Everolimus-Eluting Stent Implantation for Unprotected Left Main Stenosis: PRECOMBAT-2 Study

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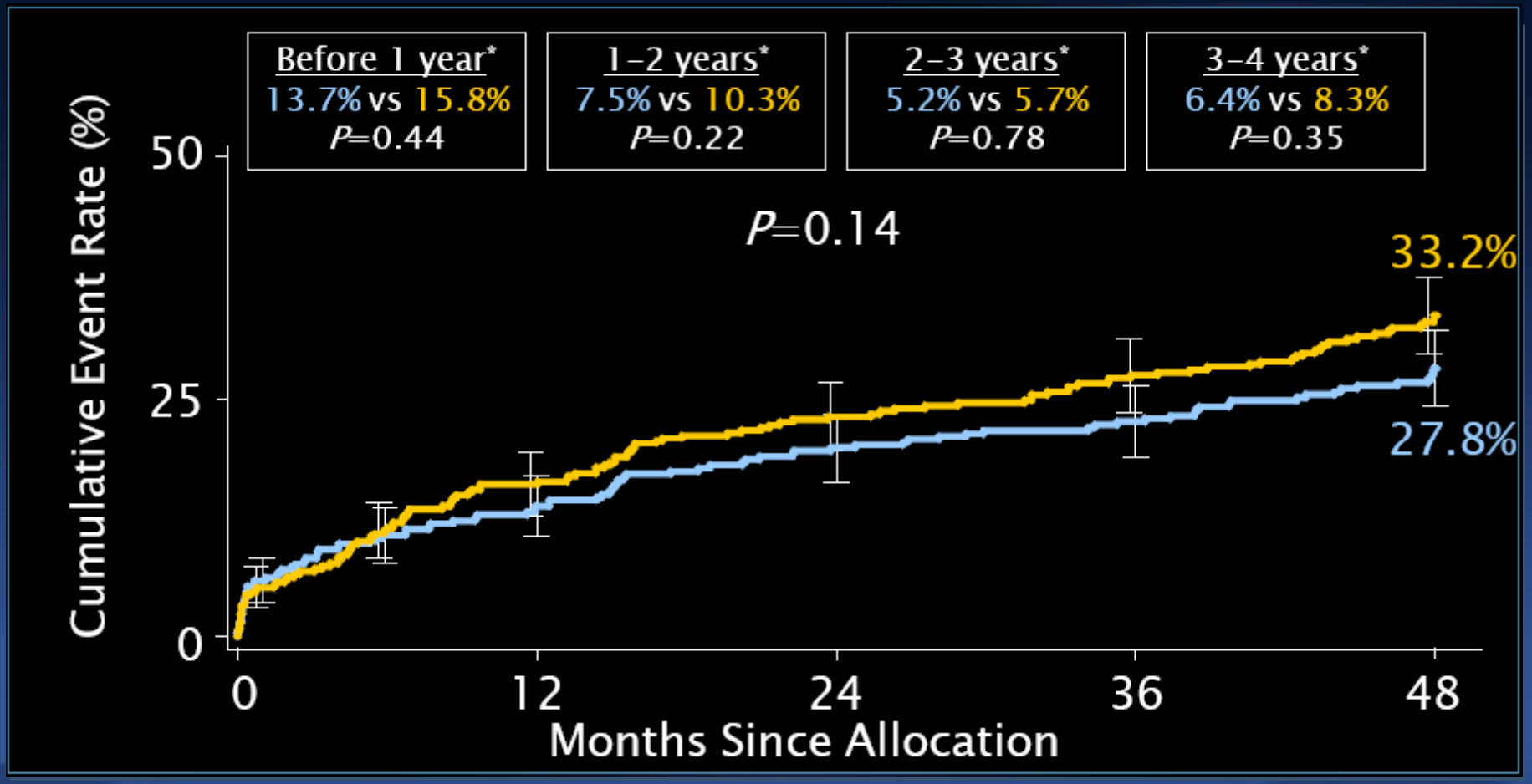
MACCE to 4 Years in SYNTAX LM
TAXUS Stent vs. CABG

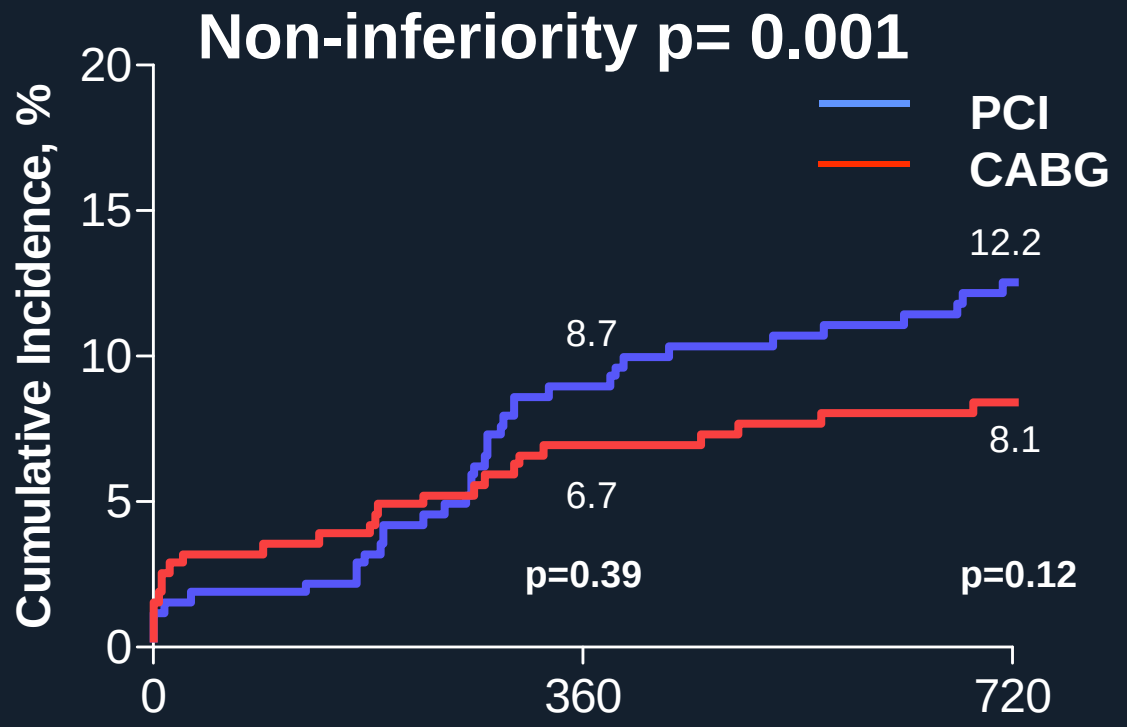


Serruys PW TCT 2011

ITT population

MACCE of PRECOMBAT Study

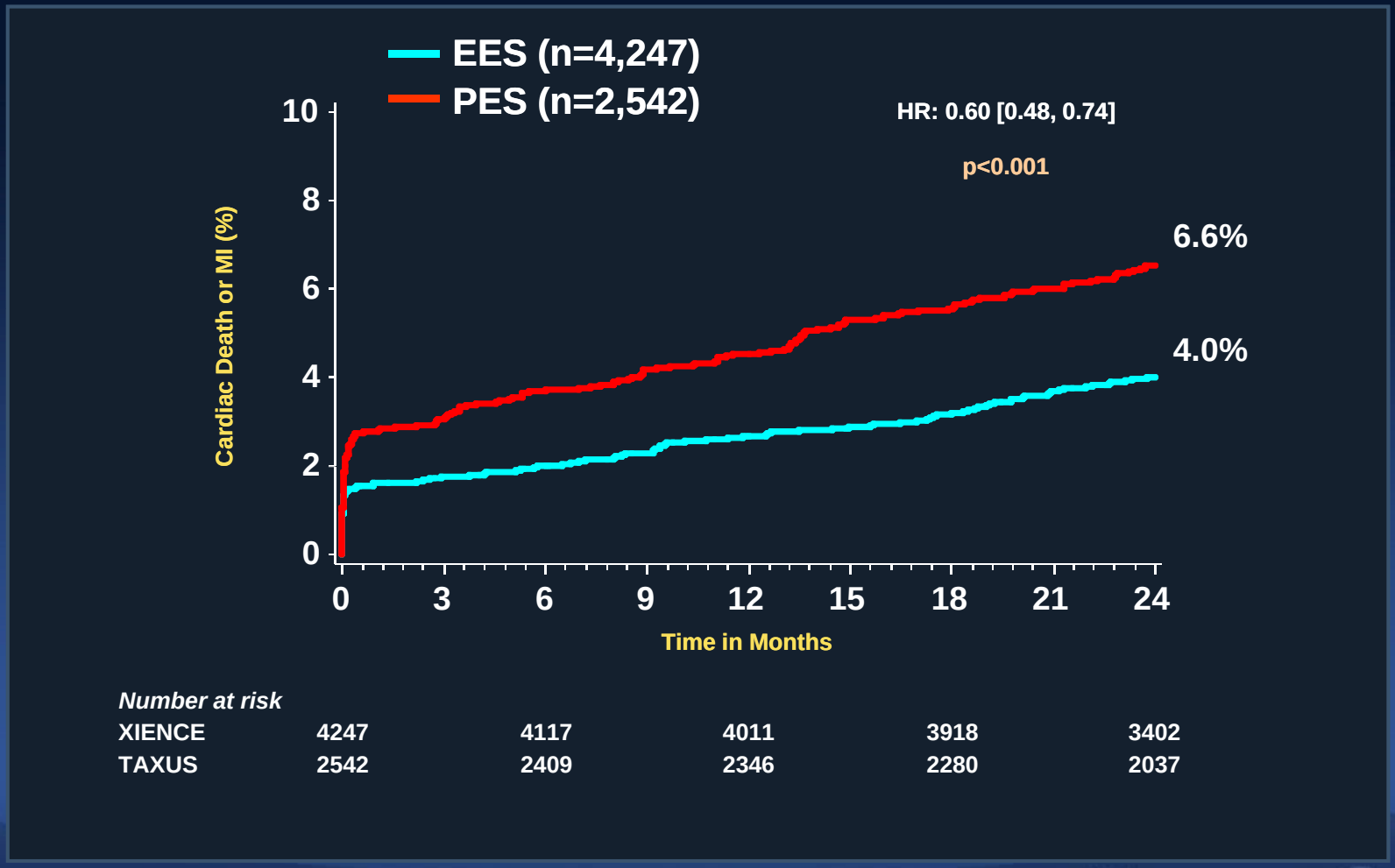
CYPHER Stent vs. CABG



No. at Risk			
PCI	300	272	236
CABG	300	276	239

Park SJ et al. N Engl J Med. 2011;364:1718

Cardiac death or MI
Pooled SPIRIT II, III, IV and COMPARE trials
Xience Everolimus-Eluting Stent vs. TAXUS



Number at risk

XIENCE	4247	4117	4011	3918	3402
TAXUS	2542	2409	2346	2280	2037

Purpose of PRECOMBAT-2

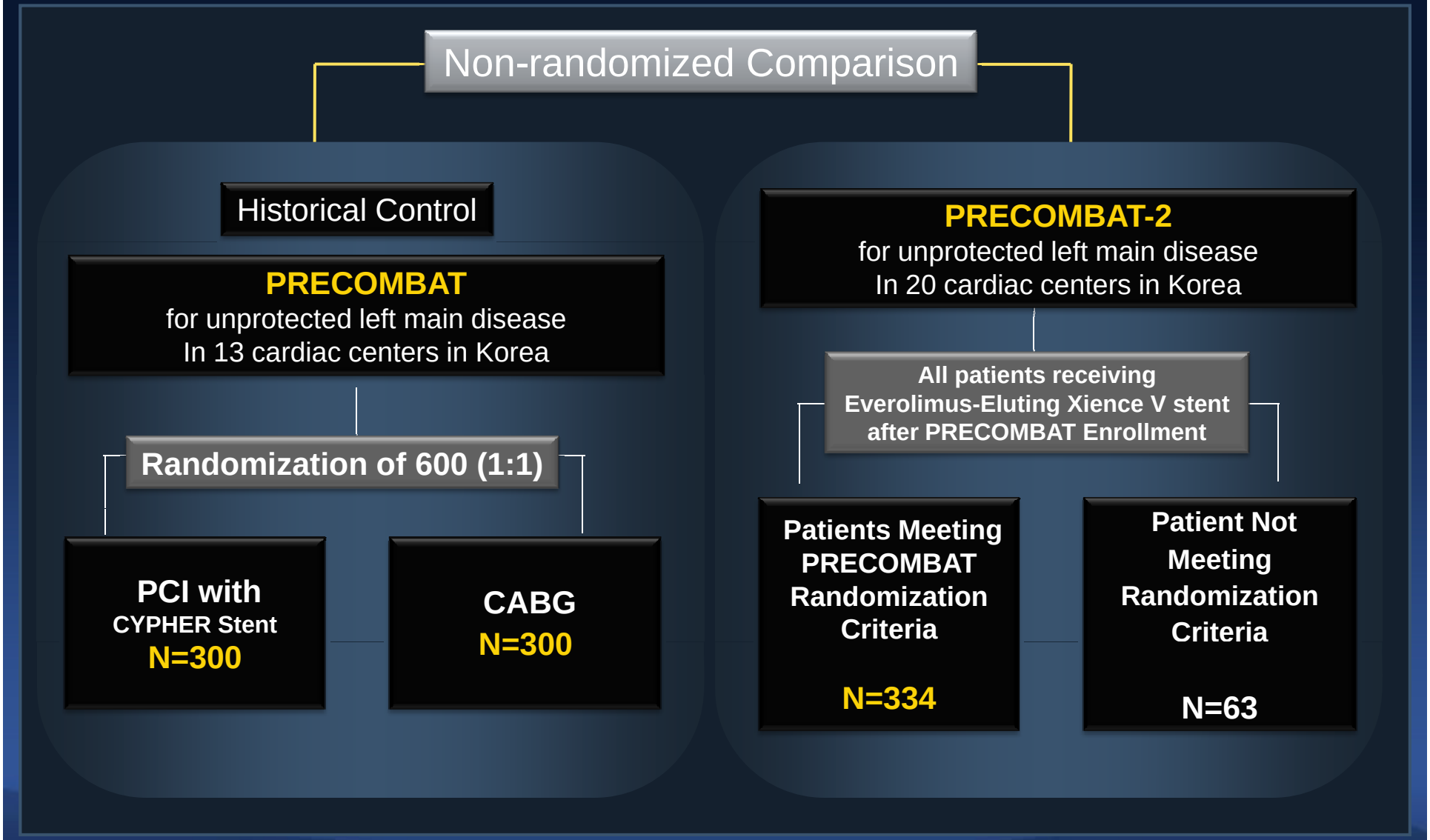
- To evaluate the safety and efficacy of PCI using everolimus-eluting Xience V stent (Abbott Vascular, Santa Clara, CA) for patients with ULMCA stenosis.
- The results were compared with those of historical controls of patients receiving PCI with SES or CABG in the PRECOMBAT randomized study

PRECOMBAT-2 Trial

Design

- DESIGN: a prospective, single arm, registry
- OBJECTIVE: To evaluate the outcomes of PCI with everolimus-eluting Xience V stents for patients with ULMCA stenosis, the results were compared with those of patients receiving SES and CABG in the PRECOMBAT trial
- PRINCIPAL INVESTIGATOR
  Seung-Jung Park, MD, PhD, Asan Medical Center, Seoul, Korea

Design


Non-randomized Comparison
Historical Control
PRECOMBAT
for unprotected left main disease
In 13 cardiac centers in Korea
Randomization of 600 (1:1)
PCI with
CYPHER Stent
N=300
CABG
N=300
PRECOMBAT-2
for unprotected left main disease
In 20 cardiac centers in Korea
All patients receiving
Everolimus-Eluting Xience V stent
after PRECOMBAT Enrollment
Patients Meeting
PRECOMBAT
Randomization
Criteria
N=334
Patient Not
Meeting
Randomization
Criteria
N=63

Subjects

- Between May 2009 and September 2010, 334 patients who met the inclusion and exclusion criteria of PRECOMBAT randomized study were entered from 392 patients undergoing ULMCA stenting with EES in 21 Korean cardiac centers.

Inclusion and Exclusion

- Identical to the PRECOMBAT randomized study
- In brief, patients with angiographic ULMCA stenosis (> 50% stenosis), who did not have ST-segment elevation myocardial infarction (MI), cardiogenic shock, other serious comorbidity or contraindication of DES, were included.

Procedures and Follow-up

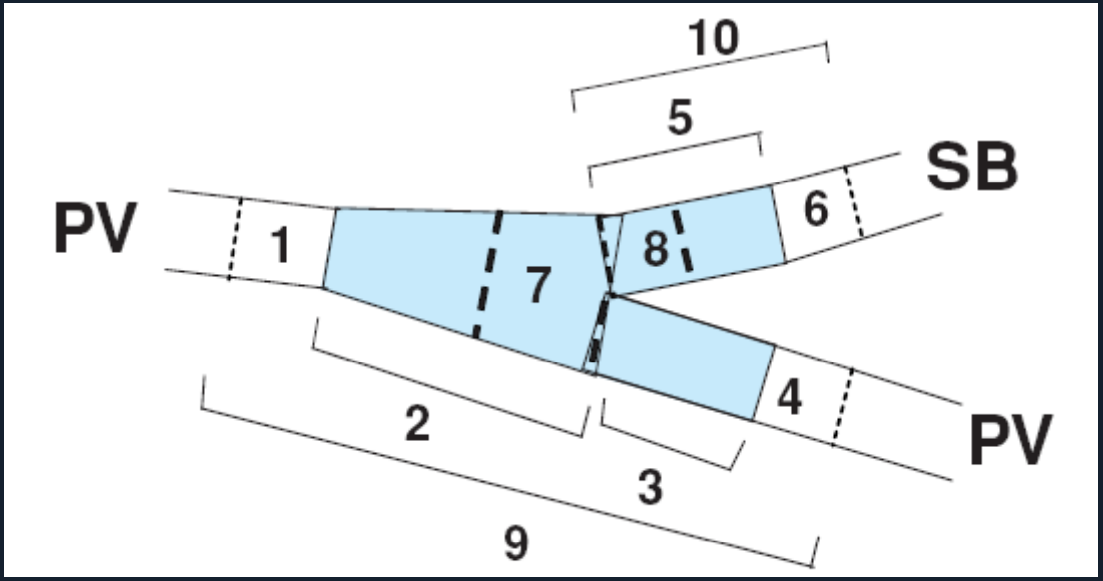
- EES was the default stent in the study period for ULMCA stenosis
- All lesions were treated with EES.
- IVUS and other devices were used at the operator's discretion.
- Patients were asked to return for follow-up angiography 8–10 months after the PCI, or earlier if angina symptoms occurred. However, due to the tendency of in-stent restenosis having a benign presentation in patients with ULMCA, angiographic surveillance was less strongly recommended in the PRECOMBAT-2 than in the PRECOMBAT study.

End Points

- Identical to those used in the PRECOMBAT.
- **MACCE** : Primary end point
  - a composite of death, MI, stroke and ischemia-driven TVR.
- **Death** : cardiac and non-cardiac deaths.
- **MI** : Q-MI within 48 hours after procedure and spontaneous MI thereafter.
- **TVR** : ischemia- (symptomatic and stenosis > 70%) and clinically (symptomatic) driven revascularization.

Quantitative Angiographic Analysis

- For 73% of SES and 59% of EES patients
- Dedicated bifurcation QCA software (CAAS 5.4)



1. Proximal edge (5 mm)
2. Proximal main stent
3. Distal main stent
4. Distal edge main (5 mm)
5. SB stent
6. Distal edge side (5 mm)
7. Polygon of confluence
8. Ostium of SB (5 mm)
9. MB stent + edges
10. SB stent + distal edge

- The proximal main branch included segments 1 and 2.
- Distal MB and side branch included 3 and 4, and 5 and 6, respectively.

Statistics

- Analysis among as-treated groups
- ANOVA and t-test for continuous variables
- Chi-square and Fisher-exact for categorical variables
- Censoring at 1.5 years (18 months) or events
- Log-rank for survival analysis
- Multivariate Cox analysis to adjust different baseline characteristics

Baseline Characteristics

	SES (N=327)	EES (N=334)	CABG (N=272)	P value
Age, years	62.0±10.0	62.9±10.4	62.5±9.4	0.49
Male sex	249 (76.1)	236 (70.7)	209 (76.8)	0.15
Diabetes mellitus	109 (33.3)	116 (34.7)	82 (30.1)	0.48
Hypertension	176 (53.8)	189 (56.6)	140 (51.5)	0.45
Hyperlipidemia	139 (42.5)	149 (44.6)	107 (39.3)	0.43
Current smoker	97 (29.7)	75 (22.5)	74 (27.2)	0.10
Previous PCI	42 (12.8)	27 (8.1)	34 (12.5)	0.098
Previous MI	16 (4.9)	13 (3.9)	17 (6.3)	0.41
Previous heart failure	0	4 (1.2)	2 (0.7)	0.15

Baseline Characteristics

	SES (N=327)	EES (N=334)	CABG (N=272)	P value
Chronic renal failure	3 (0.9)	4 (1.2)	2 (0.7)	0.84
Peripheral vascular disease	15 (4.6)	6 (1.8)	7 (2.6)	0.097
Chronic lung disease	8 (2.4)	4 (1.2)	7 (2.6)	0.40
Acute coronary syndrome	155 (47.4)	151 (45.2)	147 (54.0)	0.084
Ejection fraction, %	61.5±8.4	61.1±8.2	60.8±8.4	0.67
EuroSCORE value	2.8±1.9	2.9±2.0	2.9±2.0	0.71
Multivessel disease *	231 (70.6)	191 (57.2)	205 (75.4)	<0.001
Bifurcation left main stenosis *	219 (67.0)	240 (71.9)	163 (59.9)	0.008
SYNTAX score *	23.8±9.5	21.1±8.8	26.8±10.4	<0.001

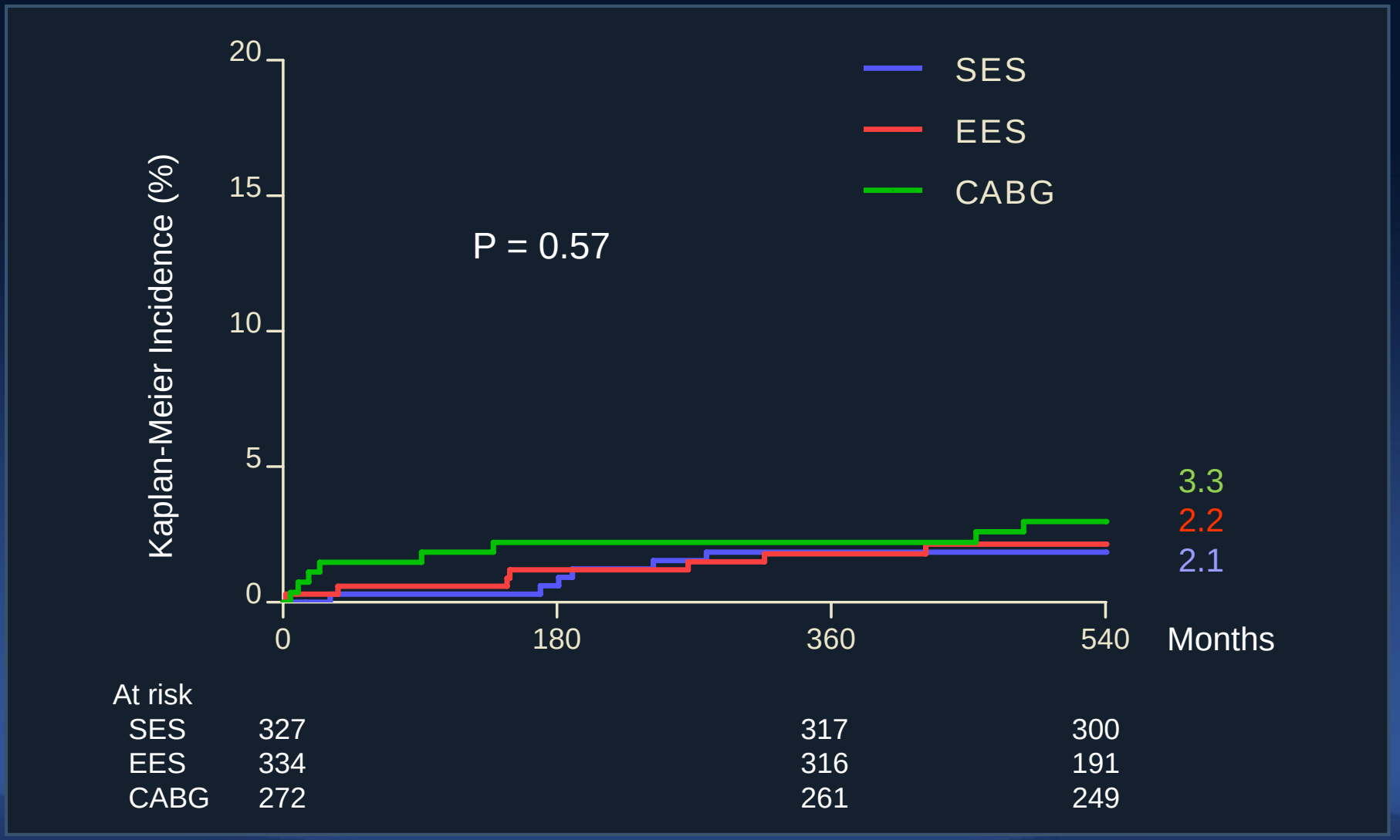
*for multivessel disease, <0.001 between SES vs. EES, 0.20 between SES vs. CABG, and <0.001 between EES vs. CABG
for bifurcation left main stenosis, 0.17 between SES vs. EES, 0.074 between SES vs. CABG, and 0.008 between EES vs. CABG
for SYNTAX score, <0.001 between SES vs. EES, <0.001 between SES vs. CABG, and <0.001 between EES vs. CABG

Procedures

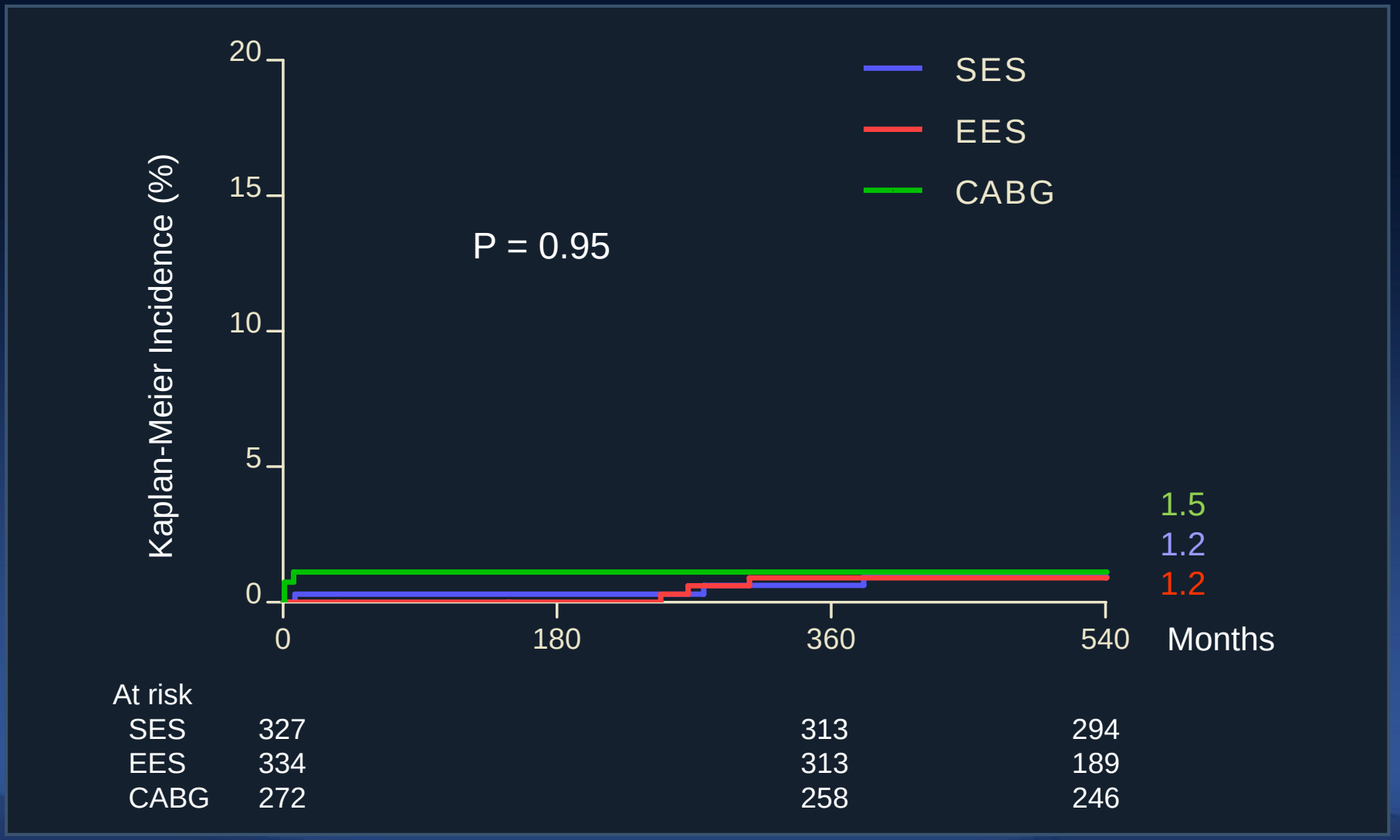
	SES (N=327)	EES (N=334)	CABG (N=272)	P value
Total stent number in left main	1.6±0.8	1.8±0.9	–	0.003
Total stent number per patient	2.6±1.4	2.3±1.3	–	0.006
Intravascular ultrasound guidance	294 (89.9)	302 (90.4)	–	0.83
Two-stent technique for left main	112 (34.3)	88 (26.3)	–	0.027
Angiographic follow-up	249 (76.1)	203 (60.8)	–	<0.001
Number of conduits	–	–	2.7±0.9	
Number of arterial conduits	–	–	2.1±0.9	
Off-pump surgery	–	–	166 (61.0)	
Use of LIMA	–	–	254 (93.4)	

Clinical Outcomes

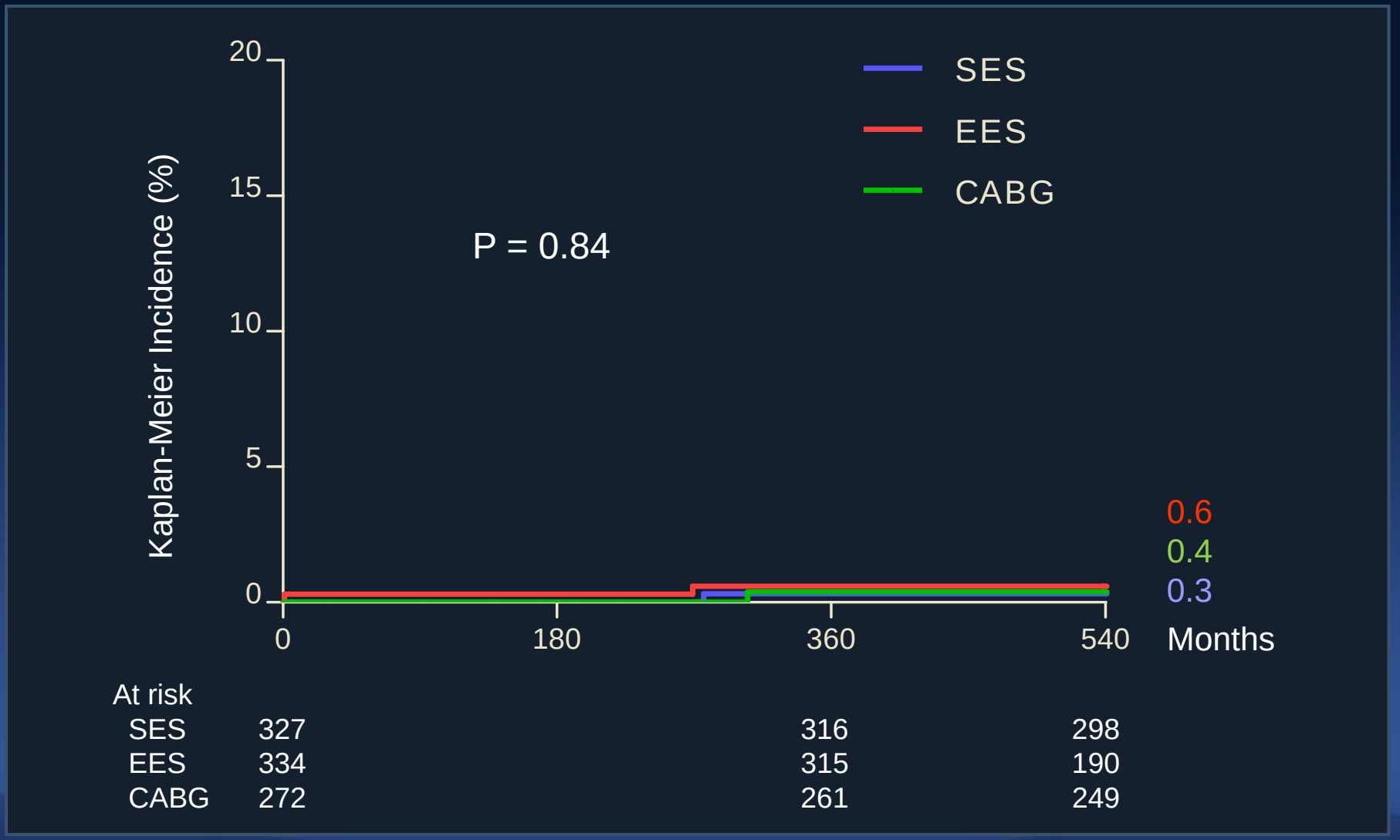
Death


20
15
10
5
0
Kaplan-Meier Incidence (%)
SES
EES
CABG
P = 0.57
3.3
2.2
2.1
0
180
360
540
Months
At risk
SES 327 317 300
EES 334 316 191
CABG 272 261 249

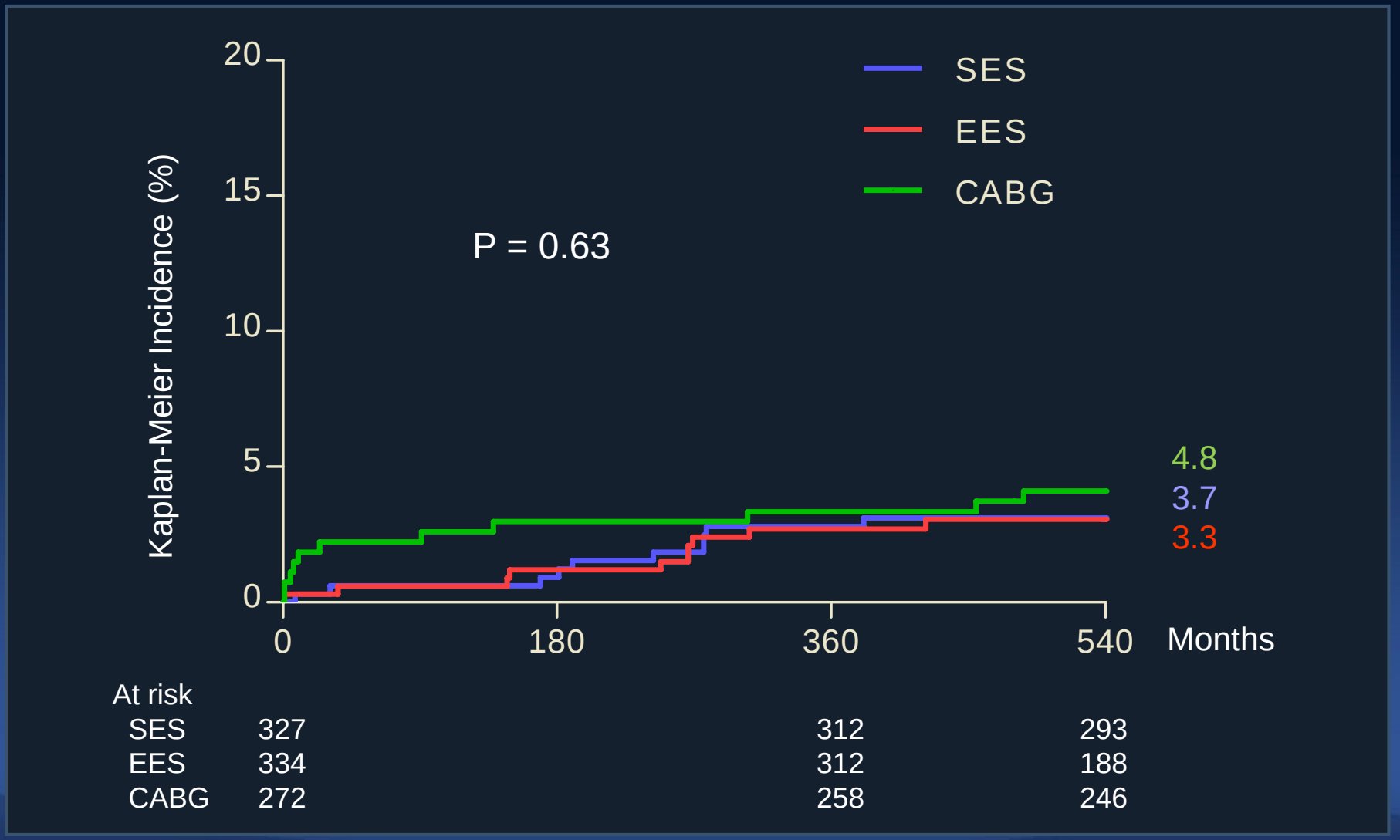
MI


20
15
10
5
0
Kaplan-Meier Incidence (%)
SES
EES
CABG
P = 0.95
1.5
1.2
1.2
0
180
360
540
Months
At risk
SES 327 313 294
EES 334 313 189
CABG 272 258 246

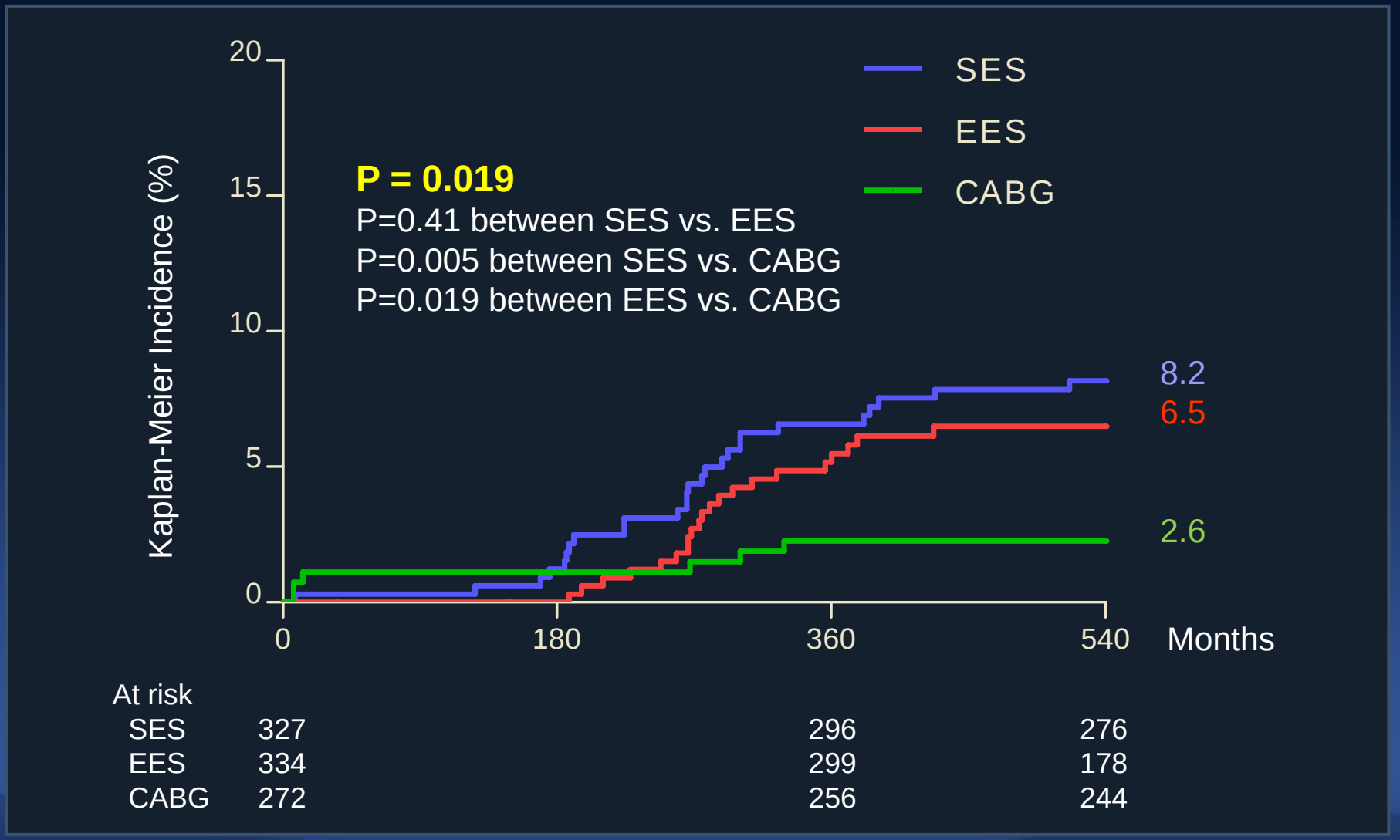
Stroke


Kaplan-Meier Incidence (%)
20
15
10
5
0
SES
EES
CABG
P = 0.84
0.6
0.4
0.3
0
180
360
540
Months
At risk
SES 327 316 298
EES 334 315 190
CABG 272 261 249

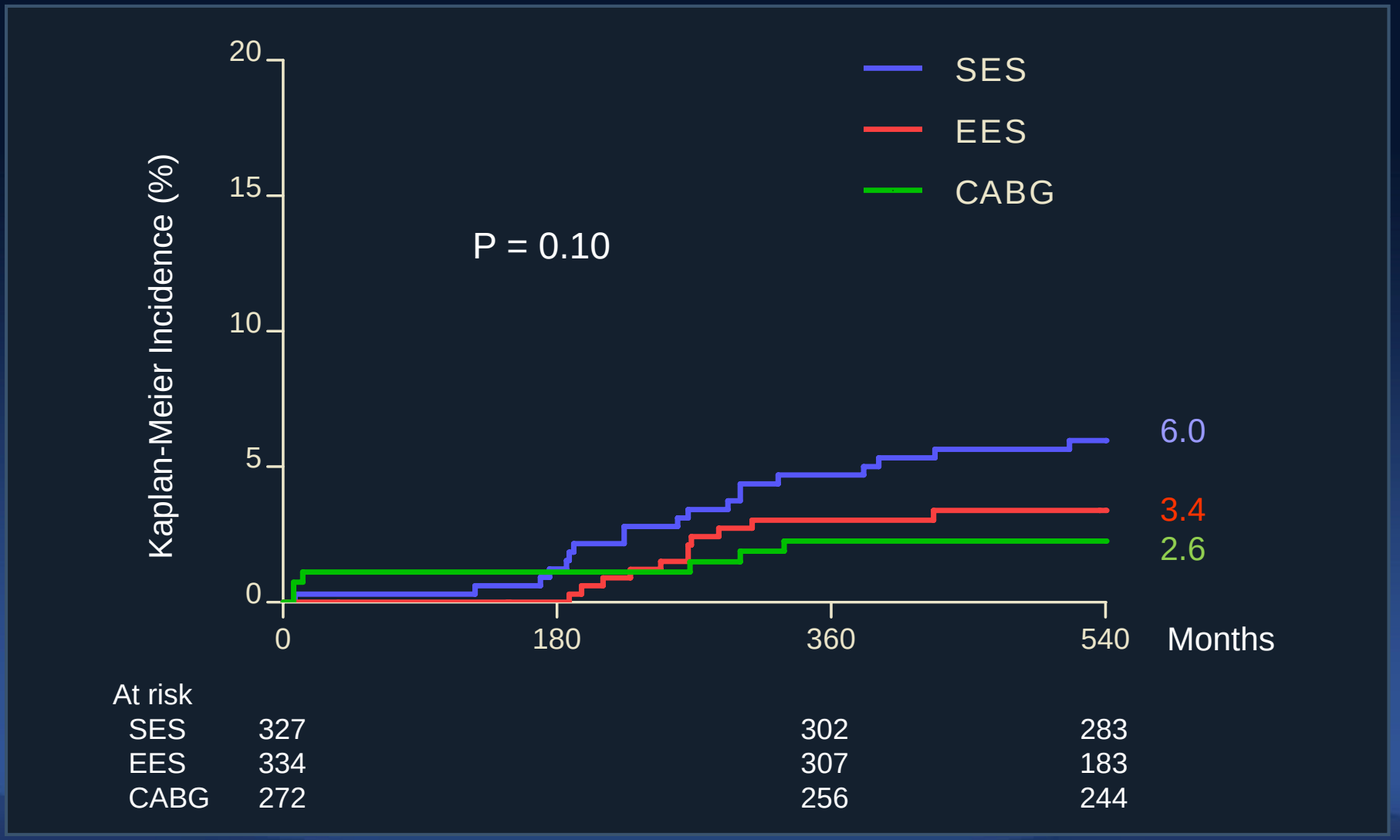
Death, MI, or Stroke



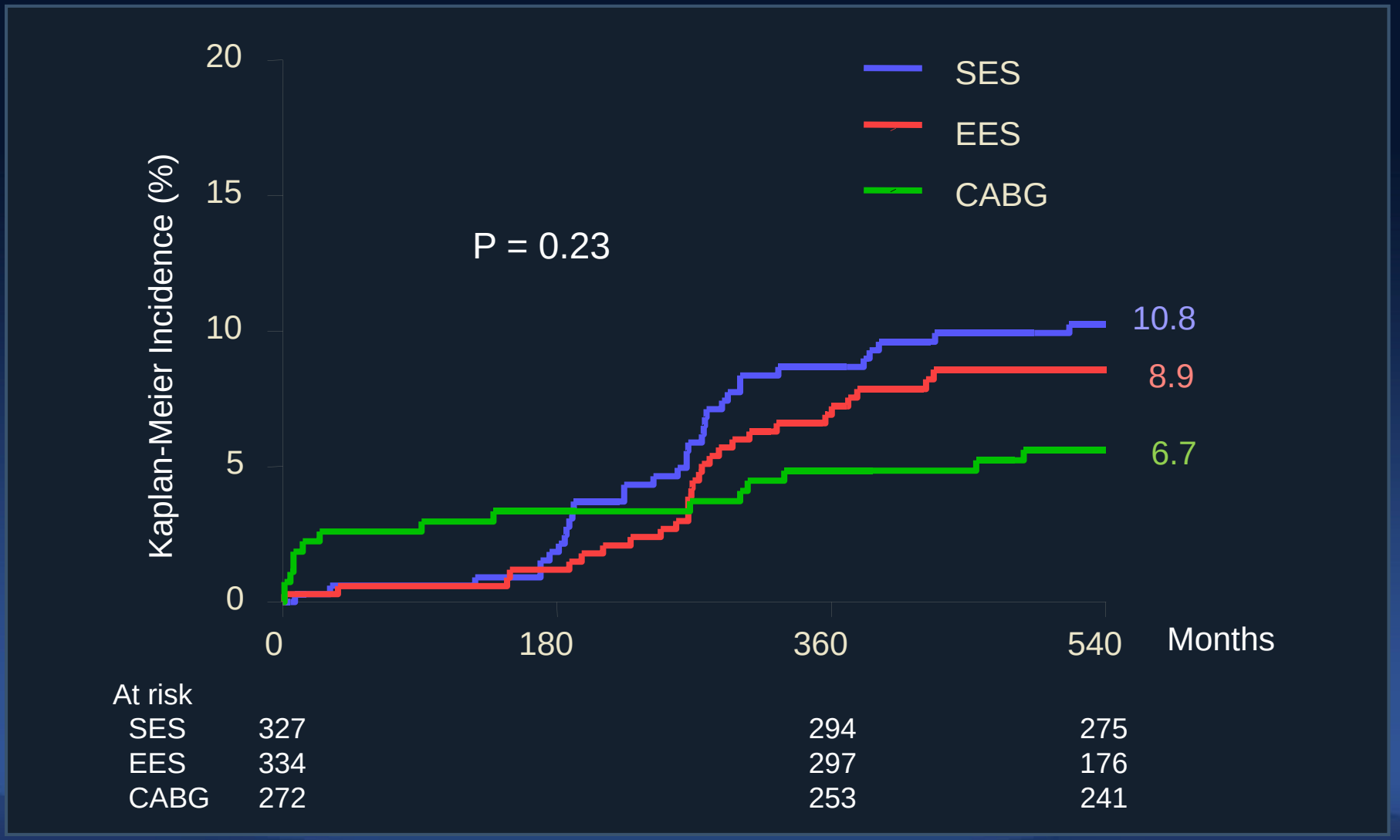
Ischemia-driven TVR



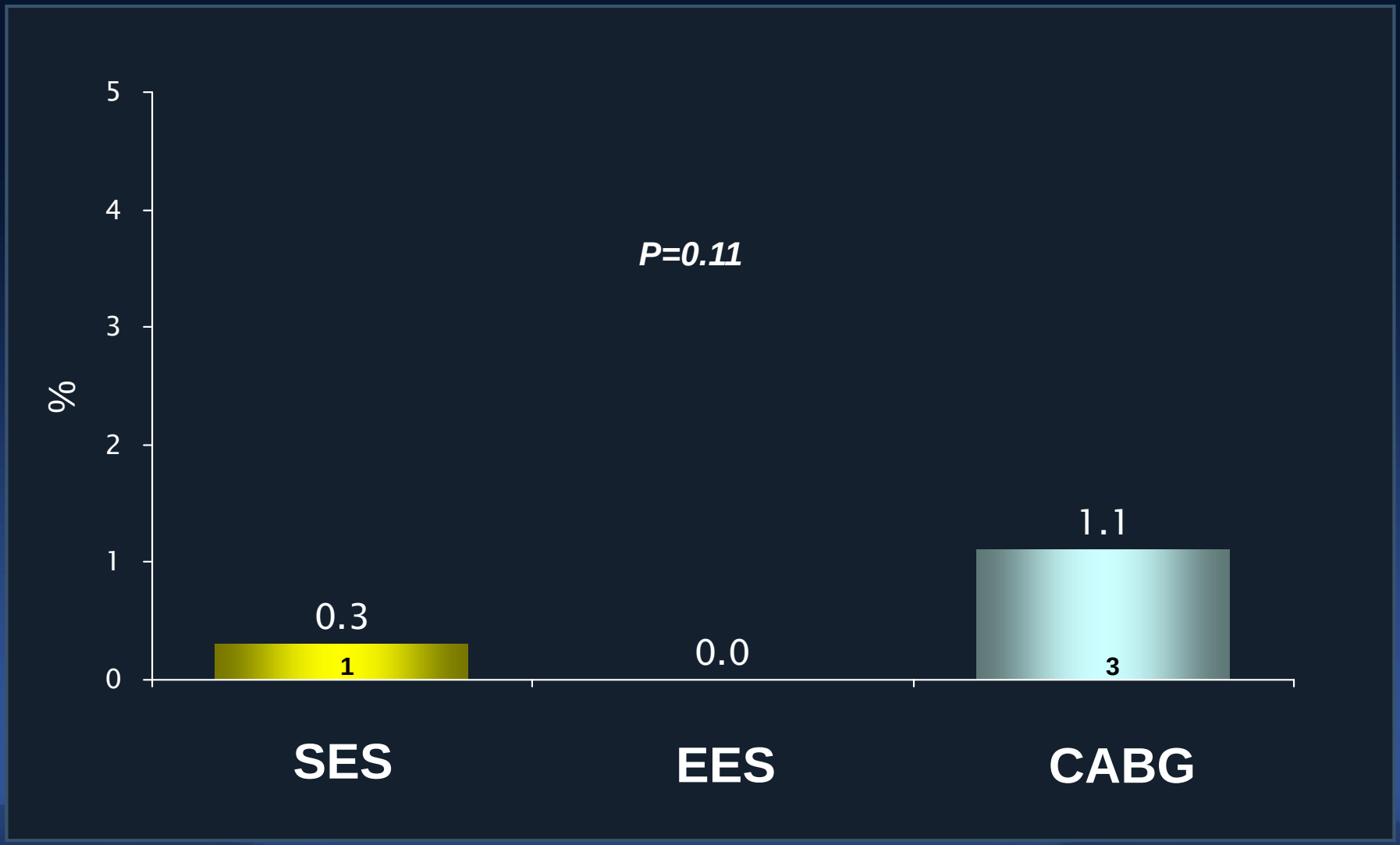
Clinical-driven TVR



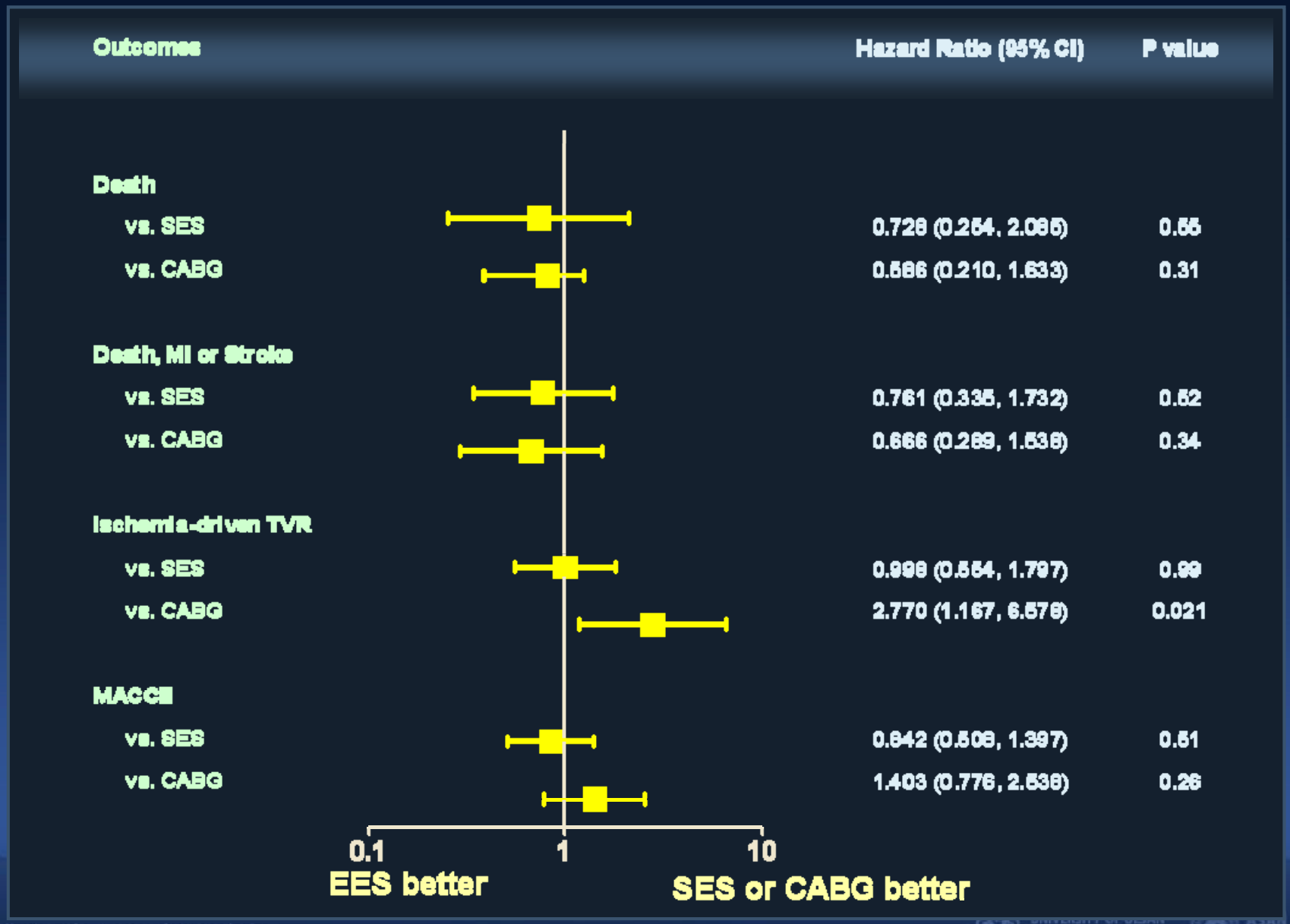
MACCE
Death, MI, Stroke or Ischemic TVR



Symptomatic Graft Occlusion & Stent Thrombosis to 18 Months



Hazard Ratios of EES after Adjustment



Angiographic Outcomes

QCA before Procedure

		SES (N=286)	EES (N=311)	p
Lesion length, mm	Main branch	28.5±15.7	23.5±15.9	<0.001
	Side branch	9.8±12.1	8.3±10.6	0.26
Reference, mm	Left main	3.64±0.49	3.71±0.46	0.12
	LAD	3.16±0.49	3.18±0.51	0.55
	LCX	2.96±0.50	3.00±0.55	0.45
MLD, mm	Left main	1.68±0.63	1.72±0.55	0.46
	LAD	1.66±0.78	1.77±0.77	0.087
	Side branch	1.91±0.66	2.10±0.72	0.001
DS, %	Left main	53.8±16.3	53.5±14.0	0.83
	LAD	47.2±23.4	44.6±22.0	0.17
	Side branch	34.5±20.78	29.7±20.4	0.006

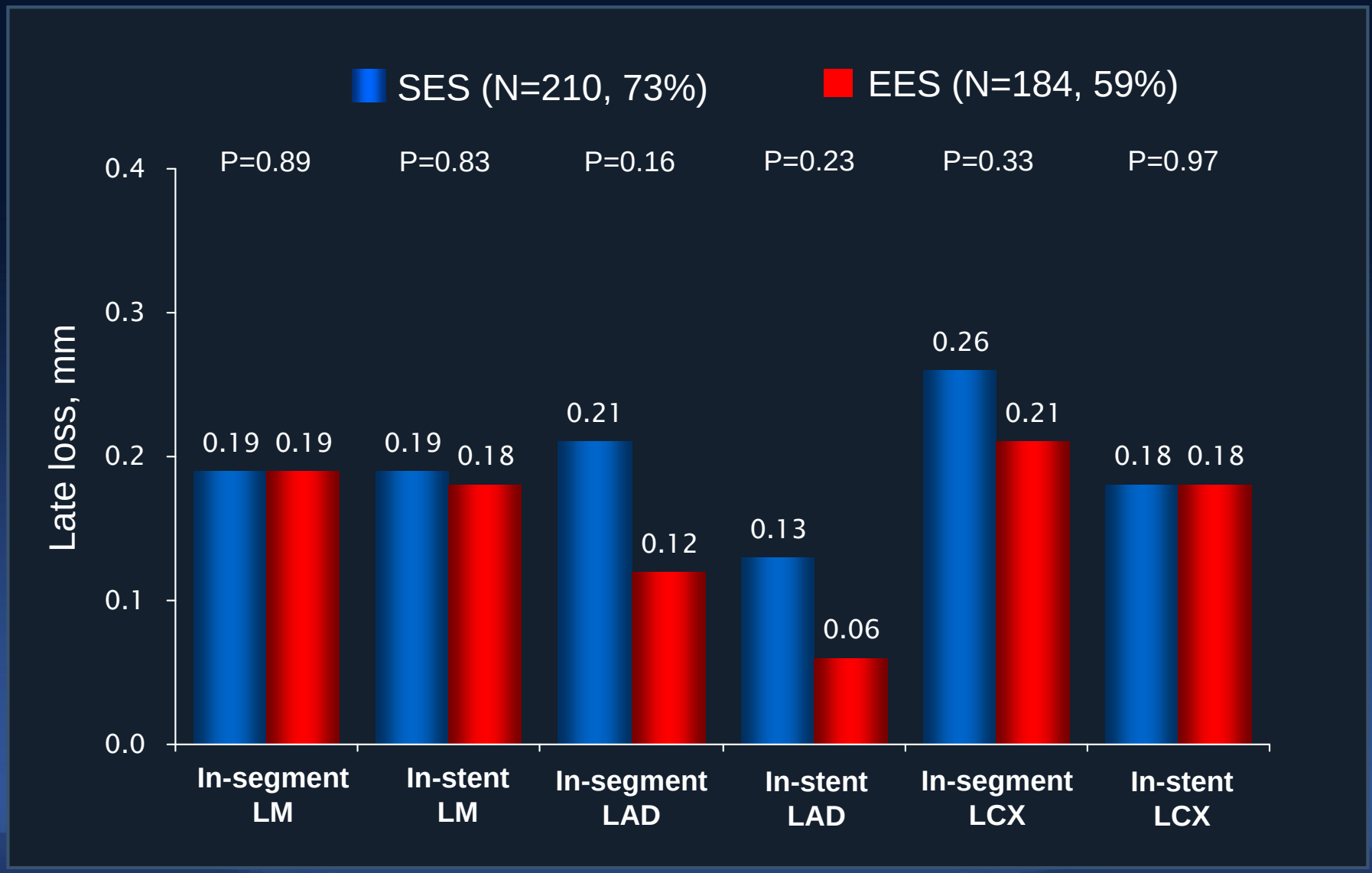
QCA after Procedure

		SES (N=286)	EES (N=311)	p
Stent length, mm	Left main	13.7±4.4	13.1±4.5	0.15
	LAD	20.3±14.7	17.8±14.8	0.045
	Side branch	10.5±11.6	6.8±8.4	<0.001
In-stent MLD, mm	Left main	3.24±0.45	3.32±0.48	0.036
	LAD	2.76±0.49	2.81±0.56	0.25
	Side branch	2.44±0.54	2.41±0.59	0.64
In-segment MLD, mm	Left main	3.23±0.45	3.31±0.48	0.046
	LAD	2.47±0.55	2.42±0.60	0.29
	Side branch	2.24±0.55	2.23±0.57	0.86
DS, in-stent, %	Left main	9.4±9.4	6.1±9.8	<0.001
	LAD	10.1±9.4	5.9±9.8	<0.001
	Side branch	16.6±13.5	19.0±14.0	0.040
DS, in-segment, %	Left main	10.1±9.1	8.4±8.2	0.017
	LAD	16.2±10.5	15.6±10.8	0.49
	Side branch	21.0±12.9	23.4±13.0	0.028

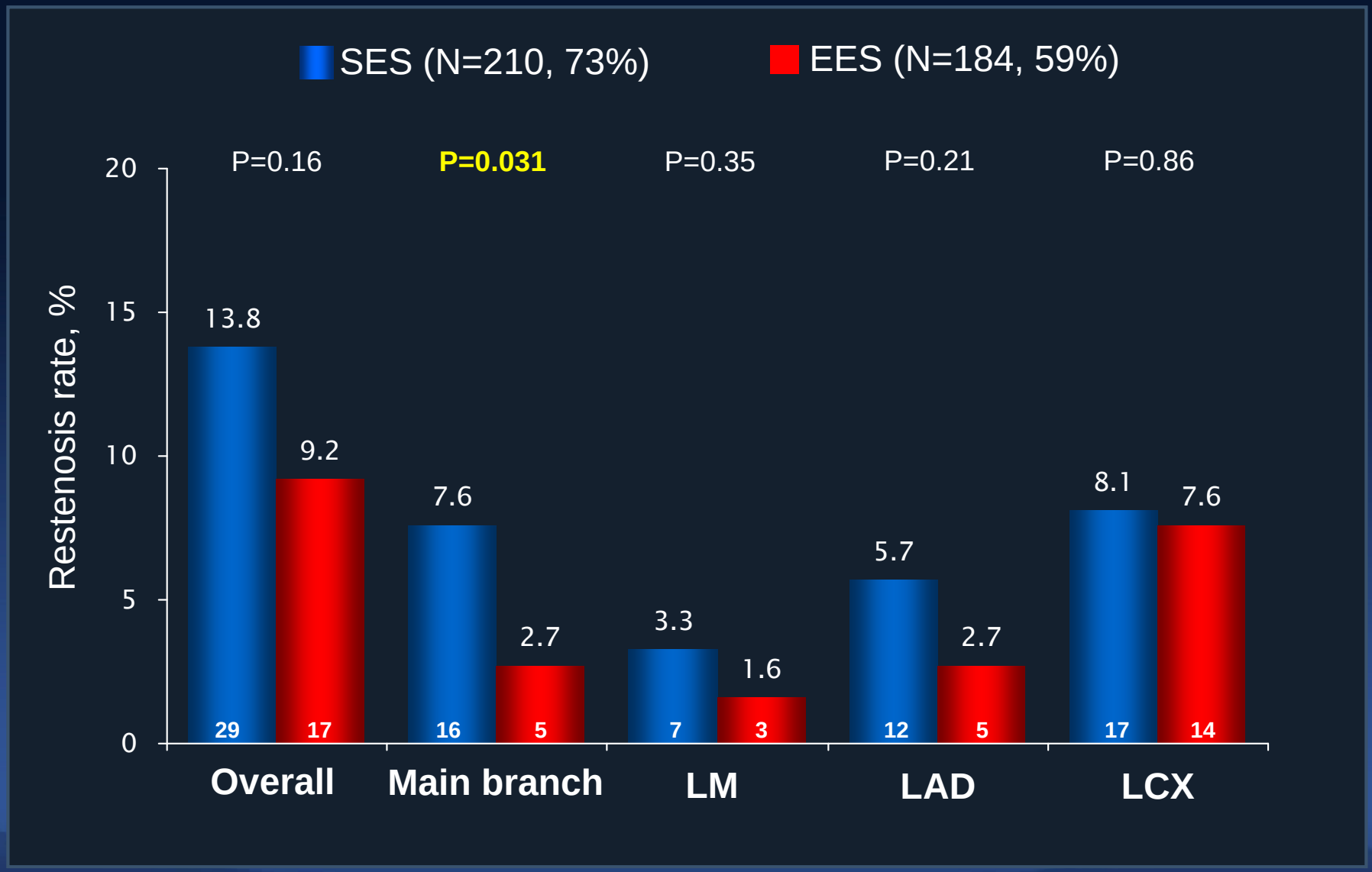
QCA at Follow-up

		SES (N=210)	EES (N=184)	p
In-stent MLD, mm	Left main	3.09±0.60	3.13±0.60	0.53
	LAD	2.58±0.68	2.68±0.72	0.17
	Side branch	2.16±0.66	2.20±0.63	0.54
In-segment MLD, mm	Left main	3.08±0.60	3.13±0.60	0.48
	LAD	2.35±0.65	2.32±0.60	0.63
	Side branch	2.05±0.63	2.05±0.61	0.92
DS, in-stent, %	Left main	13.7±14.6	12.8±14.0	0.52
	LAD	15.7±17.3	12.6±14.0	0.059
	Side branch	25.7±20.8	26.6±17.7	0.67
DS, in-segment, %	Left main	14.5±14.4	14.2±12.8	0.83
	LAD	20.2±16.7	20.1±13.7	0.99
	Side branch	28.4±19.6	29.7±16.9	0.48

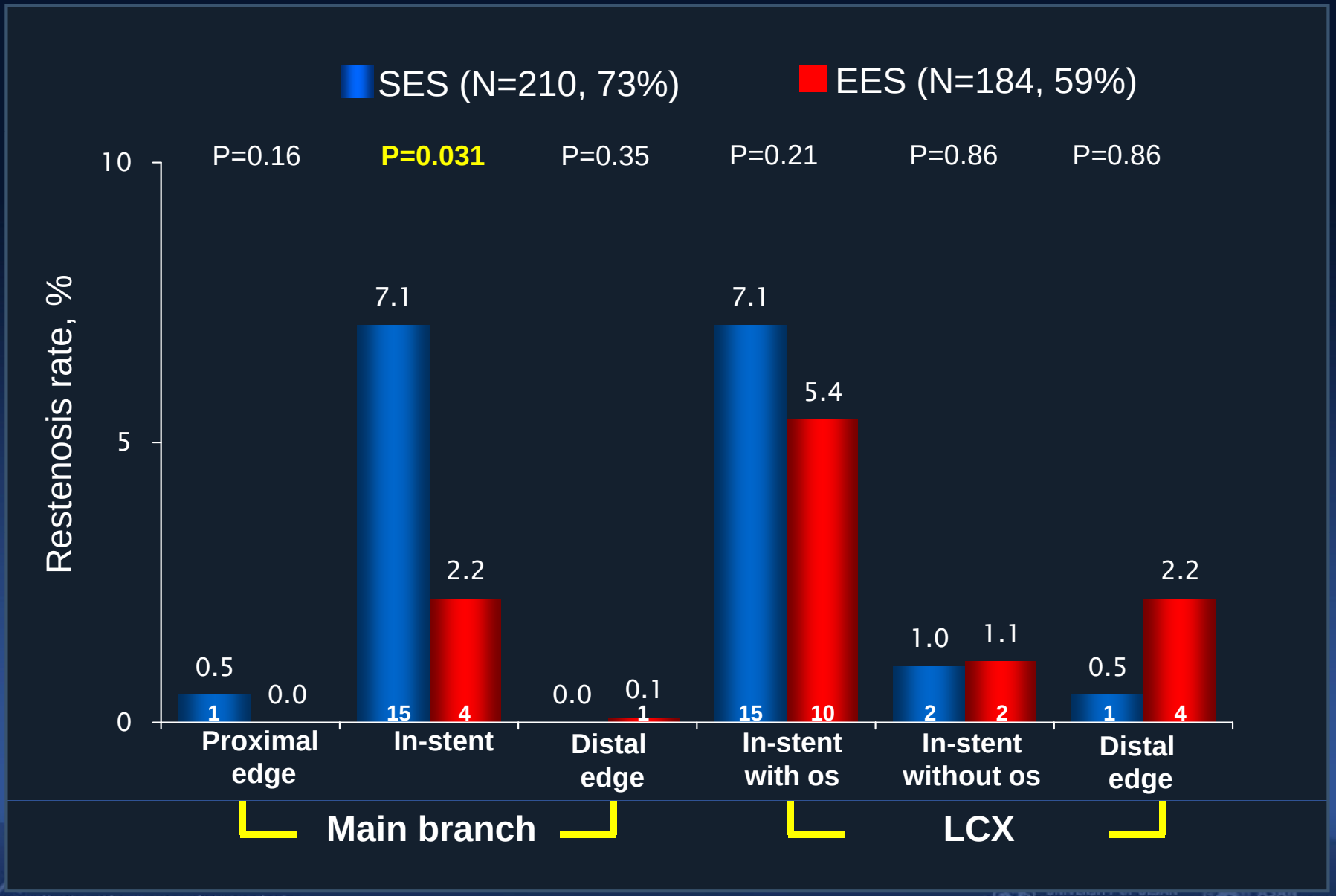
Late Luminal Loss



Restenosis Rate



Restenosis Location

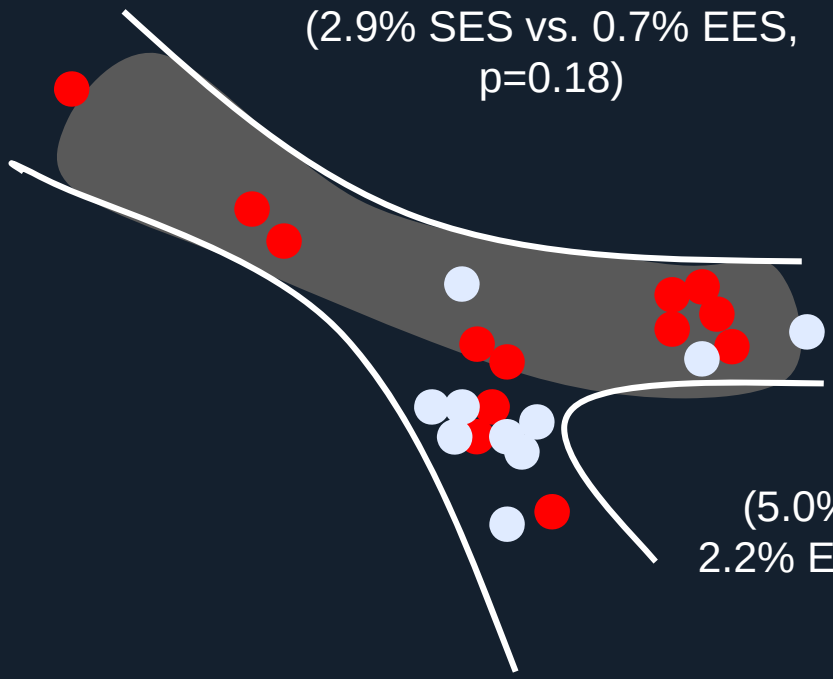


Restenosis Pattern

		SES	EES	p
Main branch	Focal	15 (7.1)	3 (1.6)	0.009
	Diffuse	1 (0.5)	2 (1.1)	0.49
	Proliferative	0	0	
	Total occlusion	0	0	
Side branch	Focal	16 (7.6)	14 (7.6)	>0.99
	Diffuse	1 (0.5)	0	>0.99
	Proliferative	0	0	
	Total occlusion	0	0	

Single-Stent Technique (N=139 SES, 138 EES)

SES



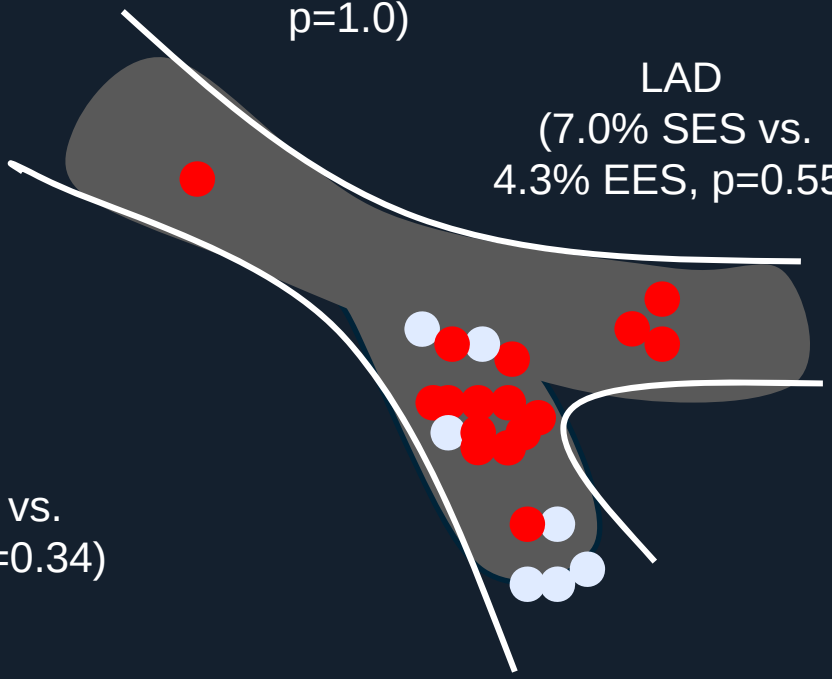
Left main (2.9% SES vs. 0.7% EES, p=0.18)

LAD (5.0% SES vs. 2.2% EES, p=0.34)

Left circumflex (3.6% SES vs. 5.1% EES, p=0.55)

Two-Stent Technique (N=71 SES, 46EES)

EES



Left main (4.2% SES vs. 4.3% EES, p=1.0)

LAD (7.0% SES vs. 4.3% EES, p=0.55)

Left circumflex (16.9% SES vs. 15.2% EES, p=0.81)

Conclusion

- The use of EES for ULMCA stenosis was comparably safe and effective with regard to the incidence of 18-month MACCE, as compared with SES or CABG.
- Although the need of repeat revascularization is higher than CABG, the second-generation EES had comparable risk of angiographic and clinical restenosis with the first-generation SES.
- Complete 3-year follow-up data will be available soon.