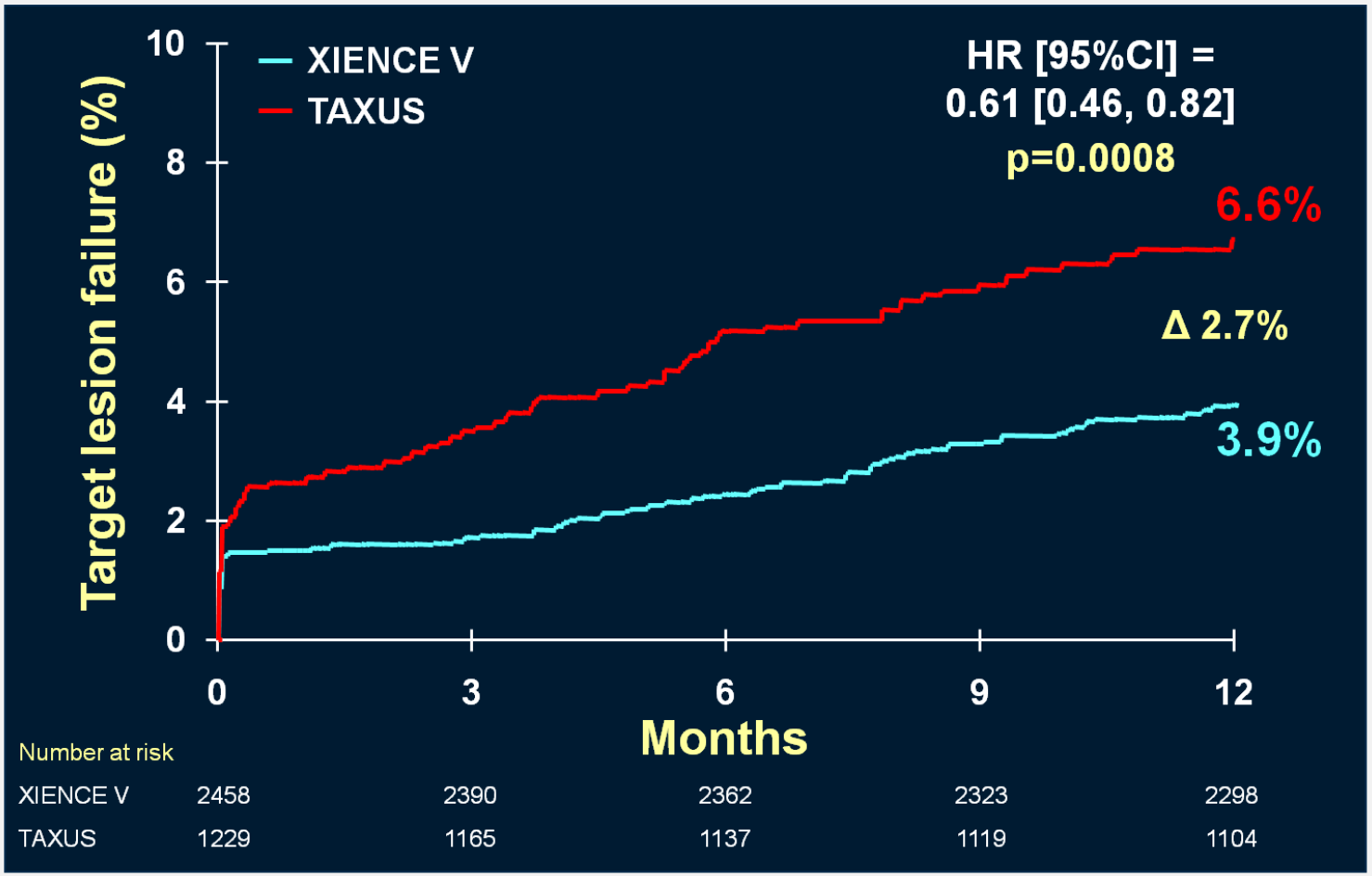
Everolimus-eluting stents in LM ?

- EES was superior to PES in inhibiting neointima formation and clinical outcomes in randomized trials and meta-analyses.

- However data comparing the clinical outcomes of EES with first generation DES in the treatment of ULMCA lesions is very limited.

EES vs. PES

SPIRIT IV: TLF at 1 year → 40% RRR



TLF = cardiac death, target vessel MI, or ischemia-driven TLR

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Stone et al. N Engl J Med 2010;362:1663-74.

Study Objective

- To evaluate the efficacy and safety of stenting with everolimus-eluting stent (EES) compared with sirolimus-eluting stent (SES) for the treatment of unprotected left main coronary artery (ULMCA) stenosis in the “real world” setting.

EXCELLENT-Registry

Efficacy of Xience/Promus versus Cypher to rEduce Late Loss after stENTing Registry

- An open label, multi-center, all-comer registry
- Prospective cohort of EES
- Retrospective historical cohort of SES

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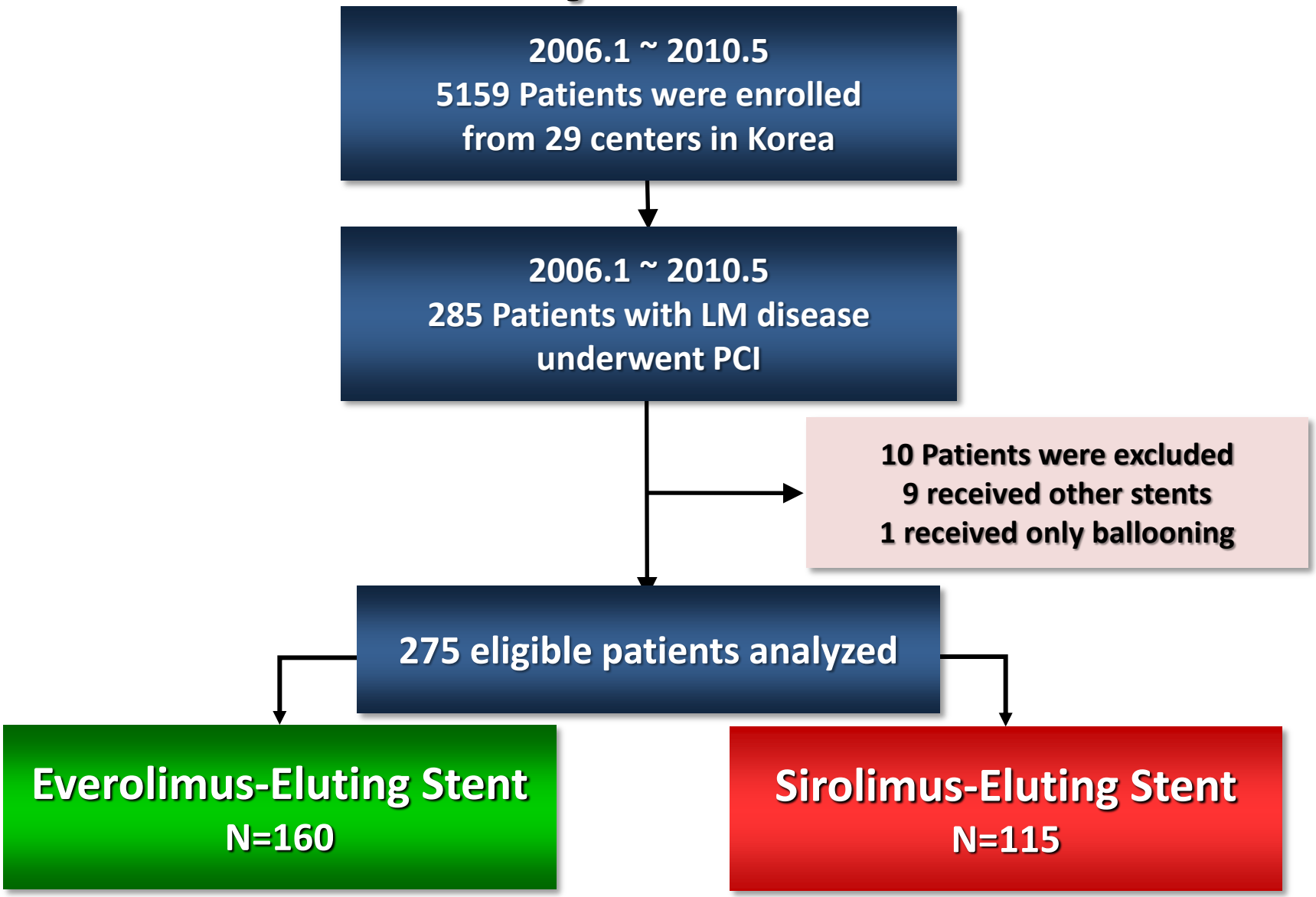
Study Scheme



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Study Endpoints

- **Primary Endpoint:** 1-year Major Adverse Cardiac Events (MACE; a composite of death, MI, ID-TVR)

- **Other Clinical Endpoints:**

✓Any death, cardiac death, MI, ID-TVR at 30 days, 6months, 1 year

✓Stent Thrombosis at 24 hours (acute), 30 days (subacute), 1 year (late)

✓Hard endpoint: composite of death and MI at 1 year

✓Clinical device and procedural success

Baseline Clinical Characteristics

Variables — no. (%)	EES (N=160)	SES (N=115)	p-value
Demographic characteristics			
Age, years — mean±SD	64.7±10.6	64.0±10.8	0.591
Males	114 (71.2)	84 (73.0)	0.744
Body-mass index, kg/m^2	24.8±3.4	24.5±2.6	0.379
Risk factors or Coexisting conditions			
Diabetes mellitus	62 (39.0)	46 (40.0)	0.866
Hypertension	95 (61.3)	57 (50.0)	0.065
Dyslipidemia	120 (75.5)	87 (75.7)	0.973
Current smoker	43 (27.0)	31 (27.4)	0.943
Chronic renal failure	4 (2.5)	4 (3.5)	0.724
Family history of CAD	15 (10.1)	7 (6.5)	0.303
Cerebrovascular disease	17 (10.8)	7 (6.2)	0.187

Baseline Clinical Characteristics

Variables — no. (%)	EES (N=160)	SES (N=115)	p-value
Risk factors or Coexisting conditions			
Previous MI	14 (8.8)	11 (9.6)	0.812
Previous PCI	22 (13.9)	22 (19.1)	0.248
Previous CABG	6 (3.8)	7 (6.1)	0.380
Previous CHF	4 (2.5)	2 (1.8)	1.000
Peripheral arterial disease	2 (1.3)	1 (0.9)	1.000
Left ventricular ejection fraction, %	59.3±12.0	60.4±11.0	0.505
Clinical indications			0.407
Silent ischemia	5 (3.1)	1 (0.9)	
Chronic stable angina	63 (39.6)	48 (41.7)	
Unstable angina	66 (41.5)	45 (39.1)	
NSTEMI	17 (10.7)	10 (8.7)	
STEMI	8 (5.0)	11 (9.6)	

Medication at discharge

Variables — no. (%)	EES (N=156)	SES (N=110)	p-value
Aspirin	154 (98.7)	109 (99.1)	1.000
Clopidogrel	154 (98.7)	110 (100.0)	0.513
Statin	143 (91.7)	89 (80.9)	0.010
ACE inhibitor	47 (30.3)	40 (36.7)	0.278
Angiotensin II-receptor antagonist	54 (34.8)	40 (36.4)	0.798
Beta-blocker	91 (58.3)	68 (61.8)	0.568
Calcium-channel blocker	40 (25.6)	36 (32.7)	0.208

Angiographic and procedural characteristics

Variables — no. (%)	EES (N=160)	SES (N=115)	p-value
Before index procedure			
Disease extent			0.273
Left main only	27 (16.9)	11 (9.6)	
Left main + 1 vessel disease	82 (51.2)	68 (59.1)	
Left main + 2 vessel disease	44 (27.5)	33 (28.7)	
Left main + 3 vessel disease	7 (4.4)	3 (2.6)	
Left main + multivessel disease	51 (31.9)	36 (31.3)	0.920
Significant RCA disease	22 (13.8)	15 (13.0)	0.866
Total occlusion	7 (4.4)	5 (4.5)	1.000
Thrombus-containing	4 (2.5)	1 (0.9)	0.652
Calcification	64 (39.6)	43 (38.7)	0.884

Angiographic and procedural characteristics

Variables — no. (%)	EES (N=160)	SES (N=115)	p-value
Before index procedure			
Lesion location			0.774
Ostium and shaft	53 (33.1)	40 (34.8)	
Bifurcation	107 (66.9)	75 (65.2)	
Distal LM involvement	67 (41.9)	49 (42.6)	0.903
SYNTAX score	20.53 ± 11.64	20.93 ± 11.26	0.618
SYNTAX score ≥ 33	24 (15.0)	16 (14.0)	0.824
Minimal luminal diameter (mm)	1.14 ± 0.57	0.98 ± 0.53	0.014
Reference vessel diameter (mm)	3.40 ± 0.58	3.37 ± 0.50	0.658
Diameter stenosis (%)	66.65 ± 14.73	71.03 ± 15.00	0.017
Lesion length (mm)	18.49 ± 14.78	17.98 ± 13.41	0.774

Angiographic and procedural characteristics

Variables — no. (%)	EES (N=160)	SES (N=115)	p-value
After index procedure			
No. of stents used in LM	1.31 ± 0.60	1.25 ± 0.51	0.436
No. of stents per patient	1.60 ± 0.99	1.57 ± 0.82	0.817
Total stent length in LM (mm)	28.34 ± 17.27	29.20 ± 15.34	0.671
Use of glycoprotein IIb/IIIa inhibitors	6 (4.0)	2 (1.8)	0.473
Use of intraaortic balloon pump	8 (5.0)	5 (4.3)	0.802
Use of intravascular ultrasound	117 (75.0)	86 (75.4)	0.934
Final balloon pressure (atm)	15.01 ± 4.50	16.02 ± 4.27	0.075
Treatment of RCA disease	20 (12.5)	12 (10.4)	0.598

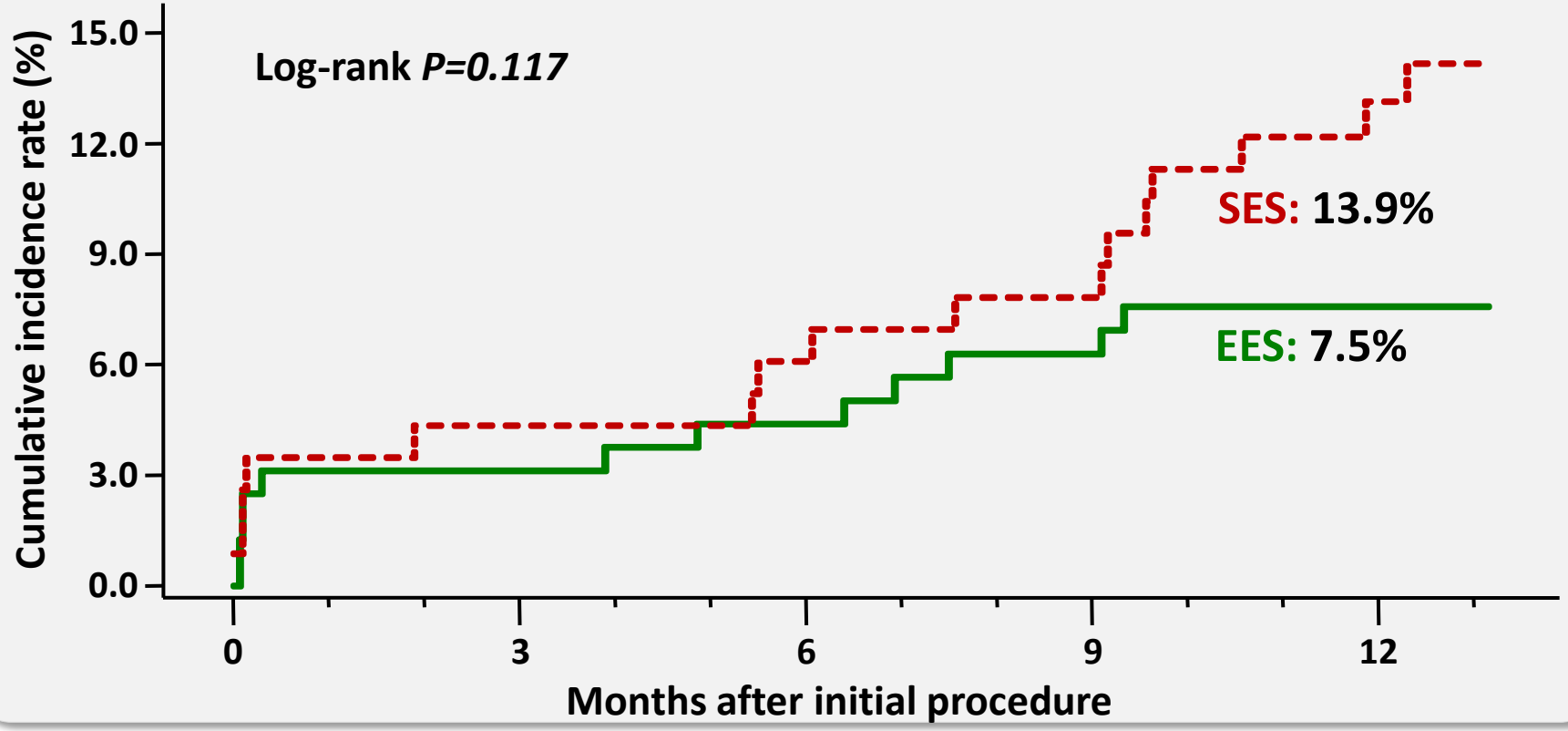
Angiographic and procedural characteristics

Variables — no. (%)	EES (N=160)	SES (N=115)	p-value
After index procedure			
Minimal luminal diameter — mm			
In stent	2.94±0.58	2.91±0.45	0.596
In segment	2.47±0.60	2.42±0.59	0.516
Diameter stenosis — %			
In stent	12.38±9.16	9.63±8.65	0.015
In segment	22.51±11.32	20.22±11.84	0.112
Acute gain — mm			
In stent	1.81±0.57	1.91±0.54	0.155
In segment	1.34±0.60	1.41±0.64	0.349
Lesion success	153 (96.8)	111 (96.5)	1.000
Device success	154 (97.5)	112 (97.4)	1.000
Procedure success	154 (97.5)	112 (97.4)	1.000

Clinical Outcomes

Major Adverse Cardiac Event

: Composite of death, MI, or ID-TVR



Patient Number at Risks

EES	160	153	151	146	101
SES	115	110	108	106	90

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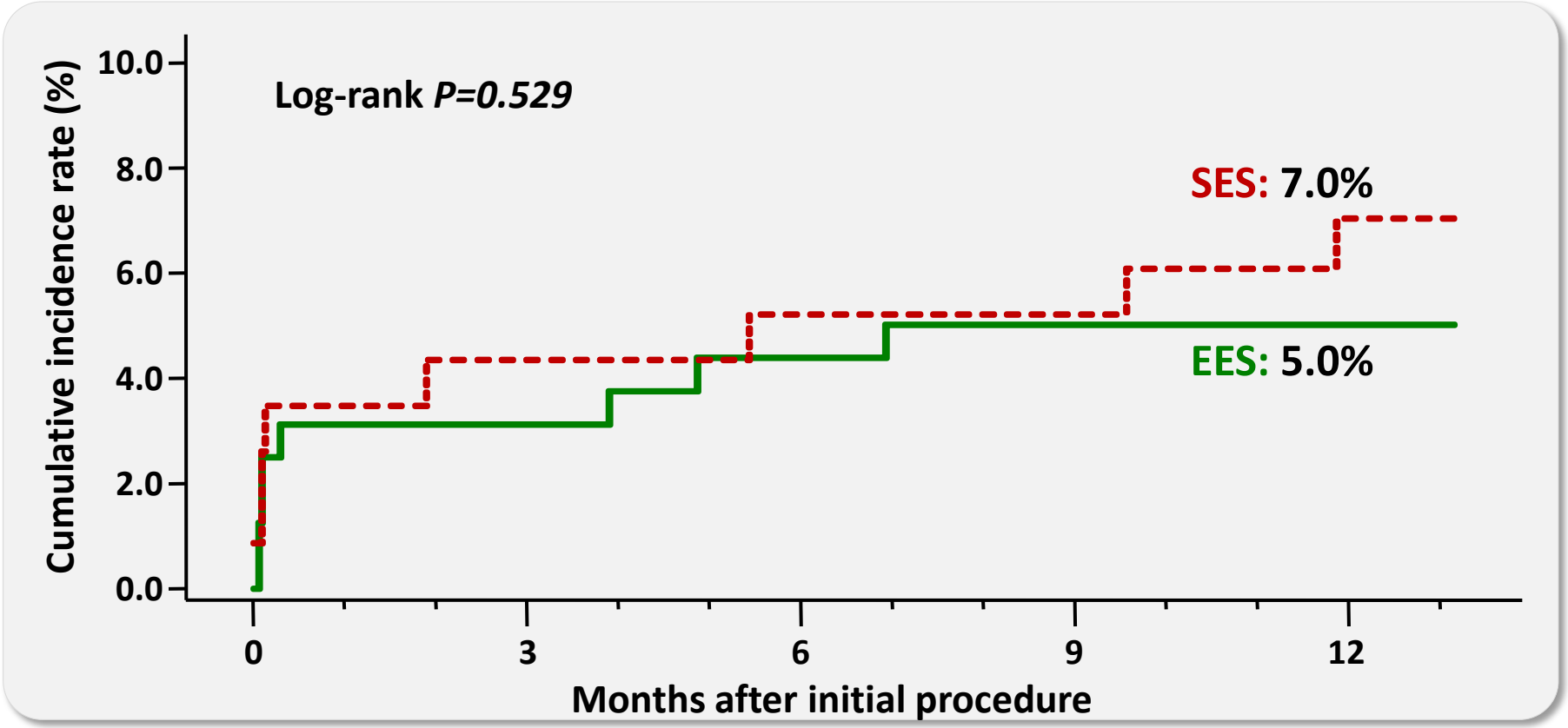
Hard Endpoint

: Composite of all-cause death, or MI

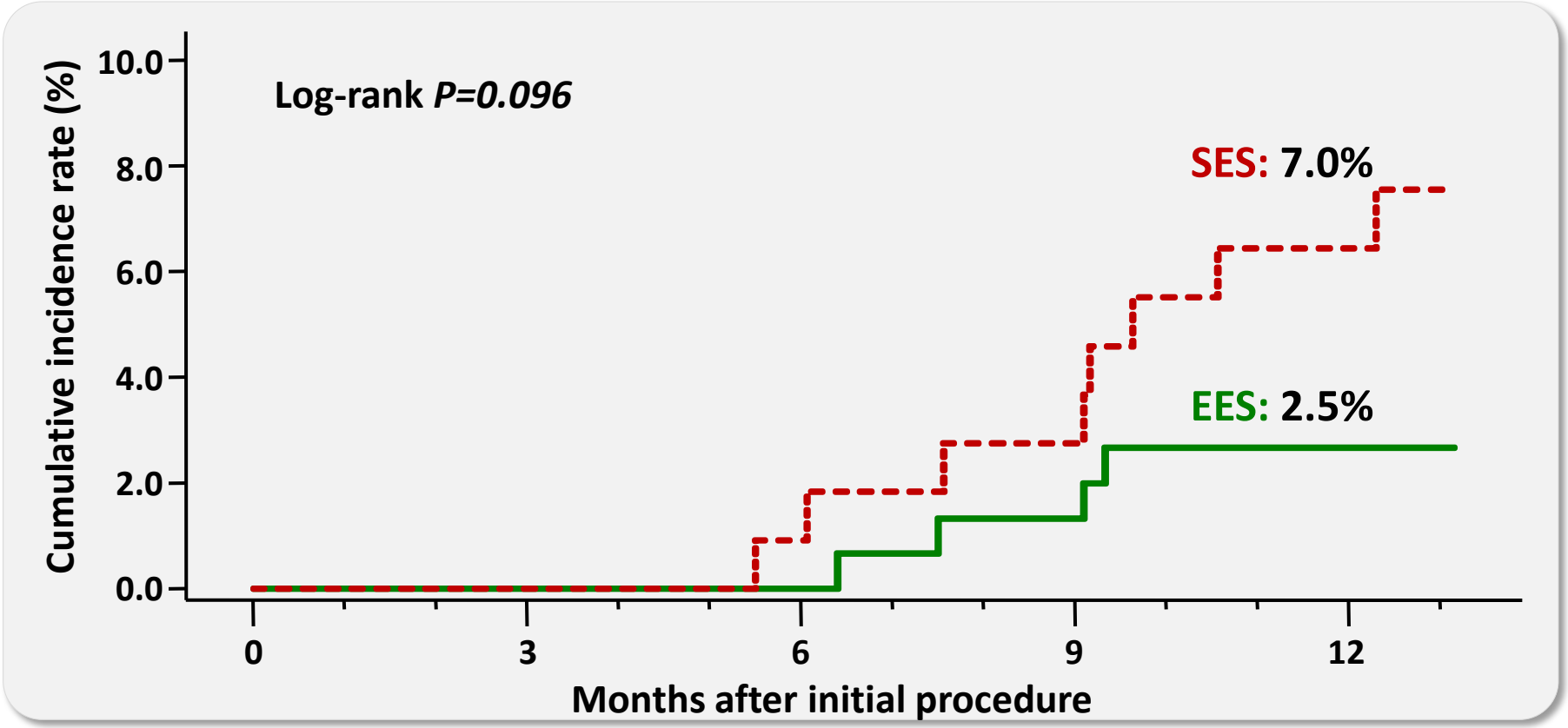


Patient Number at Risks

EES	160	153	151	148	103
SES	115	110	109	109	97

Soft Endpoint

Ischemia-driven TVR

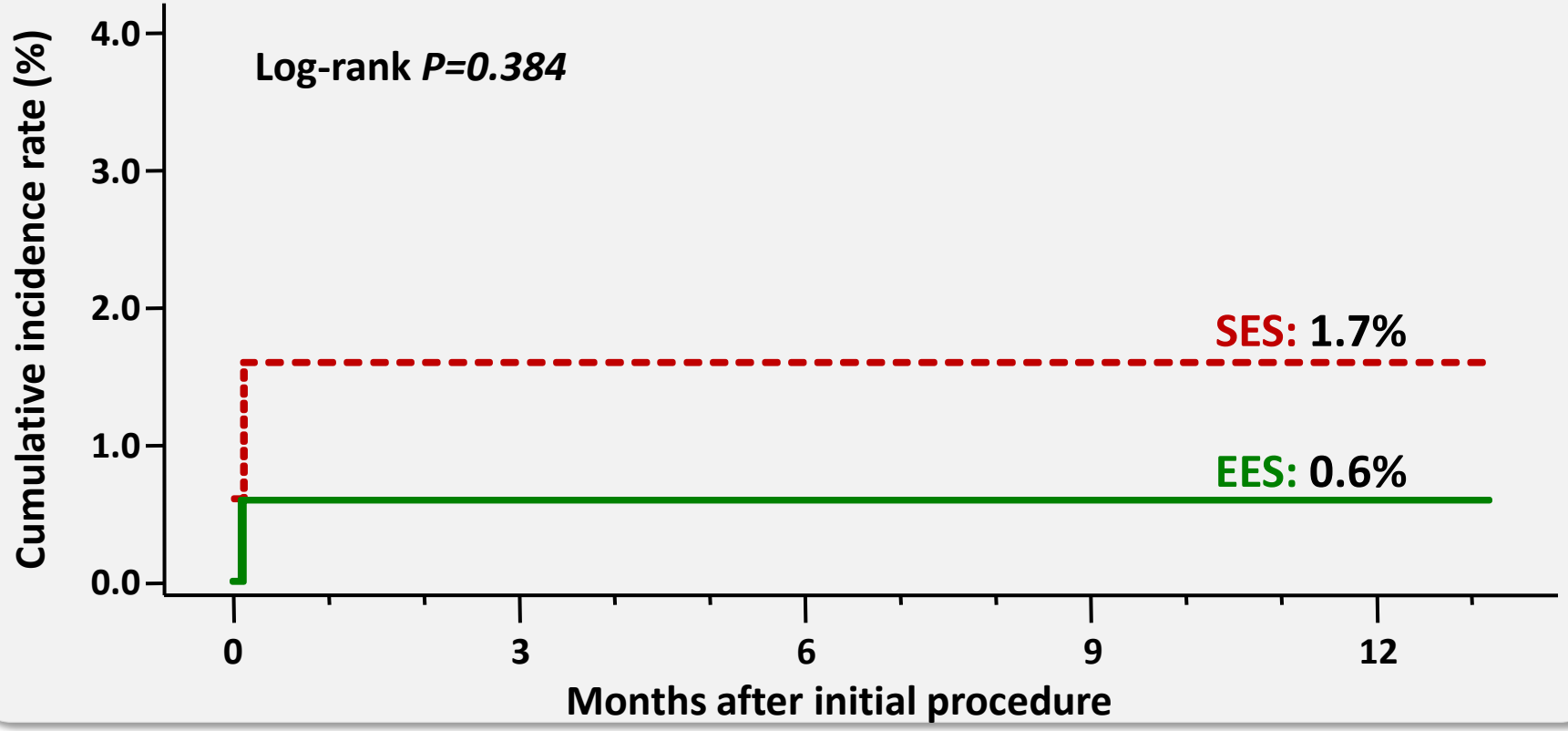


Patient Number at Risks

EES	160	153	151	147	102
SES	115	110	108	106	90

Stent Thrombosis

: Definite/Probable ST by ARC definition



Patient Number at Risks

EES	160	153	151	149	104
SES	115	110	109	109	97

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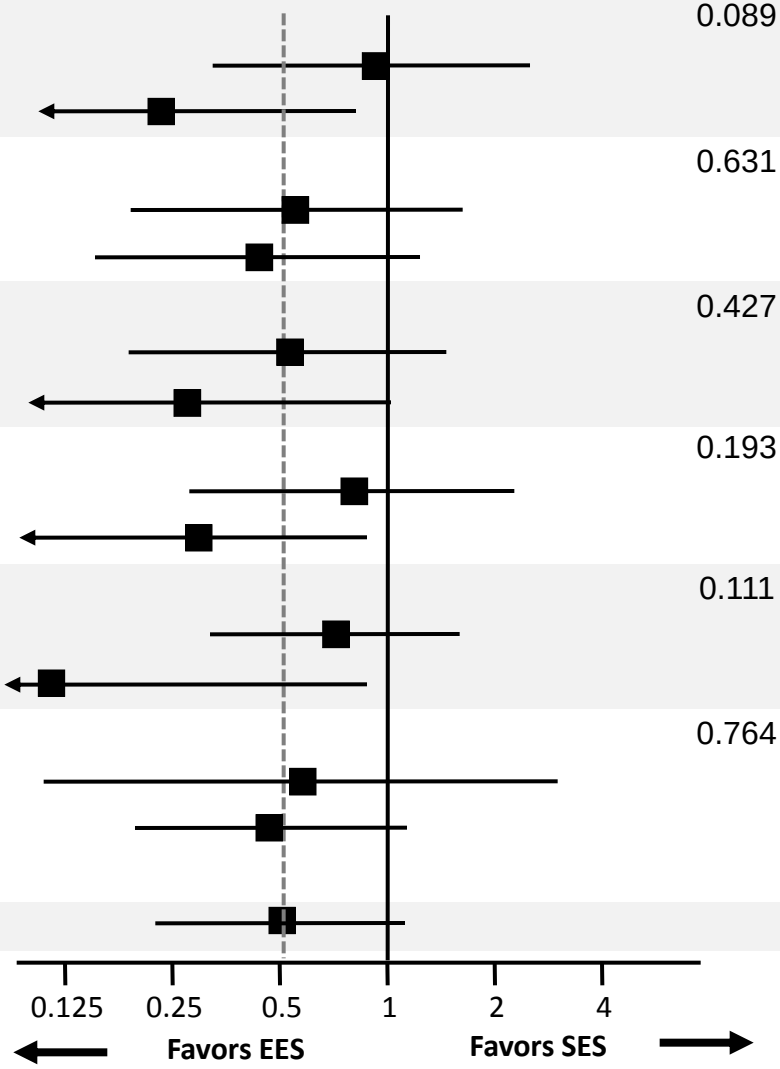
Subgroup analysis regarding MACE

Subgroups	No. of patients	MACE (%) EES	MACE (%) SES	Relative Risk (95% CI)	Interaction P
Diabetes mellitus					0.089
Yes	108	14.5	15.2		
No	166	3.1	13.0		
Age					0.631
≥ 70	136	8.4	13.2		
< 70	139	6.5	14.5		
Renal dysfunction					0.427
CCr ≤ 60	103	12.9	21.2		
CCr > 60	170	3.3	11.2		
Disease extent					0.193
LM + 1VD	188	6.4	7.6		
LM + MVD	87	9.8	27.8		
Bifurcation					0.111
Yes	180	10.4	13.5		
No	95	1.9	14.6		
RCA involvement					0.764
Yes	37	13.6	20.0		
No	238	6.5	13.0		
Overall	275	7.5	13.9		



Not a Randomized Controlled Trial !

- To adjust multiple variables

  → Multivariable Cox-regression analysis

- To overcome the allocation bias

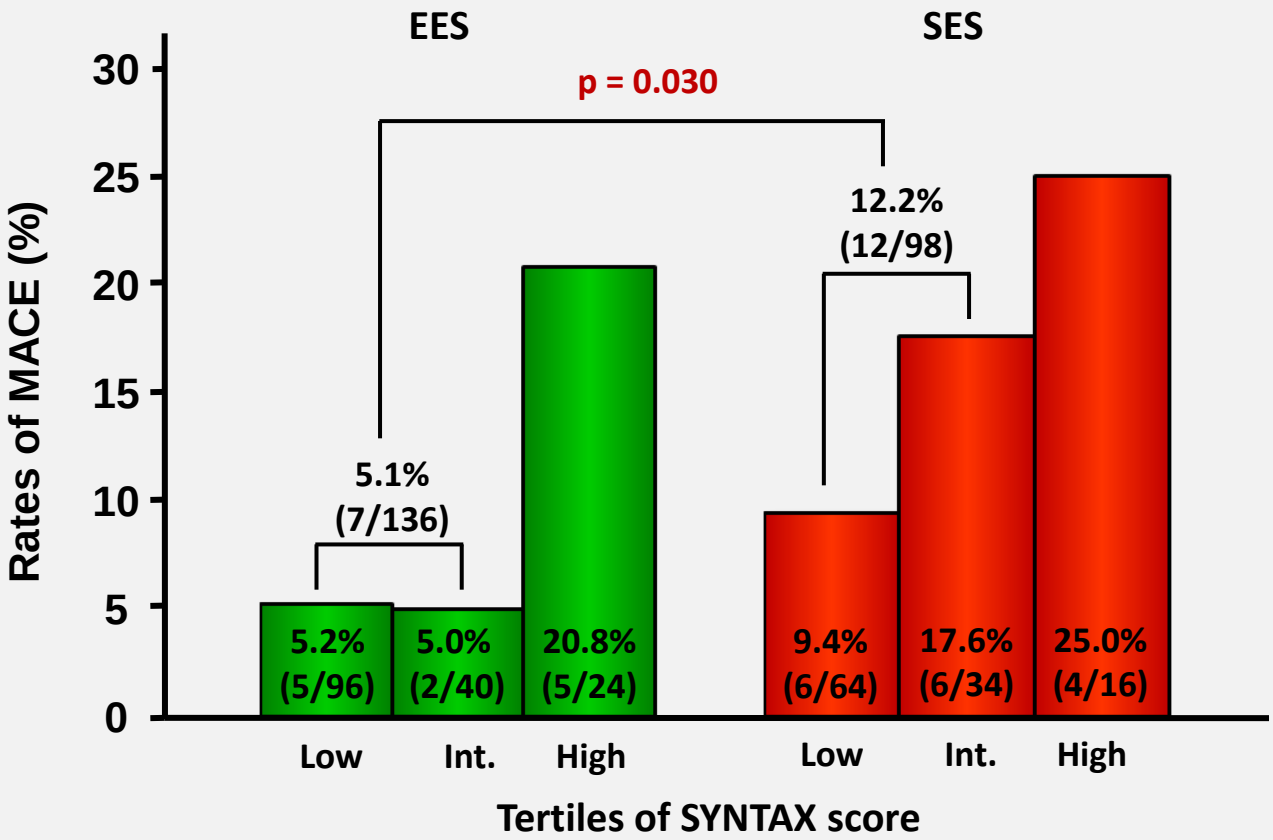
  → Propensity score adjusted Cox-regression analysis

Hazard Ratios of Clinical Outcomes

1-year outcome	Events		Unadjusted		Multivariable adjusted		Propensity score adjusted	
	EES (n=160)	SES (n=115)	Hazard Ratio (95% CI)	P	Hazard Ratio (95% CI)	P	Hazard Ratio (95% CI)	P
Primary endpoint								
MACE	12 (7.5)	16 (13.9)	0.55 (0.26-1.17)	0.123	0.45 (0.21-0.97)	**0.042**	0.41 (0.18-0.90)	**0.027**
Clinical outcomes								
All-cause death	7 (4.4)	8 (7.0)	0.64 (0.23-1.77)	0.388	0.36 (0.10-1.28)	0.114	0.49 (0.17-1.44)	0.196
Death or MI	8 (5.0)	8 (7.0)	0.73 (0.27-1.95)	0.531	0.48 (0.15-1.53)	0.216	0.57 (0.20-1.60)	0.283
ID-TVR	4 (2.5)	8 (7.0)	0.38 (0.11-1.25)	0.110	0.38 (0.11-1.34)	0.133	0.26 (0.07-0.92)	**0.036**

Hazard ratio for EES with reference of SES

MACE according to SYNTAX tertiles



- EES may be more efficacious in the patients with low and intermediate SYNTAX score.

Limitations

- This study was not a prospective randomized controlled trial, but rather an observational registry study.
- The sample size was modest with a little less than 300 patients analyzed.
- Due to relatively short duration of follow-up period, safety issues cannot be determined.

Summary

- **EES showed at least similar or superior efficacy compared with SES in the treatment of ULMCA stenosis regarding the incidence of MACE.**
- **In the crude population analysis, clinical outcomes concerning hard endpoints (death or MI) as well as soft endpoint (ID-TVR) were not significantly different between the 2 stent groups.**
- **However, after propensity-adjusted Cox-regression analysis, the risk of MACE was significantly lower in the EES group compared with SES group, which was mainly driven from lower repeat revascularization in the EES group.**

Conclusion

- **EES seems to be at similar if not superior in several aspects compared with SES in the treatment of ULMCA stenosis.**
- **Considering the head to head data in a broad population suggesting significant improvement in outcome compared with Taxus stents, the results of the SYNTAX trial may not told true in the era of 2nd generation DES**
- **A dedicated LM trial such as the EXCEL trial will be able to answer if PCI is truly non-inferior to CABG in the treatment of ULMCA stenosis in the 2nd generation DES era.**

Thank you for your attention!