COBIS

Samsung Medical Center
Cardiac & Vascular Center
SMC

Lessons from Korean Multicenter Bifurcation Stenting Registry

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For the COBIS Investigators

JCR 2010

Bifurcation Lesions in the DES Era

- Even in this era of DES, the coronary bifurcation lesion remains a complex lesion subset to treat.
- Most of the previous studies have been focused on a certain types of stents or stenting techniques, and have been too small to show overall outcomes in various subgroups.
- To date, there has been no large, real-world registry of DES implantation in coronary bifurcation lesions.

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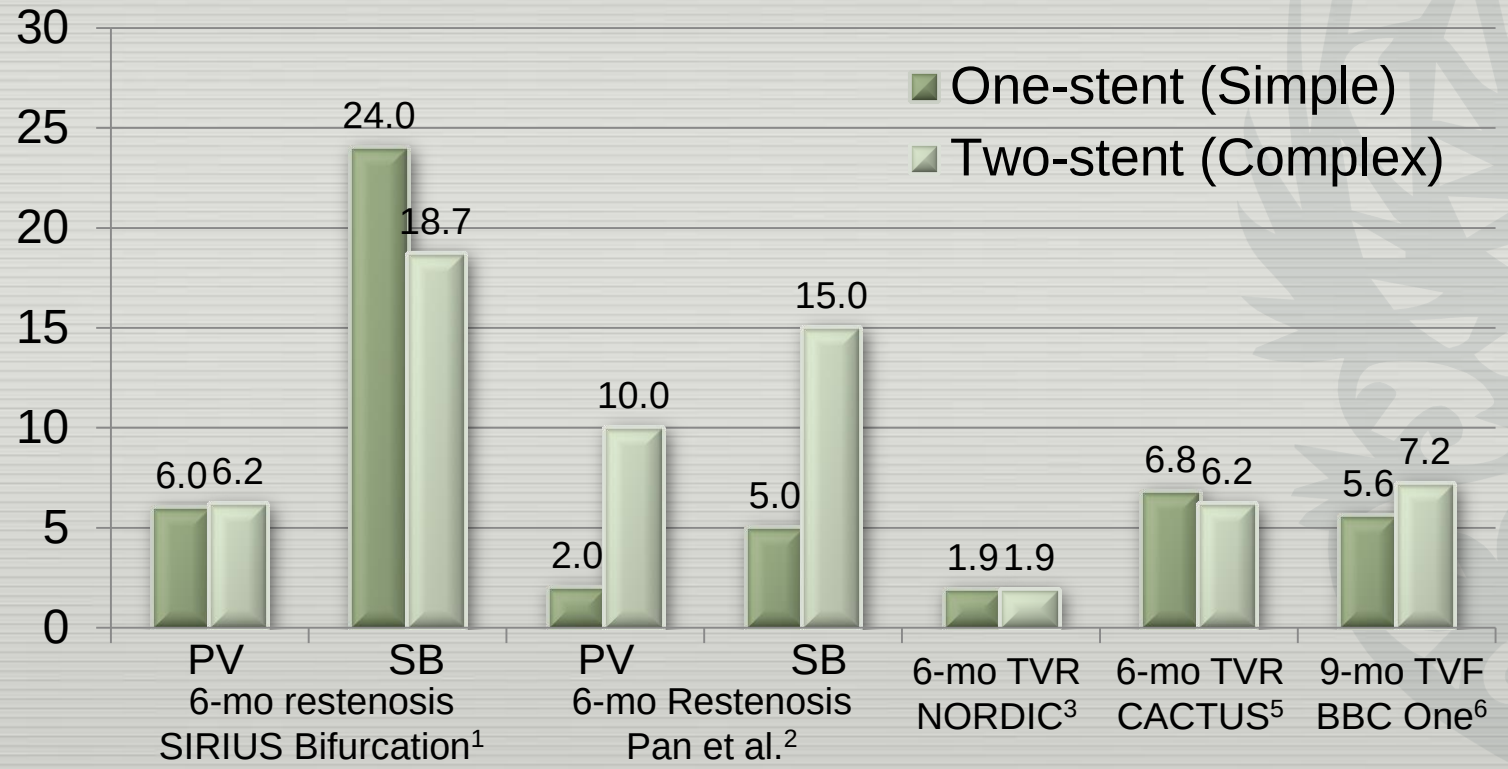
Bifurcation Lesions in the DES Era

The results varied according to stent techniques

In RCTs, patients are selected, and CAG FU rate is high, which may not reflect the real world experience



1. Colombo A, Circulation 2004
2. Pan M, AHJ 2004
3. Steigen, Circulation 2006
4. Colombo A, EuroPCR 2008
5. Hildick-Smith D. TCT 2008

Coronary Bifurcation Stent Registry

- Study design
  - Multi-center retrospective real-world registry of drug-eluting stenting for coronary bifurcation lesions from 16 cardiovascular intervention centers in Korea
- Inclusion criteria
  1) DES implantation in the coronary bifurcation lesion in 2004.1 ~ 2006.6
  2) Main vessel diameter ≥ 2.5 mm and side branch diameter ≥ 2.0 mm
- Exclusion criteria
  1) Cardiogenic Shock
  2) ST elevation MI within 48 hours
  3) Expected survival less than 1 year
  4) Left main bifurcation

clinicaltrials.gov number NCT00794014

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Baseline Characteristics

1691 lesions in 1668 patients from 16 hospitals in South Korea

Male sex	1116 (66.9%)
Age	62.1±10.3 years
Diagnosis	
Silent ischemia	61 (3.7%)
Stable angina	638 (38.2%)
UA/NSTEMI	880 (52.8%)
STEMI	89 (5.3%)
Diabetes	513 (30.8%)
Hypertension	987 (59.2%)
Dyslipidemia	521 (31.2%)
Smoking	405 (24.3%)

Periph Vasc Disease	26 (1.5%)
CVA history	87 (5.2%)
CRF	55 (3.3%)
Previous MI	139 (8.3%)
LVEF<50% (N=1195)	203(17.0%)
Location	
RCA	93 (5.5%)
LAD	1288 (76.2%)
LCX	310 (18.3%)
True bifurcation	1170 (69.2%)

UA = unstable angina; NSTEMI = non-ST elevation myocardial infarction; STEMI = ST elevation myocardial infarction; FHx of CAD = family history of coronary artery disease; CVA = cerbrovascular accident; CRF = chronic renal failure; MI = myocardial Infarction; LVEF = left ventriucular ejection fraction; RCA = right coronary artery,; LAD = left anterior descending artery; LCX = left circumflex artery

Procedural Characteristics

Transradial approach	503 (30.2%)
2-stent technique	293 (17.3%)
Final kissing ballooning	687 (41.2%)
2-stent technique	
T-stenting	140 (47.8%)
Crush	100 (34.2%)
V-stenting	43 (14.7%)
Culottes	10 (3.4%)
IVUS guidance	532 (31.9%)
Main vessel stent	
Sirolimus-eluting stent	1070 (63.3%)
Paclitaxel-eluting stent	573 (33.9%)
Others	48 (2.8%)

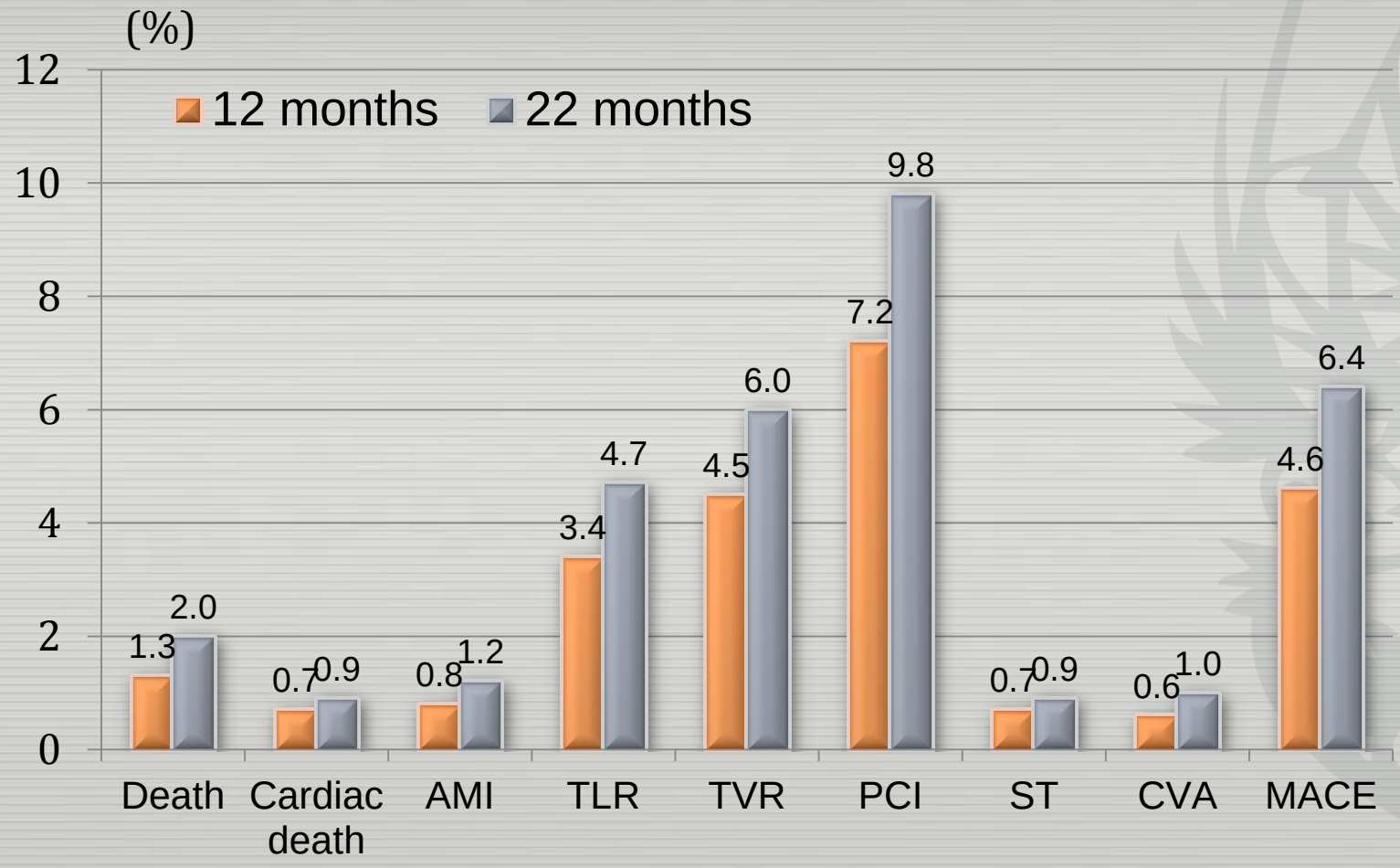
Main vessel	
Stent number ≥ 2	319 (18.9%)
Max. stent D ≥ 3.5 mm	632 (38.4%)
Total stent length ≥ 30 mm	734 (44.6%)
Side branch	
Stent number ≥ 2	10 (3.1%)
Max. stent D ≥ 3.0 mm	97 (30.4%)
Total stent length ≥ 30 mm	48 (15.0%)
Angiographic success (MV)*	1671 (98.8%)
Angiographic success (SB)*	1084 (64.1%)
Peak CK-MB>3X URL	227(15.4%)

* MV=main vessel, SB=side branch, URL = upper reference limit
* Angiographic success
  - MV: residual stenosis <30% and TIMI=3
  - SB: residual stenosis <50% and TIMI=3

Gwon HC, Circ J 2010

One-year Clinical Events

One-year FU rate 97.8%, Median FU 22.2 months



MACE = cardiac death, AMI, or TLR

Gwon HC, Circ J 2010

JCR 2010

Risk Factors for MACE

	Univariate analysis			Multivariate Cox hazard model	
	No	Yes	p value	HR [95% CI]	p value
Acute coronary syndrome	5.1%	7.2%	0.079	1.29 [0.81-2.07]	0.286
Female sex					0.590
Age ≥ 65 years					0.157
Acute coronary					0.253
Diabetes					0.842
Chronic renal f					0.499
Previous MI his					0.517
LAD location	6.5%	6.2%	0.862	0.75 [0.45-1.26]	0.282
True bifurcation					0.860
SB diameter ≥					0.224
Two-stent tech					0.982
Final kissing ba					0.043
IVUS guidance					0.526
PES in MV					0.007
SB angiograph					0.959
MV max. stent diameter ≥ 3.5 mm	7.2%	5.1%	0.085	0.70 [0.43-1.15]	0.157
MV stent total length ≥ 30 mm	4.6%	8.6%	0.001	2.17 [1.37-3.44]	0.001

Statistically Significant Independent Predictors

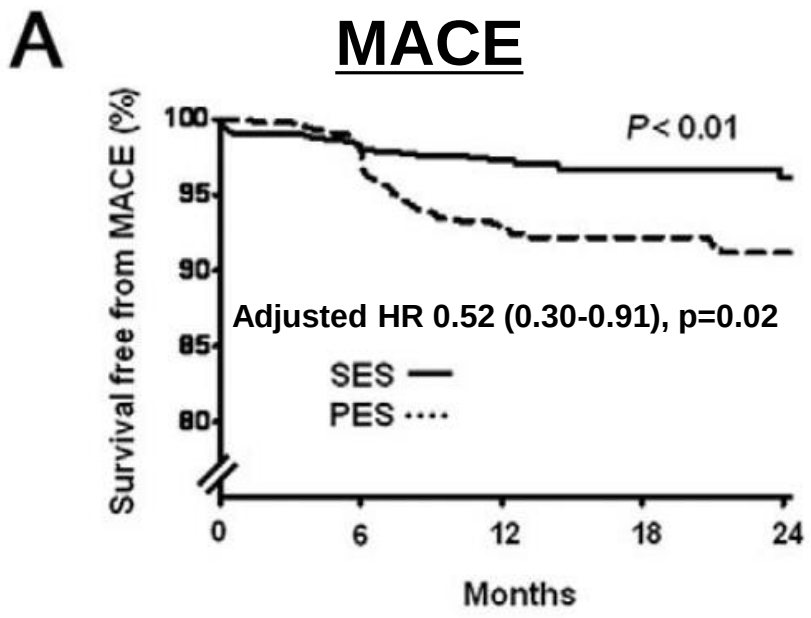
	HR [95% CI]	p value
PES in MV	1.98 [1.34-2.92]	0.001
MV stent total length	1.02 [1.01-1.03]	0.030
Final kissing ballooning	2.01 [1.29-3.13]	0.002

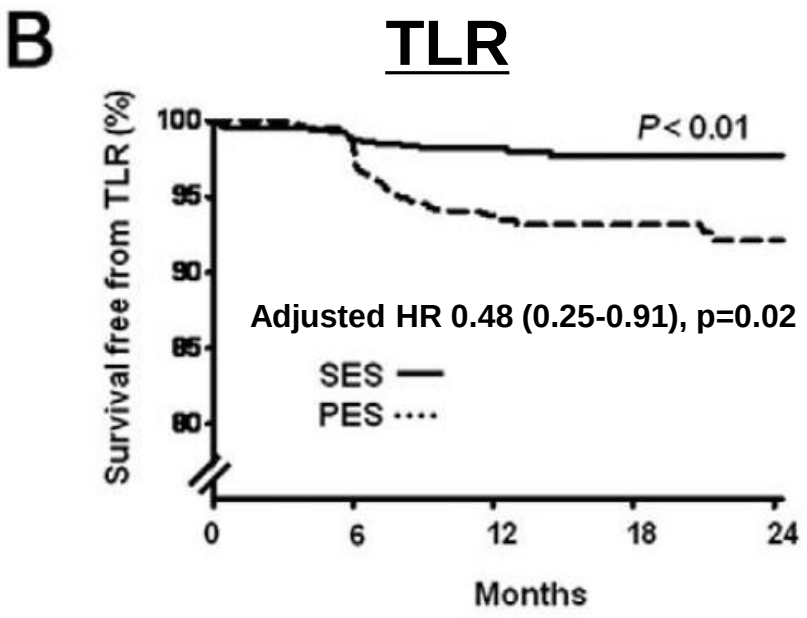
Important Non-Predictors

	HR [95% CI]	p value
True bifurcation	1.05 [0.60-1.83]	0.860
Two-stent technique	0.99 [0.54-1.82]	0.982
IVUS guidance	1.18 [0.71-1.97]	0.526
SB angiographic success	0.99 [0.56-1.74]	0.959

SES vs. PES

Propensity-Score Matched (407 pairs)





No. at risk					
SES	407	399	393	255	193
PES	407	396	369	218	154

No. at risk					
SES	407	399	393	255	194
PES	407	397	371	219	155

Song YB, Gwon HC, JACC 2010

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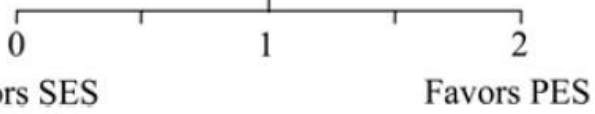
SES vs. PES

Subgroup Analysis

Subgroups	Number of patients	Hazard ratio	95% CI	P for interaction
Age				
< 65 years	917	0.57	0.33-0.98	0.93
≥ 65 years	678	0.55	0.30-0.99	
Presentation				
Non-ACS	668	0.51	0.25-1.00	0.68
ACS	927	0.60	0.37-0.99	
Diabetes				
No	1107	0.51	0.31-0.84	0.57
Yes	488	0.66	0.32-1.34	
True bifurcation				
No	493	0.51	0.23-1.12	0.80
Yes	1102	0.58	0.36-0.93	
Stenting technique				
1-stent	1322	0.56	0.36-0.89	0.85
2-stent	273	0.51	0.21-1.25	



Song YB, Gwon HC, JACC 2010

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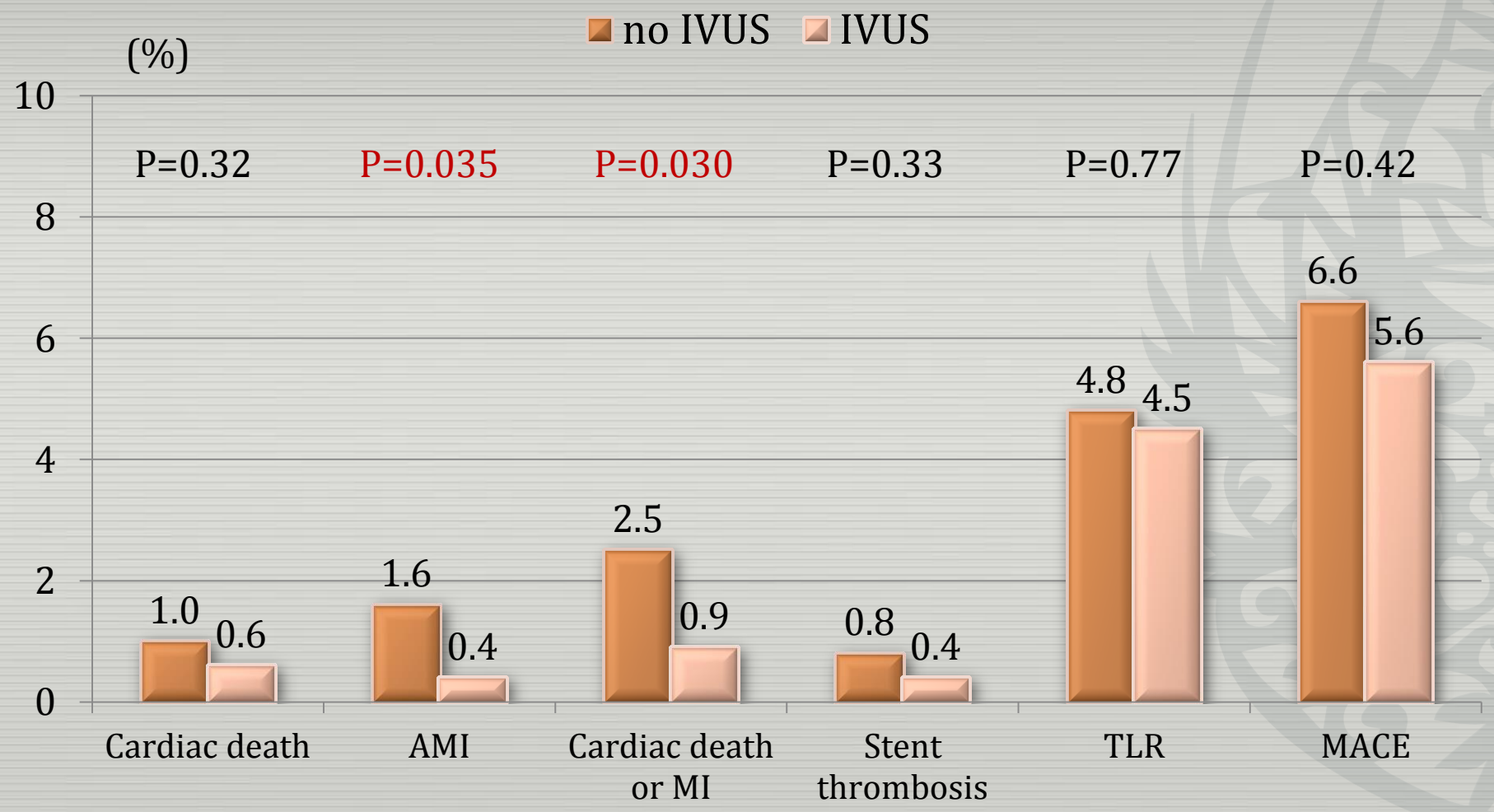
IVUS Guidance in COBIS

• MACE = cardiac death, MI, or TLR



Kim JS, Hong MK, AHJ In press 2010

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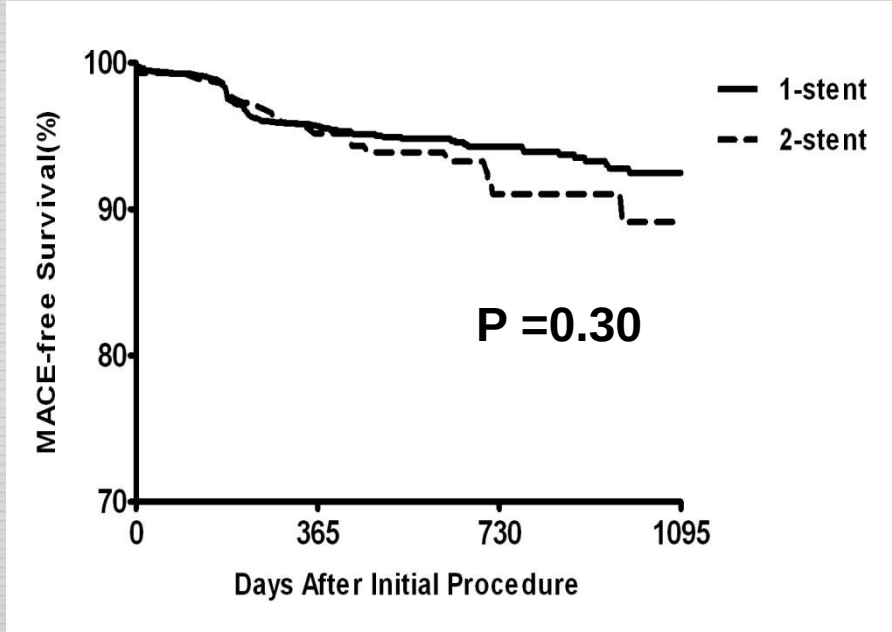
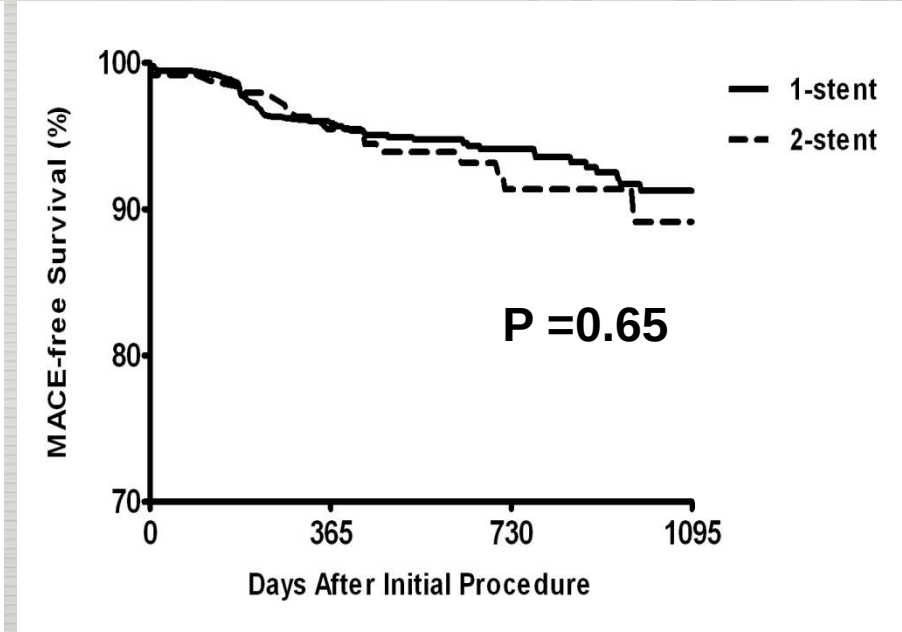
One-Stent vs. Two-Stent Technique

MACE in all patients



1-stent	1376	1283	602	258
2-stent	292	269	117	36

MACE in true bifurcation group



911	853	386	166
246	227	98	32

Gwon HC, Circ J 2010

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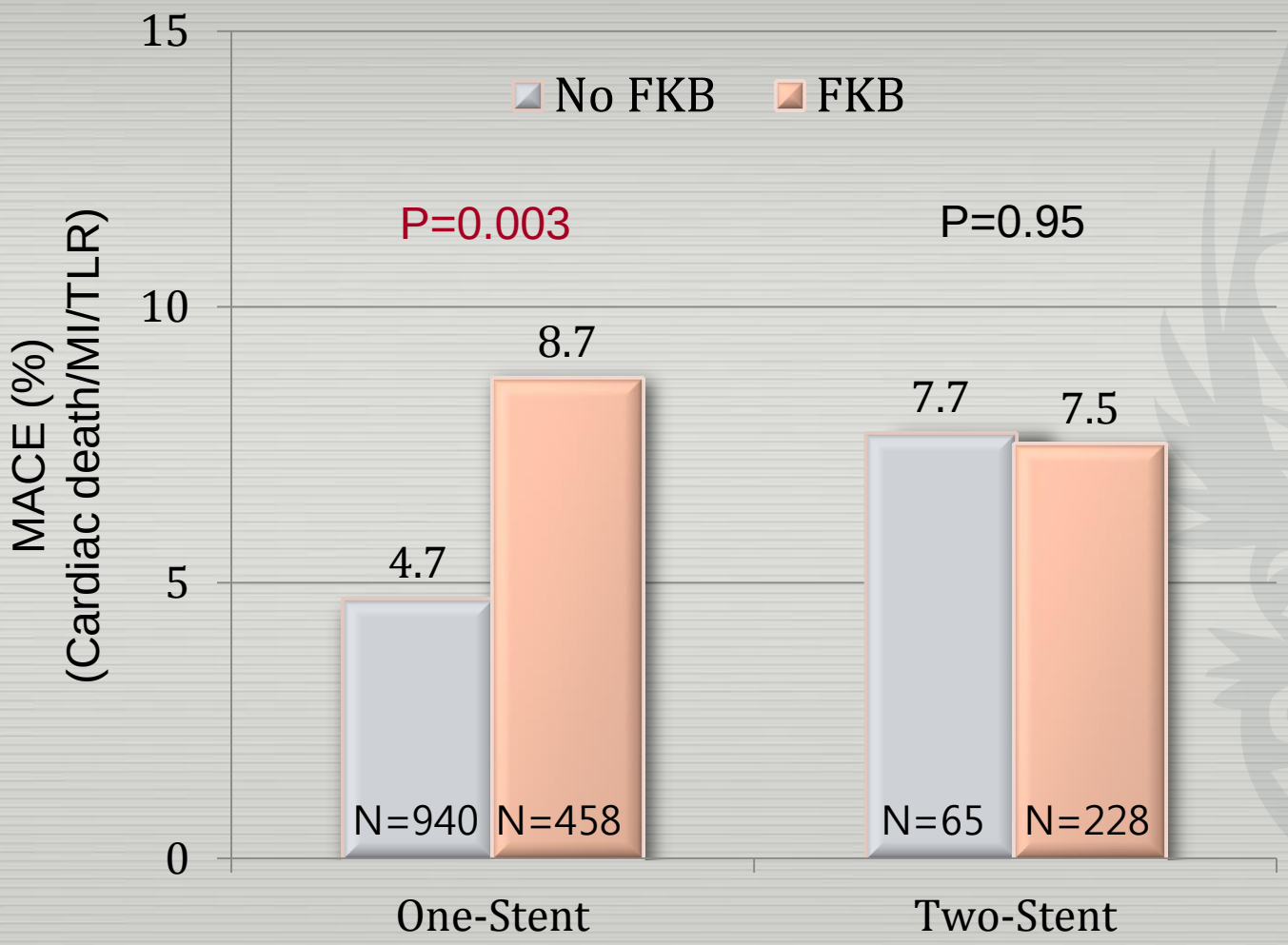
Final Kissing Ballooning

One-stent vs. Two-stent



FKB: Final kissing ballooning

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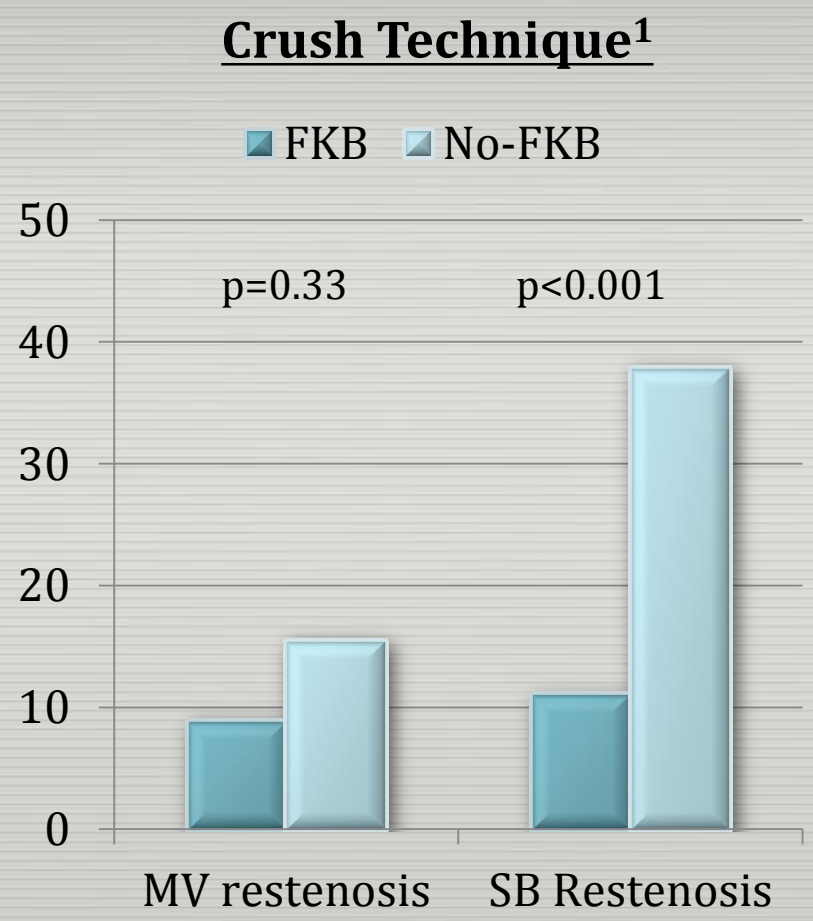
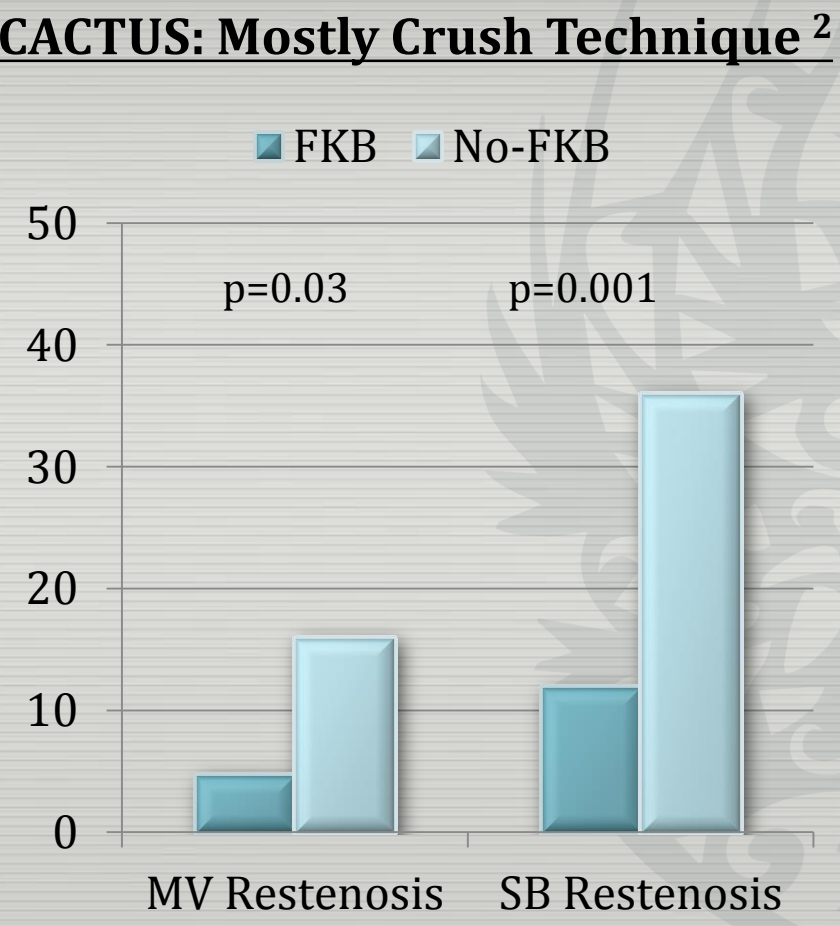
Final Kissing Ballooning Is Important in Crush Technique





1. Ge L, JACC 2005
2. Colombo A, CACTUS, Circulation 2009

NORDIC III Study

FKB vs. no FKB in 1-Stent Technique

	No Kissing (N=239)	Kissing (N=238)	P-value
Procedure time (min)	47±22	61±28	0.0001
Fluorosc. Time (min)	11±10	16±12	0.0001
Contrast (ml)	200±92	235±97	0.0001
6-mo MACE (%)	2.9	2.9	NS
6-mo Index lesion MI (%)	2.2	0.0	NS
6-mo TLR (%)	2.1	1.3	NS
6-mo Stent thrombosis (%)	0.4	0.4	NS

Short follow-up duration
Small sample size for low MACE rate

If baseline event rate is 2.9%, you need 3,200 patients to prove 50% of risk reduction (power 0.8, alpha error 0.05).

Niemela M, TCT 2009

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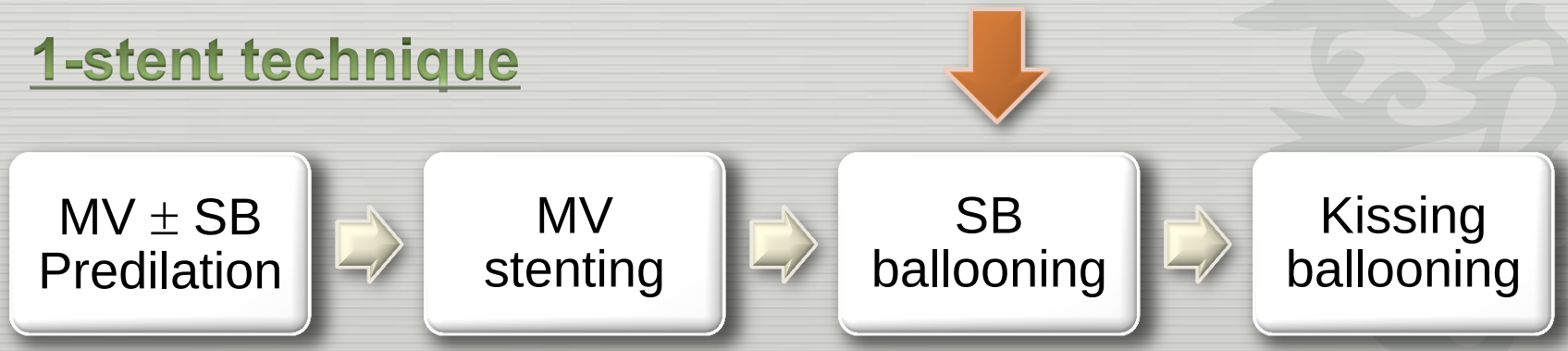
COBIS: Elective SB Ballooning

- Subjects: elective SB ballooning after MV stenting in one-stent group
  - Excluding bail-out SB ballooning due to TIMI flow < 3 or a significant dissection
- SB ballooning after MV stenting was not followed by final kissing ballooning in 20% of the lesions.

1-stent technique

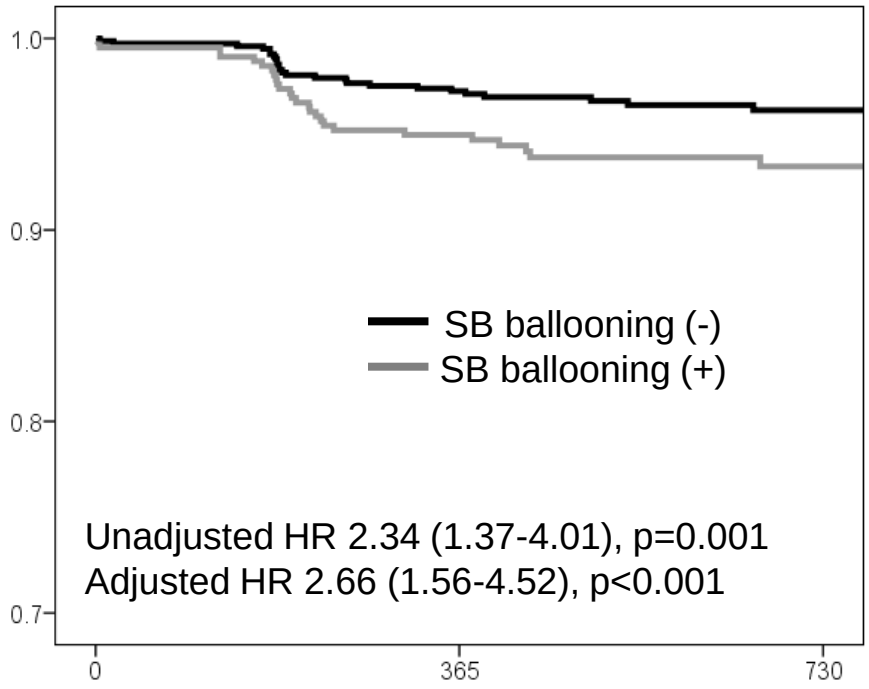


Gwon HC, TCT 2010

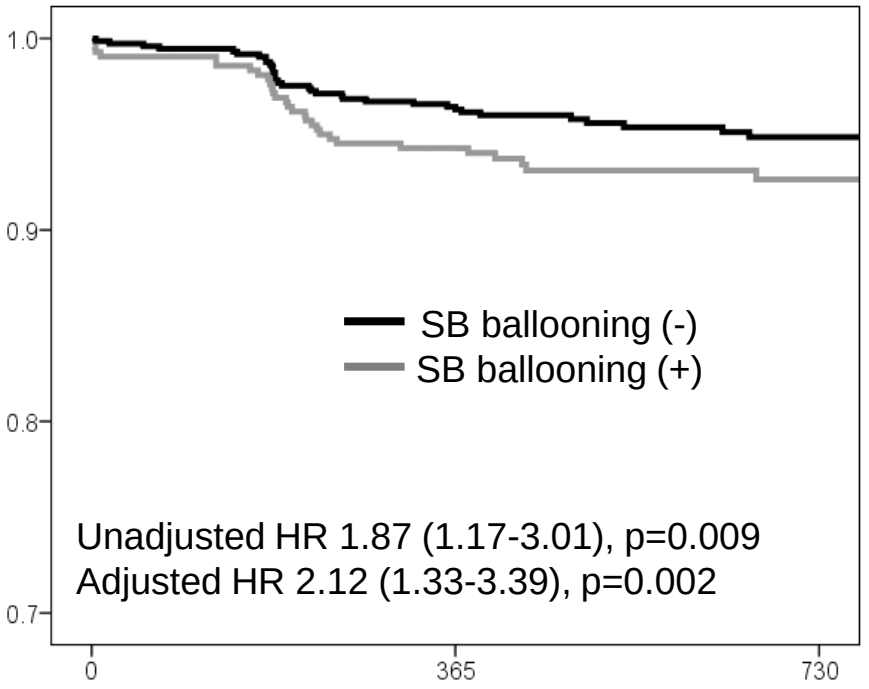
JCR 2010

Elective SB Ballooning in 1-Stent Group (N=1133)

TLR



MACE



*Adjusted covariates included age, diabetes, acute coronary syndrome, stent type, true bifurcation, intravascular ultrasound guidance, post-procedural MV MLD, post-procedural SB MLD, and lesion length of main vessel

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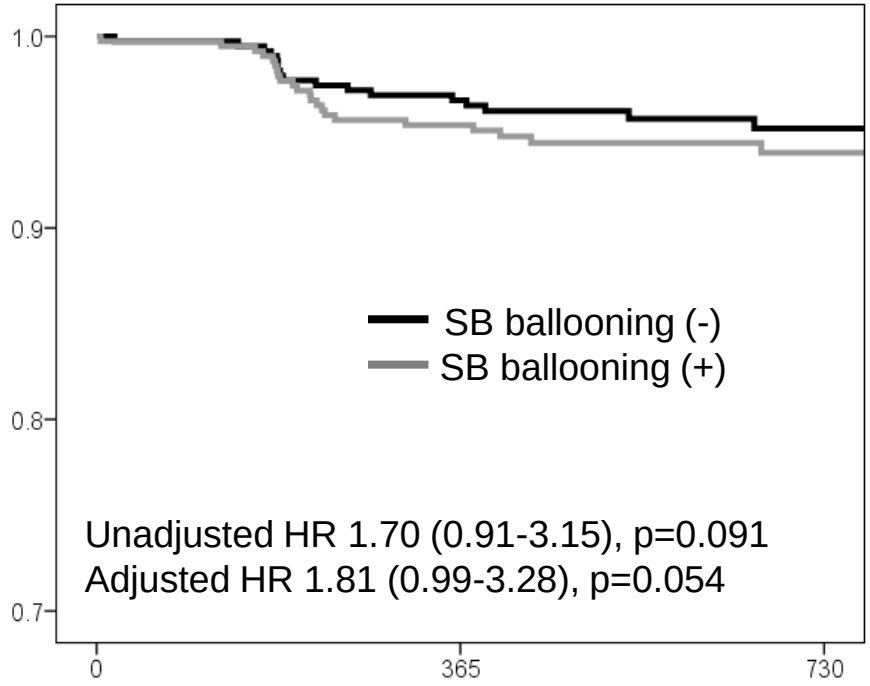
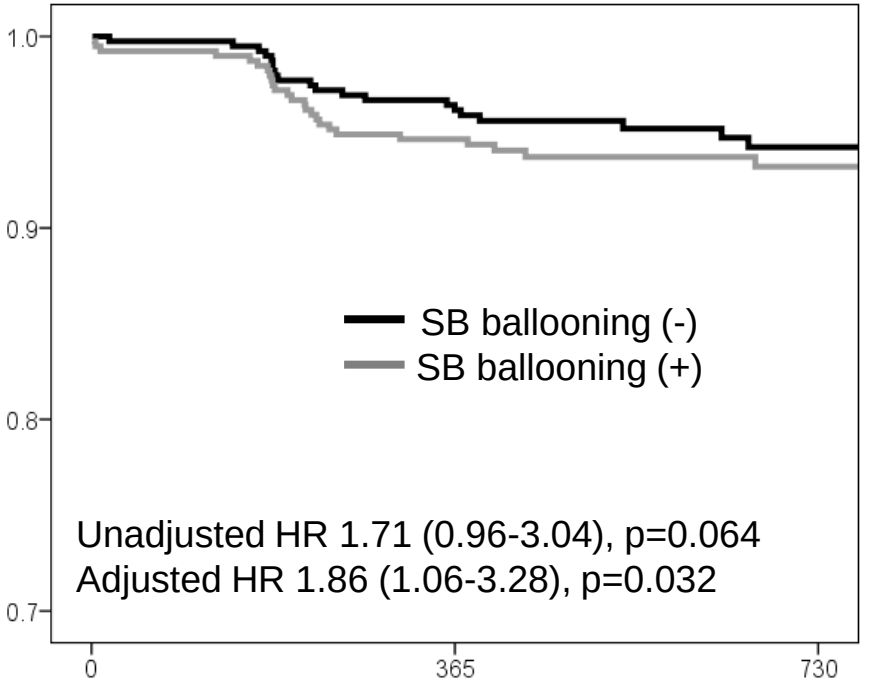
Elective SB Ballooning in 1-Stent Group

N=786 (393 pairs) of propensity score-matched group

TLR



MACE



*Adjusted covariates included age, diabetes, acute coronary syndrome, stent type, true bifurcation, intravascular ultrasound guidance, post-procedural MV MLD, post-procedural SB MLD, and lesion length of main vessel

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COBIS: Elective SB Ballooning

QCA Results of Propensity Score-Matched Population

	Pre-PCI			Post-PCI		
	No SBB (n=393)	SBB (n=393)	p Value	No SBB (n=393)	SBB (n=393)	p Value
MV proximal RD (mm)	3.07±0.52	3.07±0.51	0.99	3.16±0.52	3.14±0.52	0.46
MV distal RD (mm)	2.44±0.45	2.45±0.43	0.65	2.61±0.48	2.55±0.46	0.048
SB distal RD (mm)	2.09±0.41	2.16±0.41	0.03	2.03±0.49	2.18±0.41	<0.001
MV proximal MLD (mm)	1.45±0.85	1.47±0.79	0.69	2.74±0.51	2.86±0.47	<0.001
MB ostial MLD (mm)	1.24±0.62	1.19±0.58	0.29	2.61±0.49	2.59±0.44	0.55
MV distal MLD (mm)	1.58±0.71	1.63±0.70	0.29	2.49±0.53	2.55±0.47	0.06
SB ostial MLD (mm)	1.24±0.59	1.23±0.55	0.80	1.20±0.56	1.40±0.45	<0.001
SB distal MLD (mm)	1.55±0.56	1.66±0.57	0.007	1.53±0.56	1.73±0.52	<0.001
MV lesion length (mm)	17.6±9.8	17.2±9.7	0.63			
SB lesion length (mm)	5.0±6.0	4.7±5.6	0.46			

Better QCA results in SB ballooning group was not translated into better clinical outcome.

Gwon HC, TCT 2010

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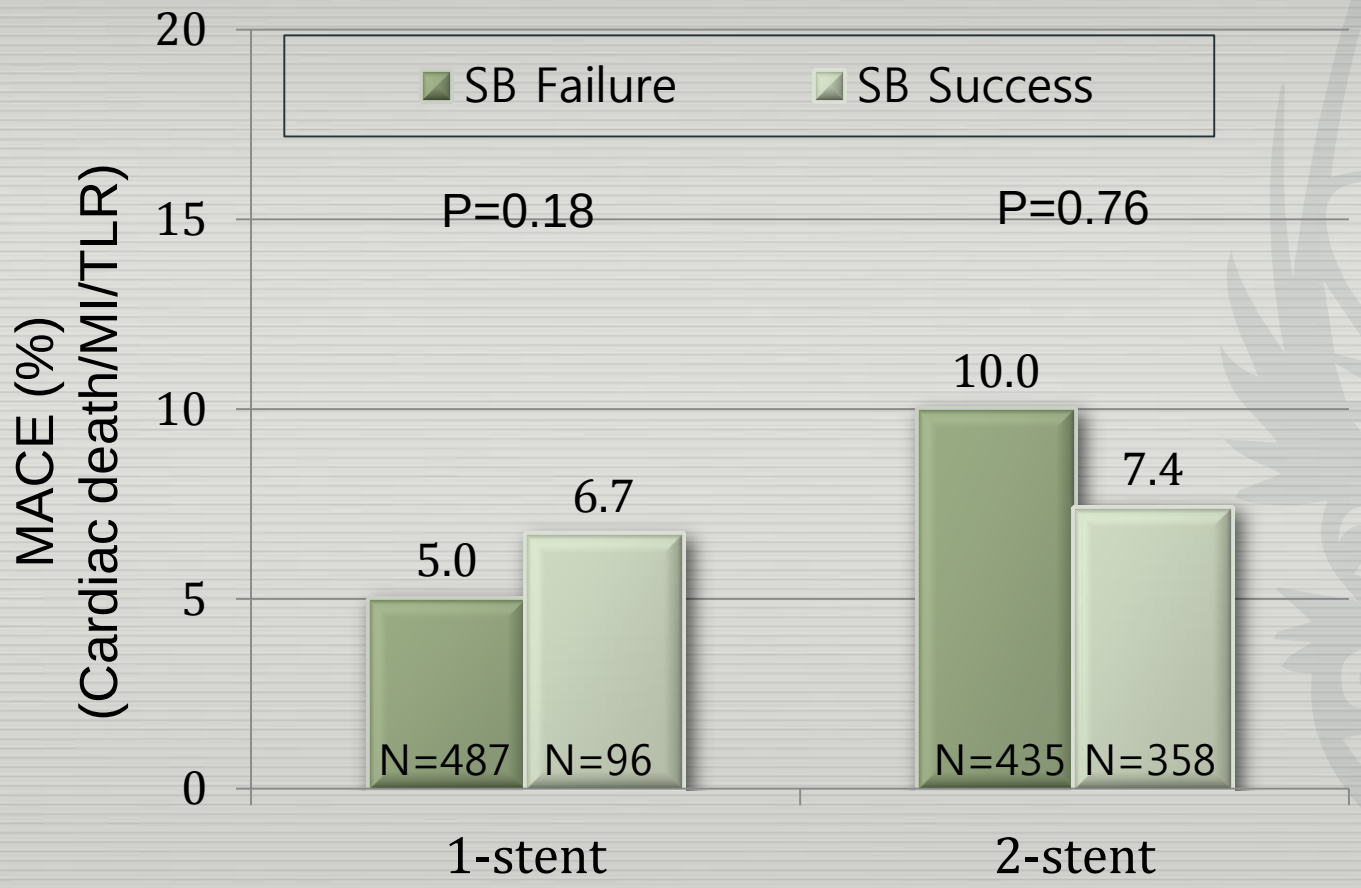
SB Ballooning Increases TLR?

Angiographic success in SB was not important



SB Angiographic Success: Residual stenosis < 50% and TIMI = 3

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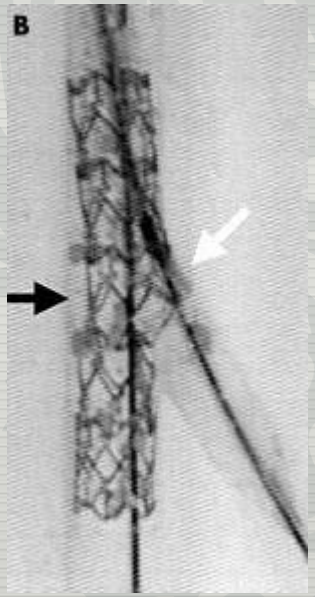
SB Ballooning Increase TLR?
Maybe due to MV stent deformation

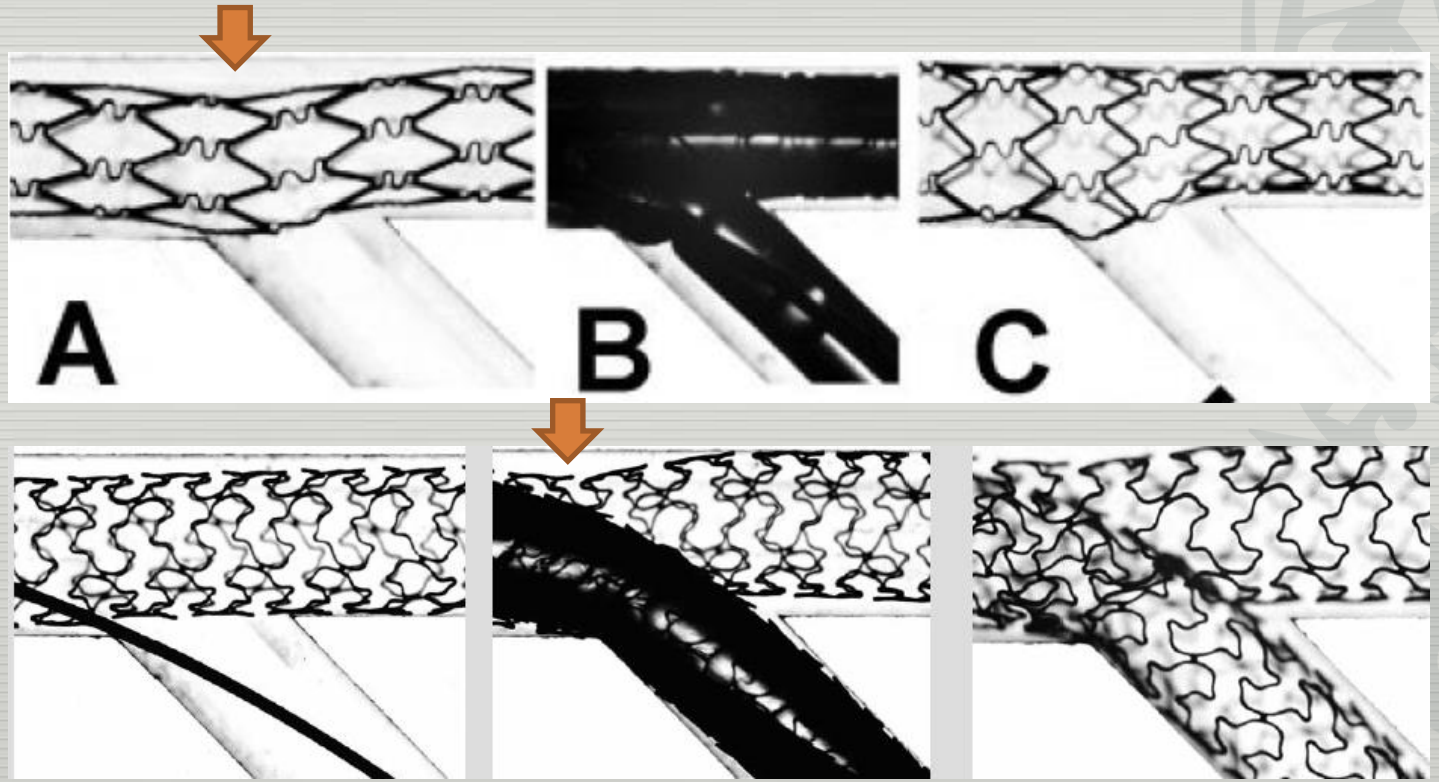
- Pros
  - Scaffolding of SB ostium
  - Access to SB preserved
  - Correct distal stent sizing
  - Optimizing proximal stent architecture
- Cons
  - Complicates procedure
  - SB ostial injury
  - MV stent deformation



Modified from Hildick-Smith D, TCT 2009
Picture from Lefevre T, Heart 2005

SB ballooning distorts MV stent struts

- Stent distortion can be corrected by kissing ballooning in the *in vitro* study .



Ormiston JA, CCI 2006

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Stent deformation was not corrected by kissing ballooning in clinical study

- N=23
  - IVUS after MV stenting
  - IVUS after SB ballooning
  - IVUS after Kissing ballooning

	Stent in MV	Dilatation of SB	Final KB
Proximal SA, mm^2	7.3 (1.9)	7.2 (1.9)	9.3 (2.9)
SA SB origin, mm^2	6.2 (1.2)	6.1 (1.6)	6.8 (1.9)
SA after SB origin, mm^2	5.9 (1.2)	5.2 (1.1)	5.6 (1.3)
Distal SA, mm^2	6.3 (1.3)	6.3 (1.2)	6.3 (1.2)

KB: kissing balloon; MV: main vessel; SA: stent area; SB: side branch.

Pan M, Rev Esp Cardiol 2008

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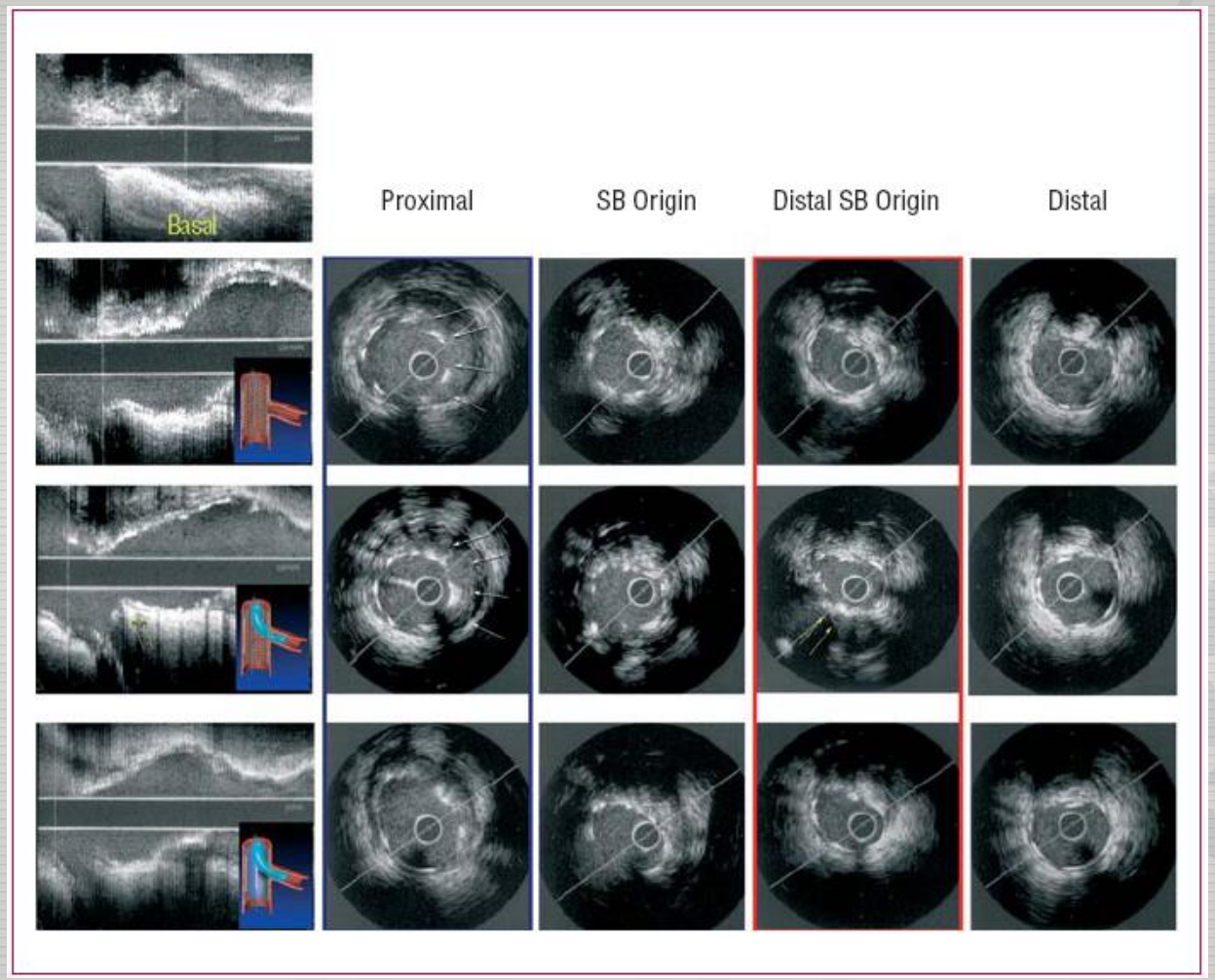
Stent deformation was not corrected by kissing ballooning in clinical study



Pan M, Rev Esp Cardiol 2008

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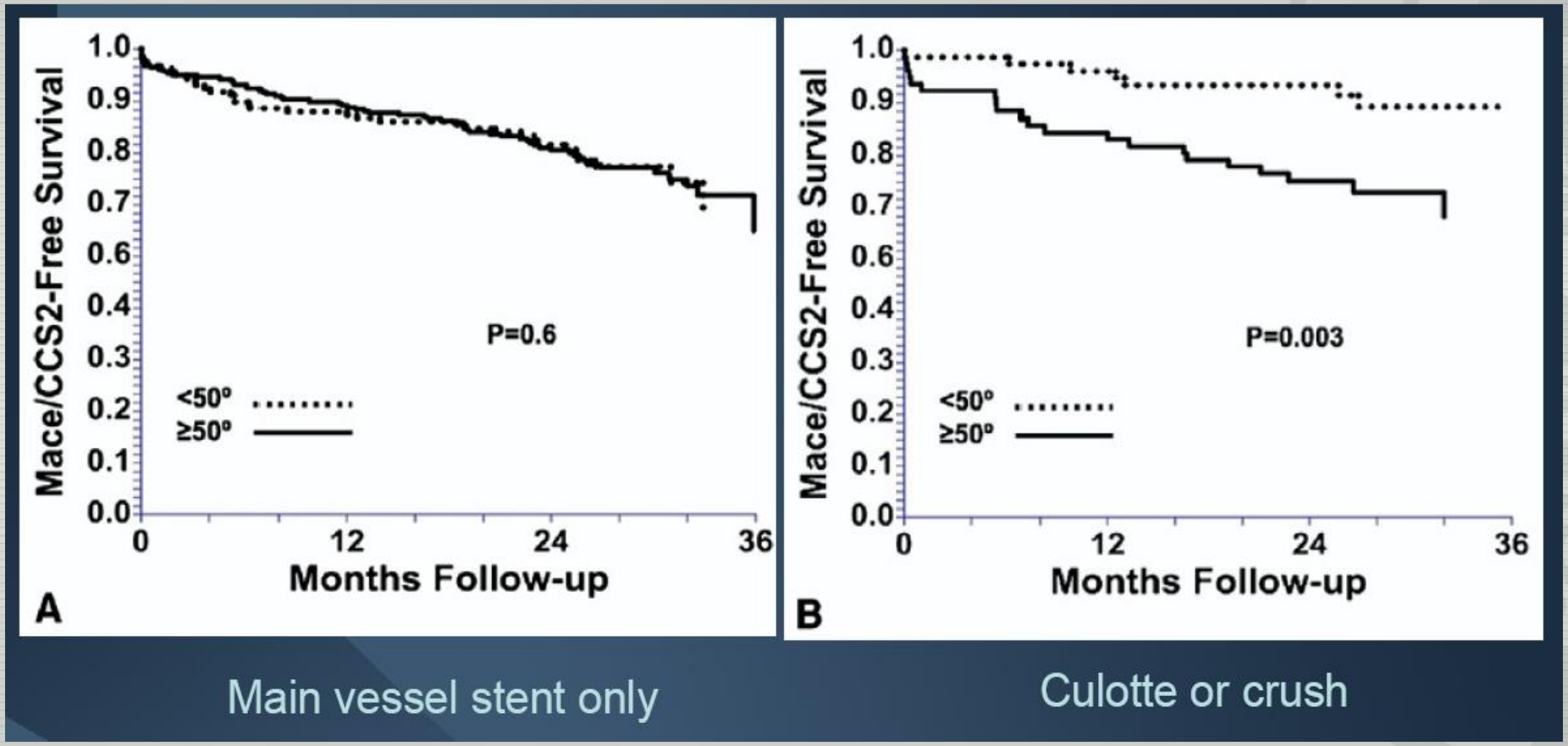
Culottes and Crush Techniques are Angle-dependent



Collins et al. Am J Cardiol 2008

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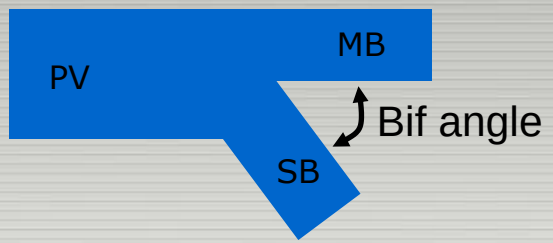
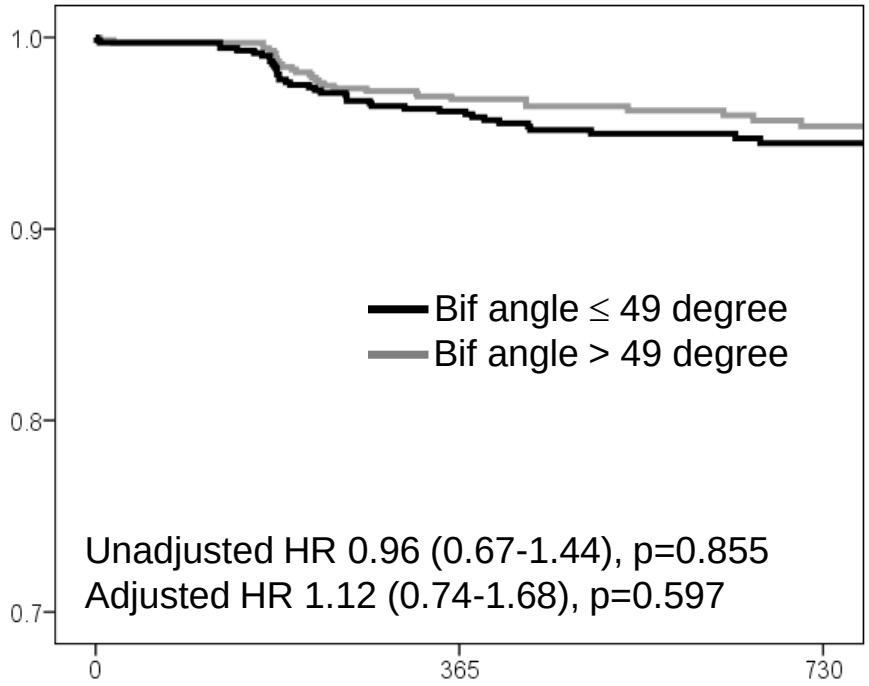
Bifurcation Angle is not Predictive

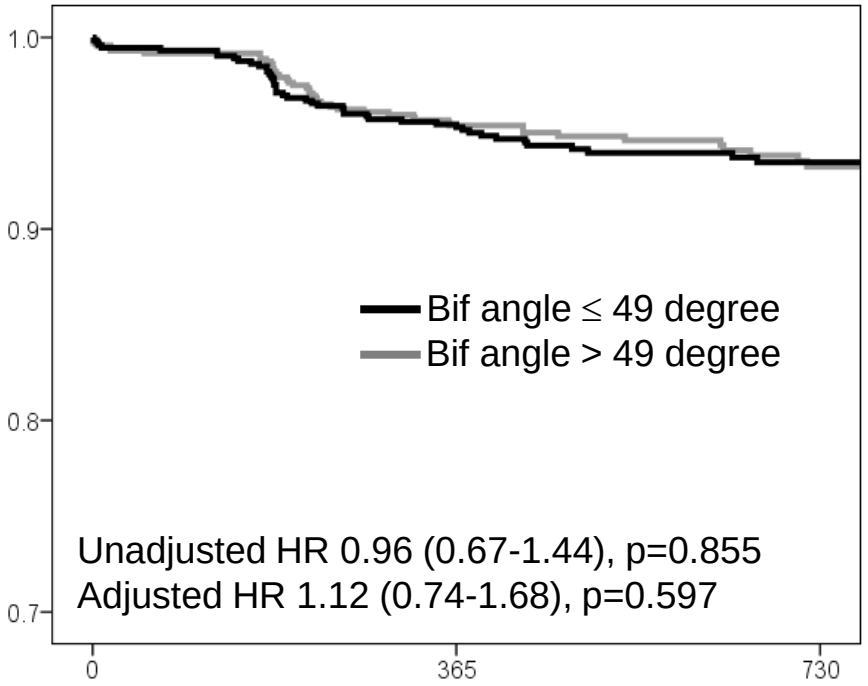


N=1455
Median: 49 degree

TLR



MACE



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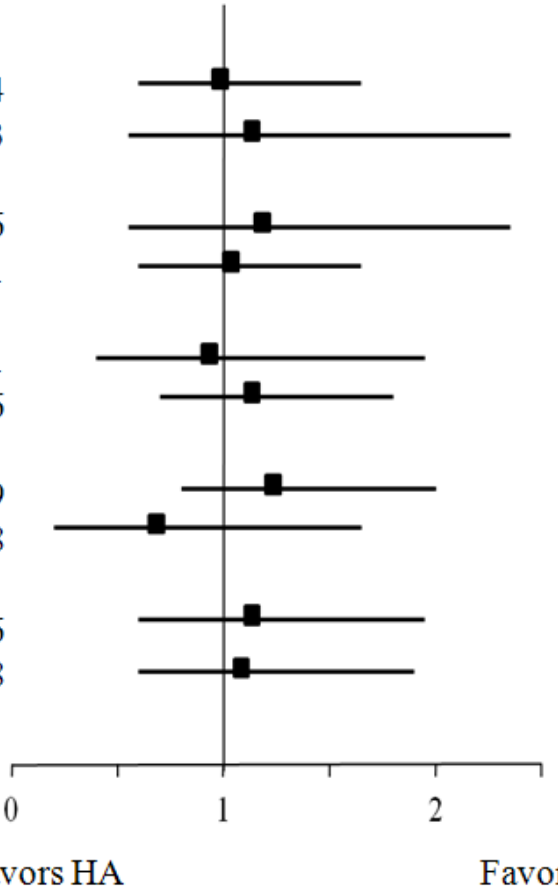
Bifurcation Angle is not Predictive

Subgroup Analysis (MACE)

Subgroups	Number of patients	Hazard ratio	95% CI	P for interaction
Diabetes				
No	1014	1.00	0.61-1.66	0.85
Yes	463	1.13	0.55-2.34	
Presentation				
Non-ACS	636	1.16	0.57-2.34	0.76
ACS	841	1.01	0.61-1.67	
True bifurcation				
No	451	0.89	0.41-1.95	0.63
Yes	1026	1.12	0.69-1.82	
Stenting technique				
1-stent	1229	1.26	0.79-2.02	0.18
2-stent	248	0.57	0.20-1.63	
PV stenting				
non-PES	926	1.10	0.62-1.96	0.99
PES	508	1.05	0.58-1.91	



HA: high angle > 49 degree, LA: low angle ≤ 49 degree

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Summary and Conclusion

- This large-scale multicenter real-world registry showed a favorable long-term prognosis in the patients with a non-left main coronary bifurcation lesion, mostly treated with a simple technique using DES.
- The simple technique is equal to, or can be better than the complex technique.
  - The angiographic success of side branch was not predictive of long-term outcomes.
  - Elective SB ballooning after MV stenting could be harmful.
- These results may not be applied to left main bifurcation, with a large side branch.

Thank you for your attention.

COBIS vs. Previous RCT Studies

	NORDIC	CACTUS	BBC-ONE	COBIS
FU duration	6-month	6-month	9-month	12-month
True bifurcation	-	94%	83%	69%
2-stent technique	50%	66%	47%	17%
TLR				
Simple technique	1.9%	6.3%	4.8%	3.5%
Complex technique	1.0%	7.3%	3.6%	2.9%
Stent thrombosis				
Simple technique	0.5%	1.2%	0.4%	0.5%
Complex technique	0.0%	1.7%	2.0%	0.4%

Steigen TK, Circulation 2006
Colombo A, Circulation 2009
Hildick-Smith D, TCT 2008

T-stenting was NOT Angle-dependent

	All lesions (N=130)	Angle < 60° (N=62)	Angle ≥ 60° (N=68)	P Value
Cardiac death	3 (2.3)	1 (1.6)	2 (2.9)	> 0.99
MI	3 (2.3)	1 (1.6)	2 (2.9)	> 0.99
TLR	20 (15.4)	9 (14.5)	11 (16.2)	0.79
Main vessel only	9 (6.9)	6 (9.7)	3 (4.4)	
Side branch only	8 (6.2)	2 (3.2)	6 (8.8)	
Both	3 (2.3)	1 (1.6)	2 (2.9)	
Stent thrombosis	2 (1.5)	1 (1.6)	1 (1.5)	> 0.99
MACE*	22 (16.9)	10 (16.1)	12 (17.6)	0.82

* MACE = cardiac death, MI, TLR

Song YB, Gwon HC, ACC/i2 2010

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