COBIS III,

where are we from and where we go?

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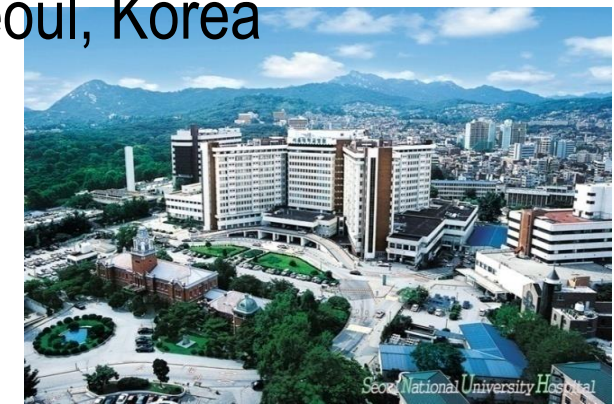


COBIS st

- Investigator-initiated nation wide multicenter regist
- Endorsed by Korean Society of Interventional Car
- Sponsored and managed by Korean Bifurcation C

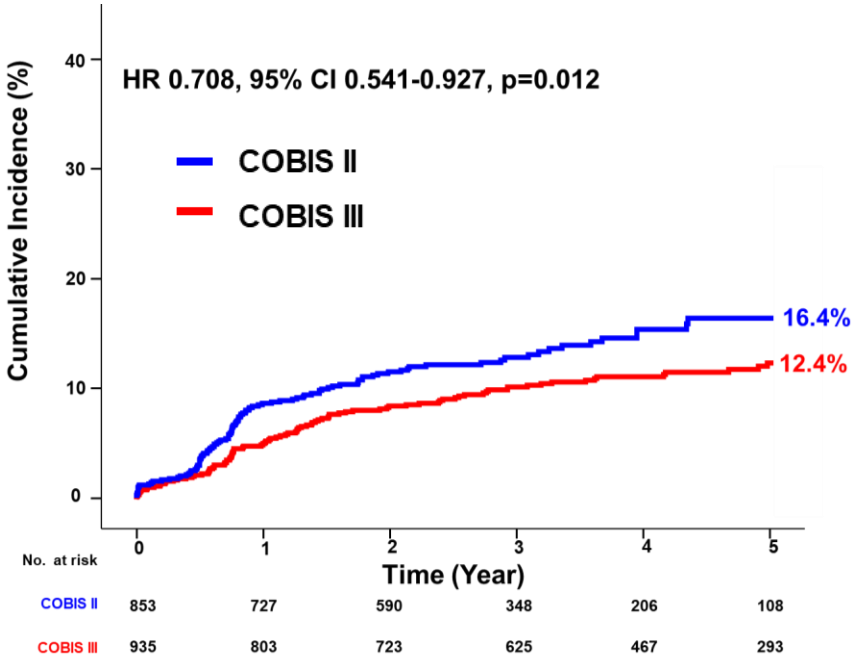
- KBC research committee
- Dedicated QCA core laboratory
- CRO
- Independent statistical analysis team
- Event adjudication committee

	COBIS I	COBIS II	COBIS III
Patients No.	**1691**	**2897**	**2648**
Enrollment period	**2004.1~2006.6**	**2003.1 ~ 2009.12**	**2010.1 ~ 2014.12**
Inclusion			
Main vessel Diameter, mm	≥ 2.5	≥ 2.5	≥ 2.5
Side branch Diameter, mm	**≥ 2.0**	**≥ 2.3**	**≥ 2.3 (by QCA)**
Left main bifurcation	**X**	**O**	**O**
DES generation	**1st**	**1st + 2nd**	**2nd only**
Median Follow-up Duration	**25 months**	**38 months**	**53 months**

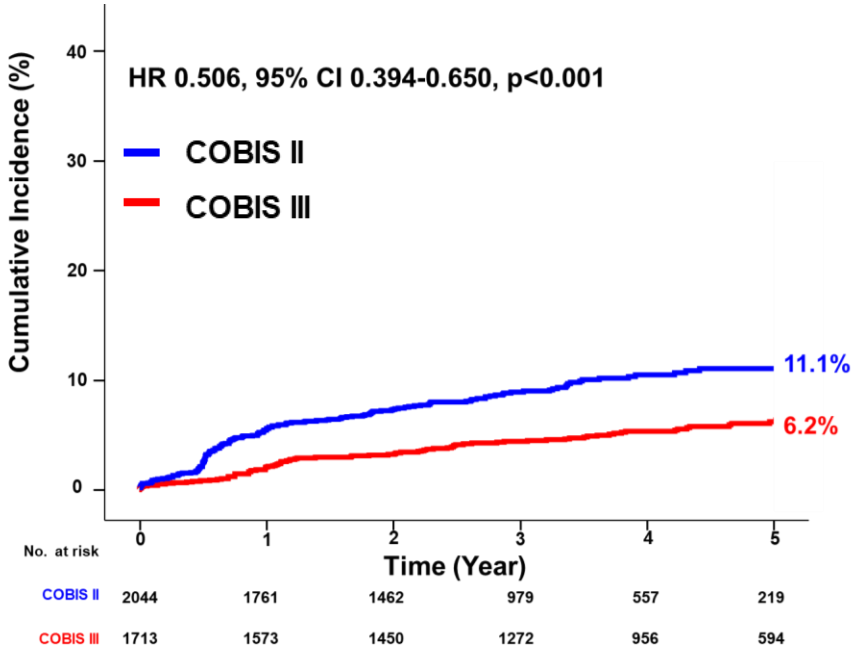
What makes the difference?

Device? Concept? Technique?

TLF in LM bifurcation



TLF in non-LM bifurcation



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- Safer access: More trans-radial approach
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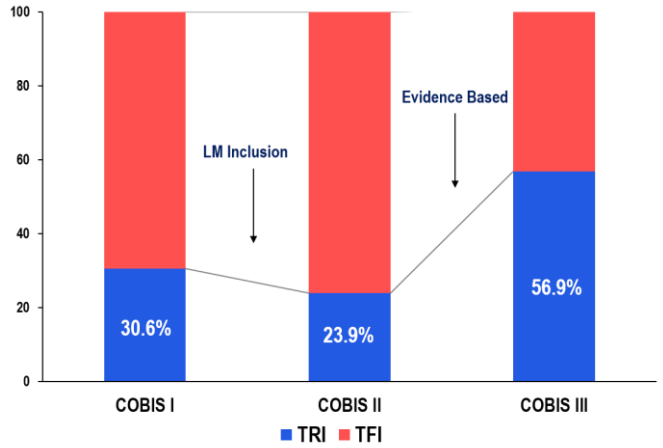
- Better concept: imaging guidance, SB relevance
- Better risk stratification: SB occlusion, risk stratification

COBIS Registry

Transradial vs. Transfemoral for Bifurcation PCI



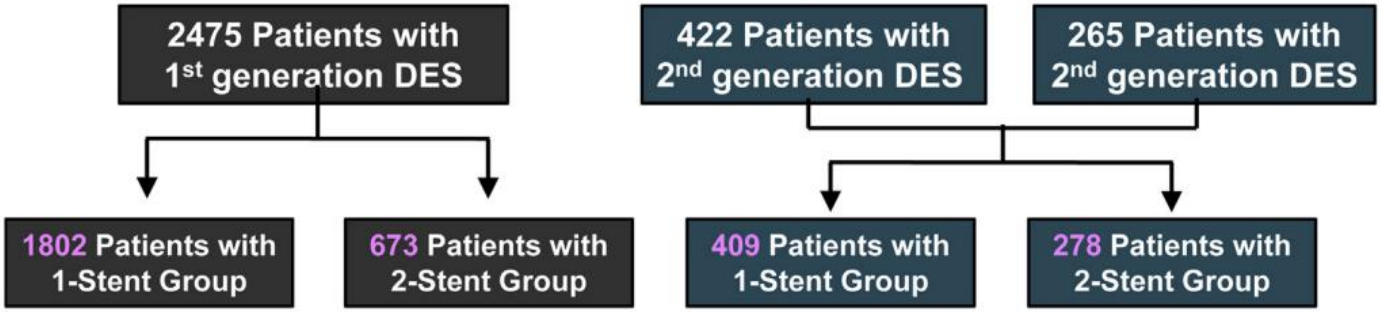
- LM bifurcation lesions from COBIS II (N=853)
- Transradial (N=212, 24.9%) vs. Transfemoral (N=641)
- Propensity score-matched analysis (1:2 ratio, 161 pairs)

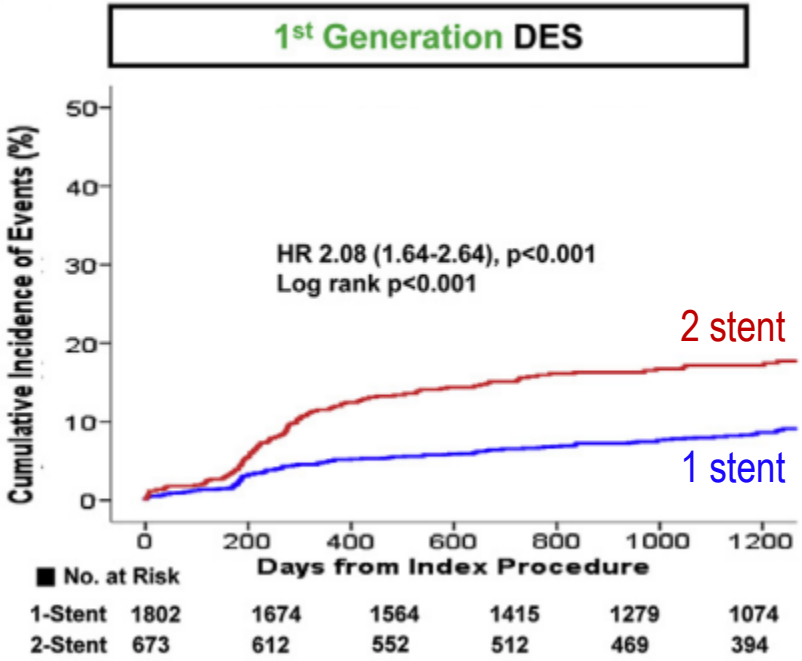
	Transradial (N=161)	**Transfemoral** (N=322)	**Adjusted HR** (95% CI)	**p**
MACE	14 (8.7)	37 (11.5)	0.48 (0.22-1.03)	0.06
Cardiac death	4 (2.5)	5 (1.6)	0.33 (0.02-4.97)	0.42
Cardiac death or MI	7 (4.3)	8 (2.5)	1.42 (0.35-5.69)	0.62
TLR	7 (4.3)	32 (9.9)	0.30 (0.11-0.81)	0.02
TIMI major or minor bleeding	4 (2.5)	27 (8.4)		0.01

Chung SM, et al., J Invasive Cardiol 2015

Korean Bifurcation Pooled Cohort

1st vs. 2nd generation DES



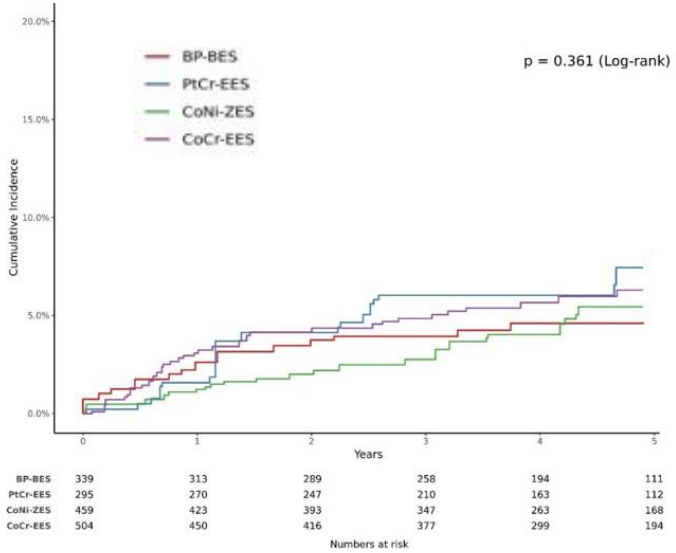


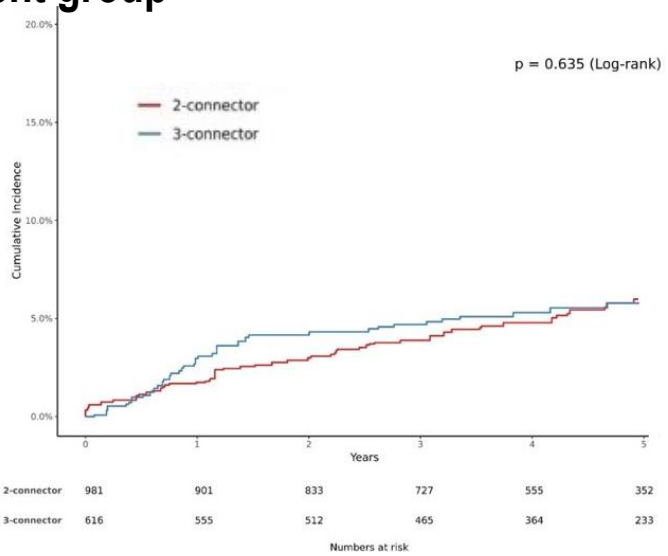
Lee JM, et al, JACC Interv 2015

COBIS III registry

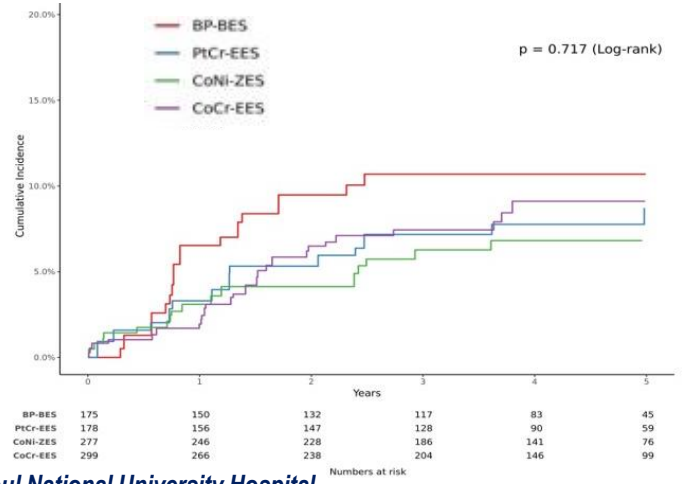
Clinical outcome among 2nd generation DES

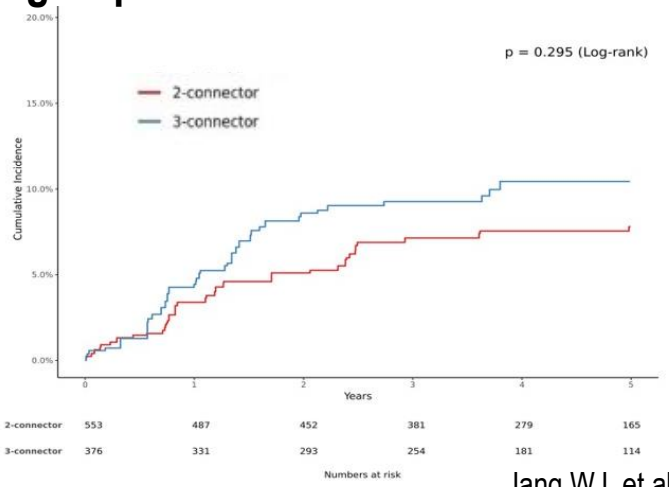
SB No treatment group





SB Treatment group

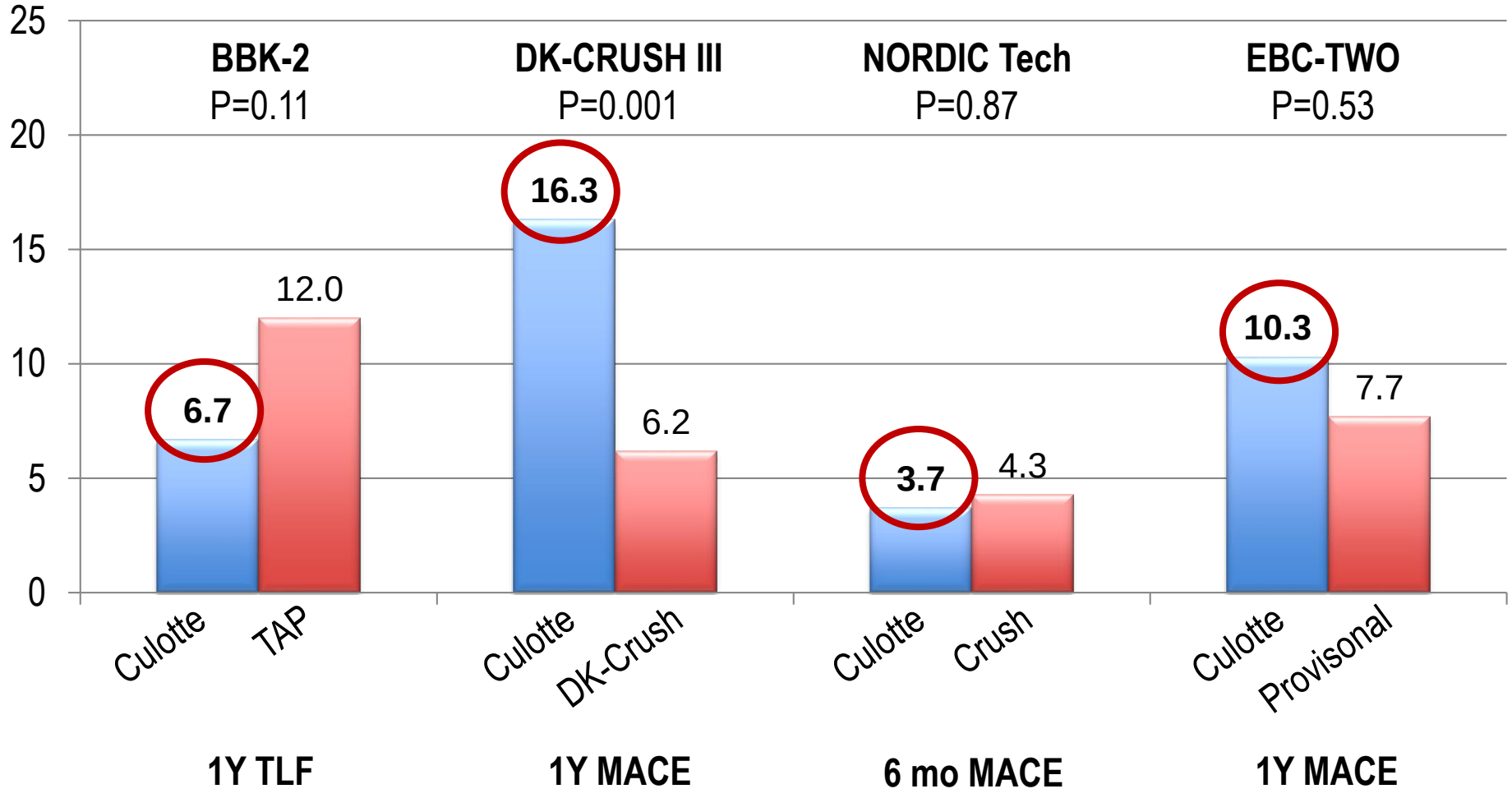




Jang WJ, et al. Under review

What is the best 2-stent technique?

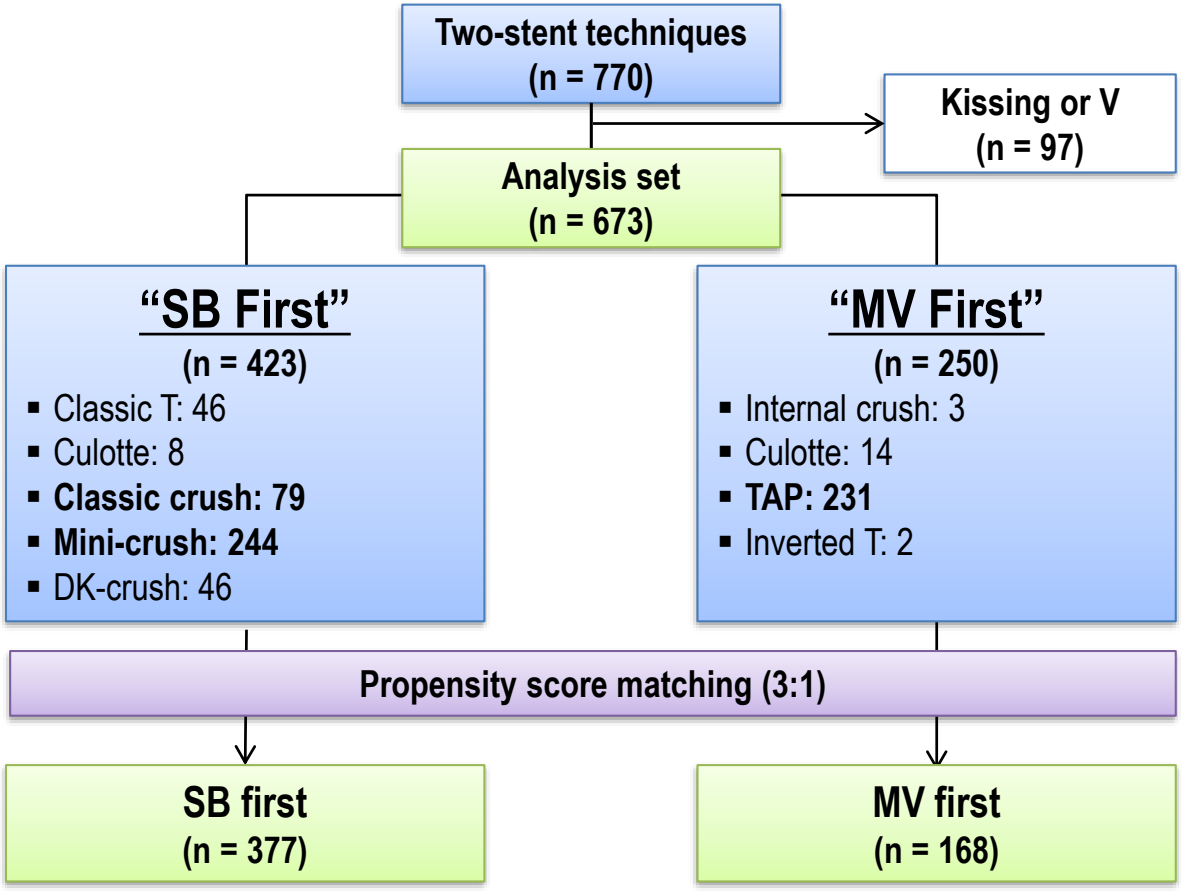
TAP technique? Culotte technique? DK crush technique?



COBIS II registry

What is the best 2-stent technique?

- N=673, treated with 2-stent technique (exclusion: kissing or V-stenting)



Park TK, et al., Eurointervention 2017

COBIS II registry

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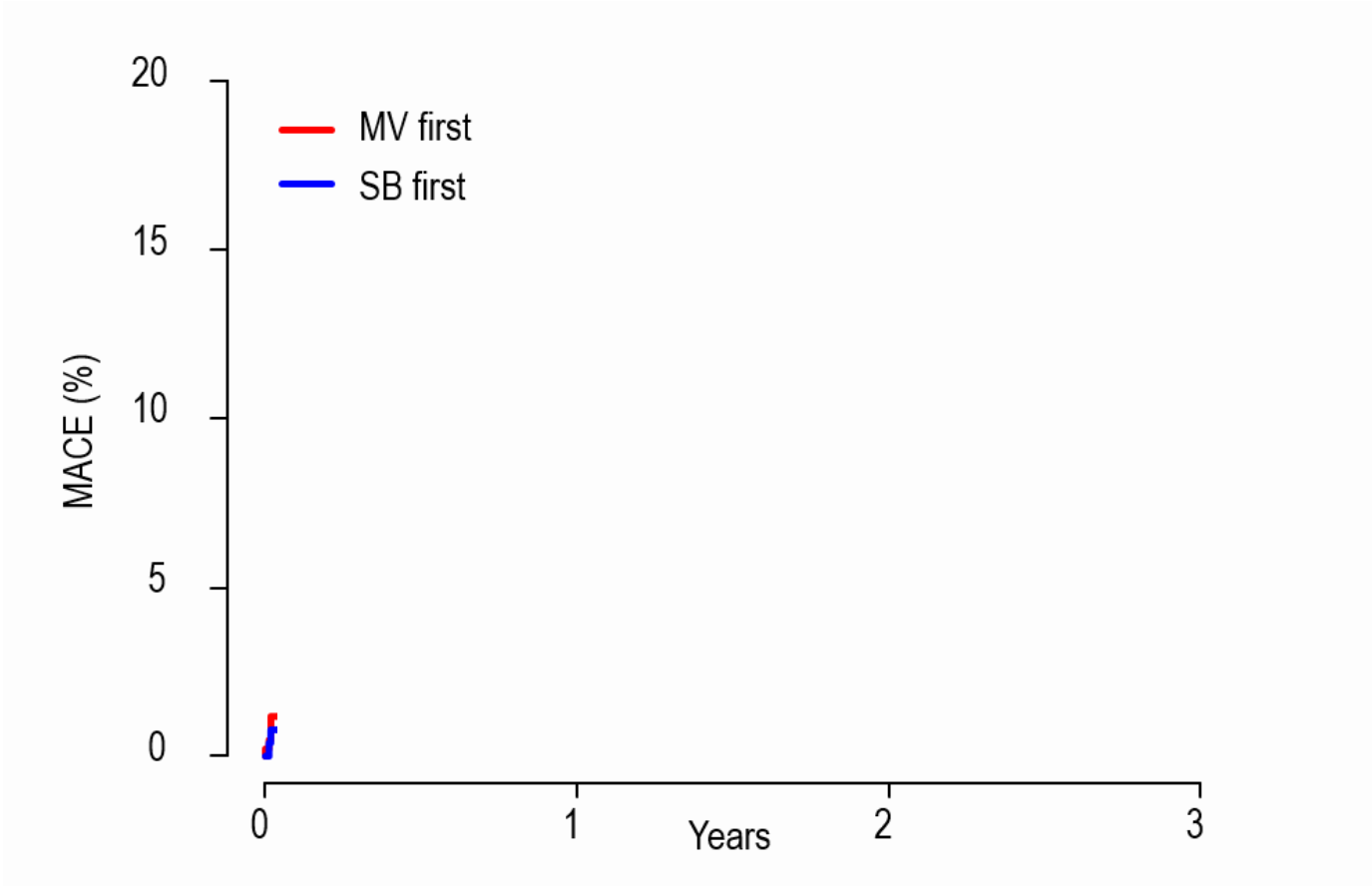

Park TK, et al., Eurointervention 2017

COBIS III registry

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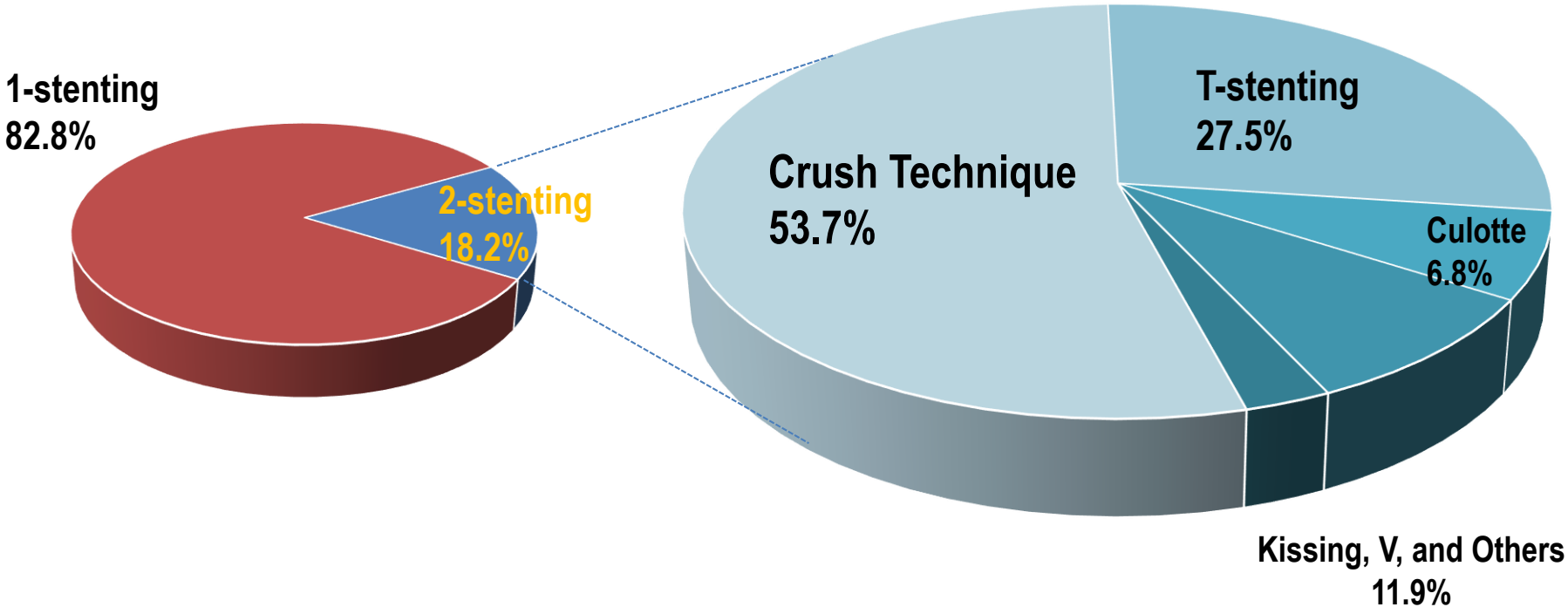
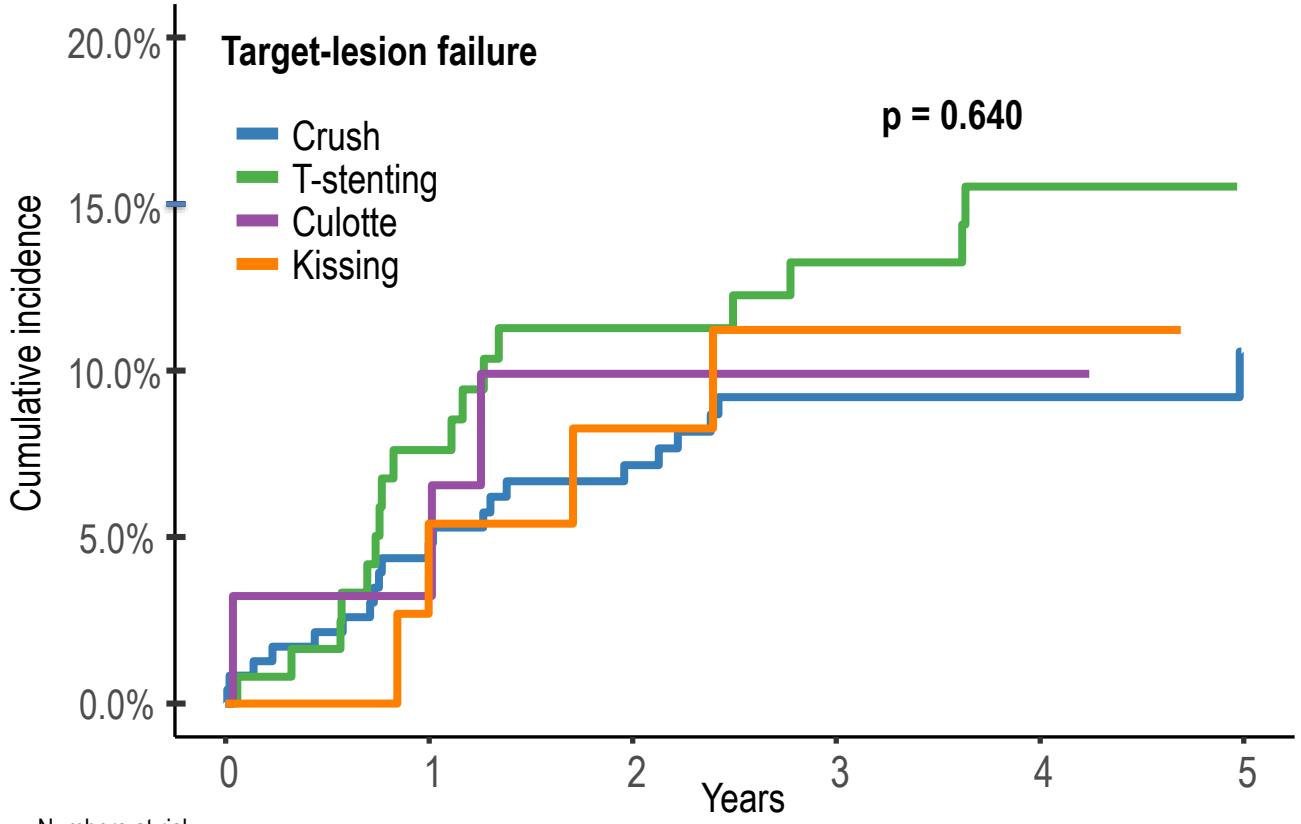


Kang JH, et al., KBC workshop 2019

COBIS III registry

What is the best 2-stent technique?



Numbers at risk

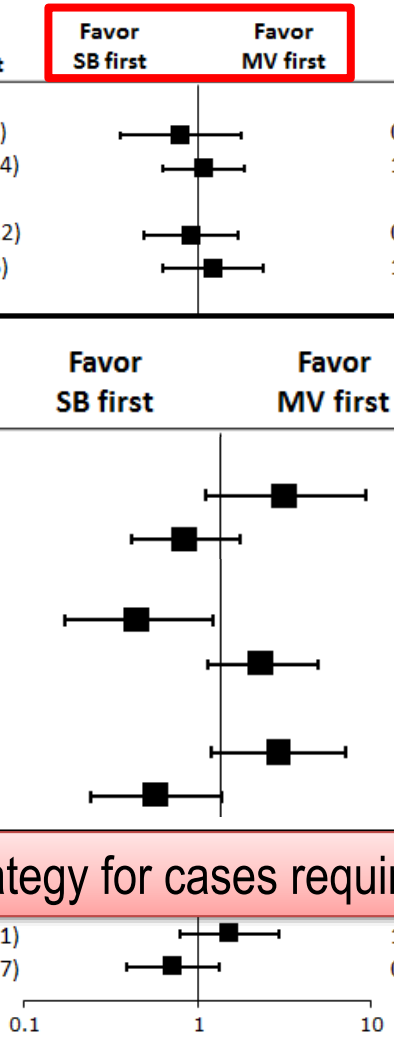
Crush	244	210	187	152	108	64
T-stenting	125	104	94	85	66	39
Culotte	31	29	26	23	13	10
Kissing	41	35	32	27	17	11

Kang JH. KBC workshop 2019

Insight from COBIS II registry

What is the best 2-stent technique?

Subgroup	Patients	TLR (%) SB first	TLR (%) MV first	Hazard ratio (95% CI)	p value	p for Interaction
MV RD						0.52
≥3.25 mm	217	12/120 (10.0)	12/97 (12.4)	0.80 (0.36-1.78)	0.59	
<3.25 mm	456	40/303 (13.2)	19/153 (12.4)	1.09 (0.63-1.88)	0.77	
SB RD						0.54
≥2.5 mm	276	20/151 (13.2)	19/125 (15.2)	0.92 (0.49-1.72)	0.79	
<2.5 mm	397	32/272 (11.8)	12/125 (9.6)	1.23 (0.63-2.38)	0.55	
SB RD > MV RD						0.78
MV DS						0.04
≥70%	257	22/156 (14.1)	8/101 (7.9)	1.94 (0.86-4.36)	0.11	
<70%	416	30/267 (11.2)	23/149 (15.4)	0.71 (0.41-1.22)	0.22	
SB DS > MV DS						0.008
Yes	252	17/189 (9.0)	12/63 (19.0)	0.44 (0.21-0.92)	0.03	
No	420	35/234 (15.0)	19/186 (10.2)	1.54 (0.88-2.68)	0.13	
MV Lesion Length						0.01
≥18 mm	329	36/215 (16.7)	11/114 (9.7)	1.79 (0.91-3.53)	0.09	
<18 mm	344	16/208 (7.7)	20/136 (14.7)	0.53 (0.27-1.01)	0.05	
≥65°	293	27/167 (16.2)	14/126 (11.1)	1.53 (0.80-2.92)	0.20	
<65°	380	25/256 (9.8)	17/124 (13.7)	0.72 (0.39-1.33)	0.29	



"MORE severe lesion FIRST" strategy for cases requiring systematic 2 stenting.

Park TK, et al., Eurointervention 2017

What makes the difference?

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- Safer access: More trans-radial approach
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"KISS" for 1-stent technique: Good or Bad?

	Number Design	Primary endpoint	Outcomes	Results	Memo
Niemela M (NORDIC III) Circulation 2011	N=477 RCT	6-mo MACE	FKB 2.9%, non-FKB 2.9% P=NS	**Neutral**	
Gwon HC (COBIS I) Heart 2012	N=1,065 Registry	2-year MACE	FKB 9.5%, non-FKB 4.5% p=0.02	**Bad**	Higher MV TLR in FKB group
Yamawaki M Circ J 2014	N=253 Registry	3-year MACE	FKB 14.6% vs. non-FKB 6.9% p=0.07	**Bad**	Higher MV restenosis in FKB-group
Kim TH Int J Cardiol 2014	N=251 Registry	3-year MACE	FKB HR=0.40 (95% CI 0.19–0.84), p=0.015	**Good**	ACS patients
Biondi-Zoccai G Heart Vessels 2014	N=2,813 Registry	2-year MACE	HR=1.01 (0.80–1.23) p=0.91	**Neutral**	
Gao Z Chin Med J 2015	N=790 Registry	4-year MACE	FKB: 7.8%, non-FKB 10.0% p=0.33	**Neutral**	Left main bifurcation
Kim YH (CROSS) JACC CVI 2015	N=306 RCT	1-year MACE	FKB 14.0%, non-FKB 11.6% p=0.57	**Bad**	Higher MV restenosis in FKB group
Yu CW (COBIS II) JACC CVI 2015	N=1,901 Registry	3-year MACE	HR=0.50 (95% CI: 0.30- 0.85),p = 0.01	**Good**	Lower MV TLR in FKB group

COBIS II Registry

"KISS" for 1-stent techniques

- Treated with 1-stent technique: N=1,901
- Final kissing ballooning (FKB): N=620 → PSM matched analysis: N=545 pairs

	Propensity-Matched Population			
	FKB (n = 545)	Non-FKB (n = 545)	p Value	Standardized Difference
After MV stenting				
Main vessel				
Proximal MLD	3.07 ± 0.55	3.02 ± 0.58	0.85	9.2
Middle MLD	2.76 ± 0.54	2.71 ± 0.56	0.72	9.6
Distal MLD	2.76 ± 0.49	2.72 ± 0.54	0.85	8.6
Side branch				
Ostial MLD	1.26 ± 0.73	1.25 ± 0.69	0.71	1.3
Distal MLD	2.02 ± 0.69	1.96 ± 0.68	0.67	7.8
Final				
Main vessel				
Proximal MLD				
Middle MLD	2.86 ± 0.50	2.72 ± 0.56	0.001	
Distal MLD	2.83 ± 0.48	2.73 ± 0.55	0.04	
Side branch				
Ostial MLD	1.85 ± 0.62	1.36 ± 0.69	<0.001	
Distal MLD	2.15 ± 0.59	1.99 ± 0.68	0.04	

FKB reduces main vessel TLR, not side branch TLR.

"Gentle KISS for MB and SB"

	Adjusted HR (95% CI)	p
MACE	**0.50** (0.30-0.85)	0.01
Cardiac death	0.50 (0.11-2.29)	0.37
MI	0.18 (0.01-20.4)	0.48
Stent thrombosis,	0.77 (0.17-3.45)	0.73
	1)	0.02
Main vessel	**0.51** (0.28-0.93)	**0.03**
Side branch	0.57 (0.24-1.37)	0.21

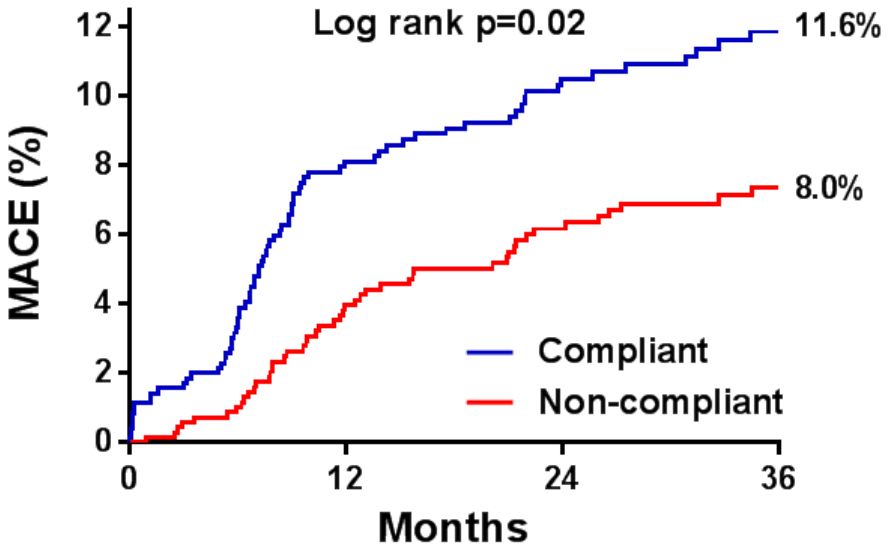
Yu CW and Yang JH, et al. JACC Interv 2015

COBIS II Registry

Clinical impact of NC balloon

- Use of non-compliant balloon: N=752, 26.0%
- Propensity score-matched analysis: N=710 pairs

	CB	NCB	p
Dissection >type B	1.1%	0.1%	0.046
Angiographic success			
Main vessel	99.0%	98.7%	0.80
Side branch	75.4%	79.7%	0.03
In-hospital MI	0.8%	0%	0.04



Park TK, et al., EuroIntervention 2016

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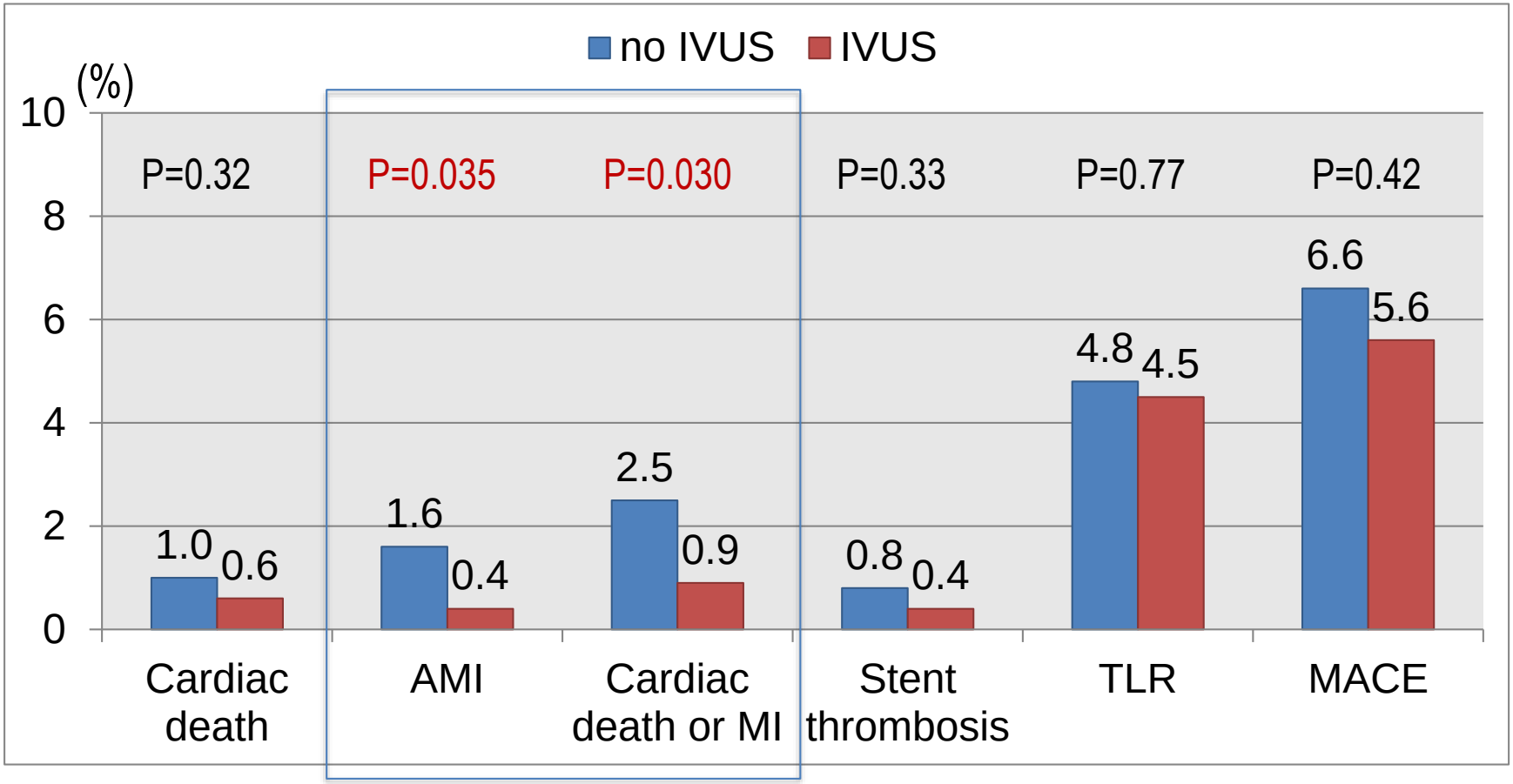
COBIS Registry
IVUS guidance improves outcomes



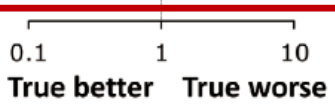
Kim JS, Am Heart J 2011

COBIS II Registry

True vs. Non-true bifurcation lesions: Clinical relevance of SB

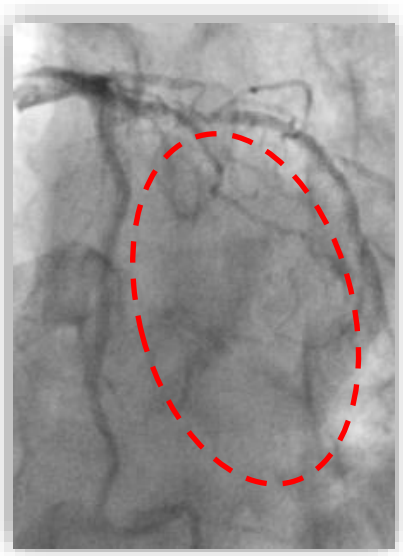
Subgroup	Patients	MACE (%) True	MACE (%) NonTrue	Adjusted HR (95% CI)	P value	P for Interaction
DM						
Yes	840	69 (15.8)	35 (8.7)	1.95 (1.24-3.07)	0.004	**0.10**
No	2057	112 (10.5)	80 (8.1)	1.18 (0.86-1.61)	0.31	
Presentation						
ACS	1798	117 (12.2)	71 (8.5)	1.35 (0.98-1.86)	0.06	**0.69**
Non-ACS	1099	64 (11.8)	44 (7.9)	1.56 (1.01-2.42)	0.05	
Left main						
Yes	853	66 (18.4)	48 (9.7)	1.22 (0.78-1.90)	0.38	**0.43**
No	2044	115 (10.1)	67 (7.4)	1.42 (1.04-1.95)	0.03	
Two stent						
Yes	770	102 (17.8)	23 (11.7)	1.54 (0.97-2.43)	0.07	**0.49**
No	2127	79 (8.5)	92 (7.7)	1.20 (0.87-1.65)	0.28	
FKB						
Yes	1349	109 (12.8)	39 (7.9)	1.56 (1.06-2.30)	0.03	**0.74**
No	1548	72 (11.1)	76 (8.5)	1.23 (0.87-1.76)	0.25	
Type						
1st						**0.53**
2nd						
SB reference diameter						
>2.5 mm	1154	72 (14.0)	43 (6.7)	2.16 (1.48-3.15)	<0.001	**0.02**
≤2.5 mm	1741	109 (11.0)	72 (9.6)	1.20 (0.89-1.62)	0.23	

Focus on true bifurcation with large SB.

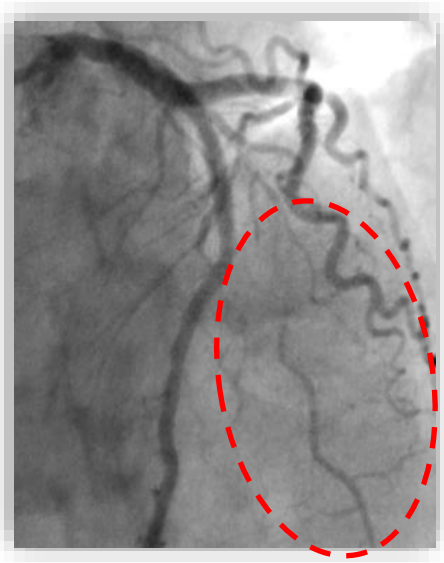


Park TK, et al., Circ J 2015

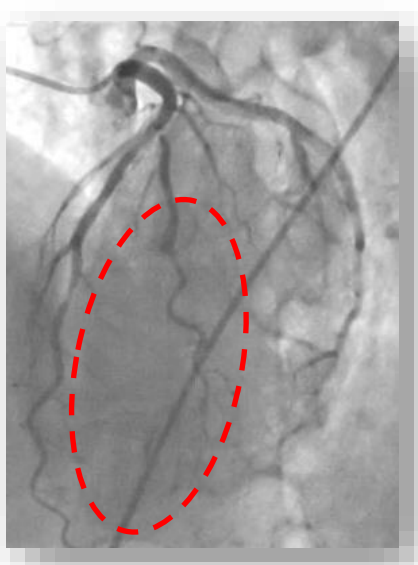
How large is large enough?



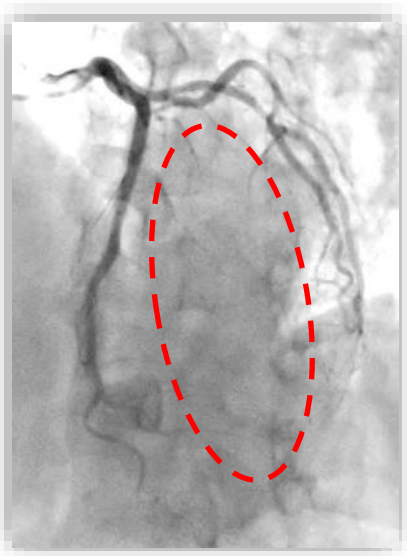
% ischemia: 15%



% ischemia: 11%



% ischemia: 10%



% ischemia: 12%

DECISION TREE LEARNING IS THE PROCESS OF CREATING/LEARNING A DECISION TREE FROM TRAINING DATA

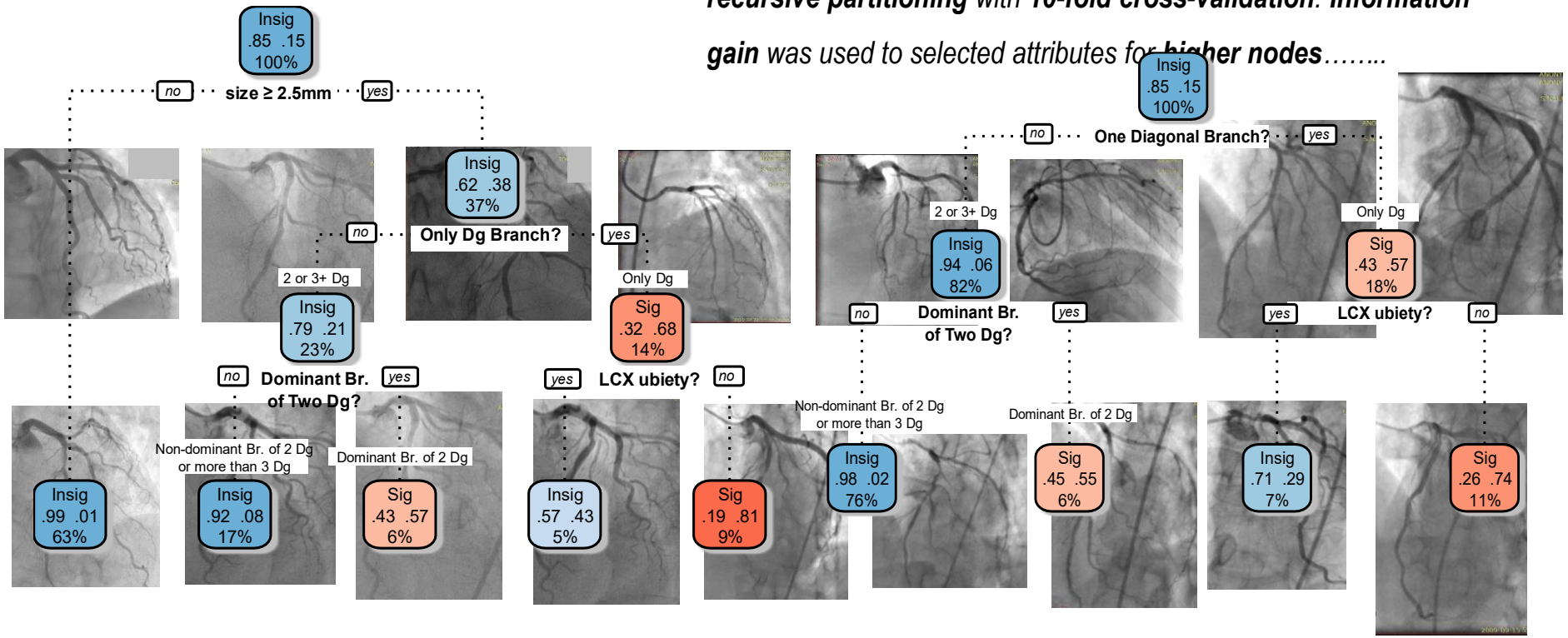
RECURSIVE PARTITIONING IS THE MOST COMMON STRATEGY FOR DECISION TREE LEARNING

ID3 C4.5 CART CHAID

DECISION TREE LEARNING ALGORITHMS BASED ON RECURSIVE PARTITIONING

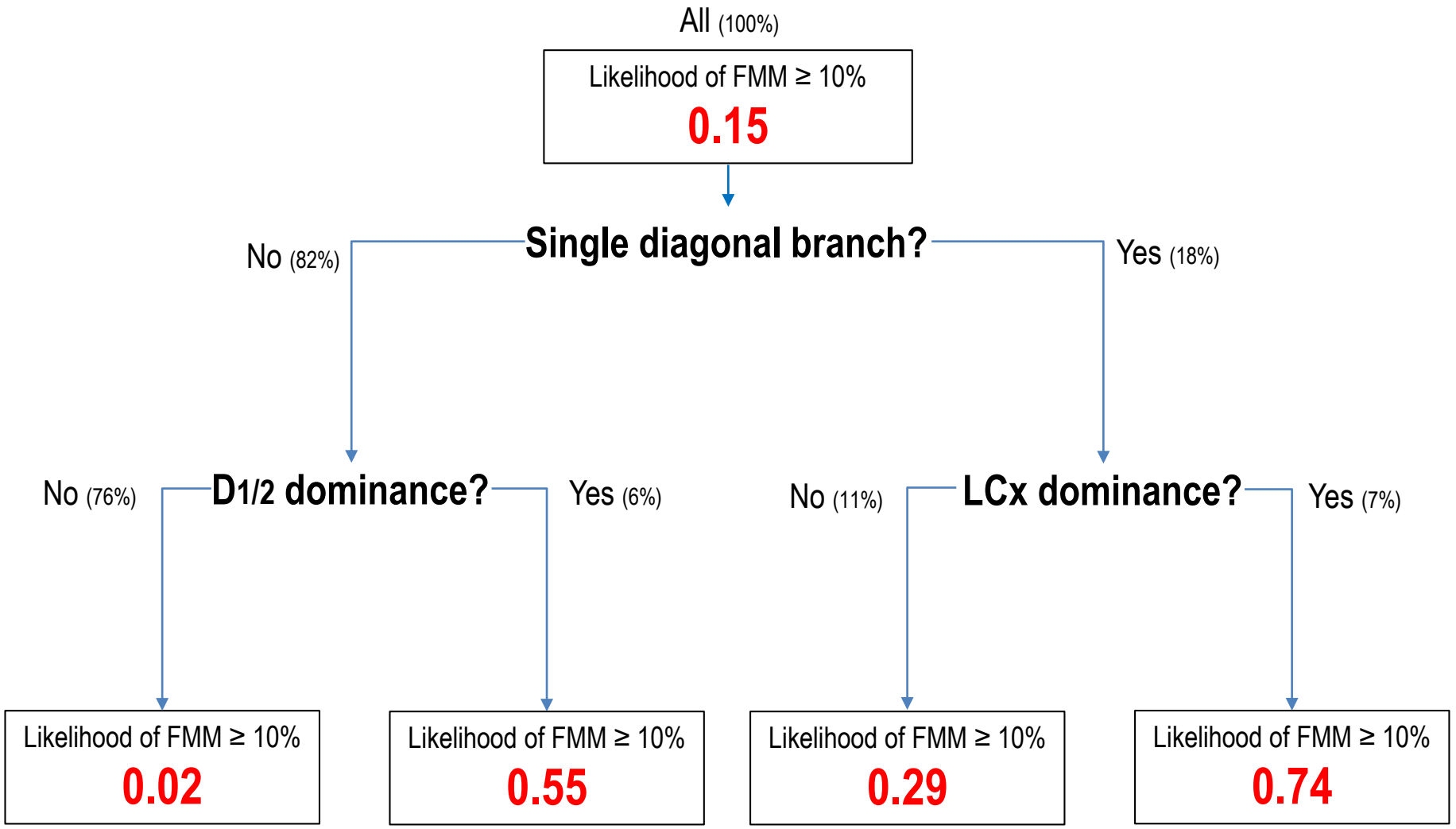
One branch? 2 branch? 3 branch? 2.8mm? 2.3mm? LCx dominance? D1/2 dominance? Non-dominant? ……..

…..To train and validate models to predict % FMM ≥ 10%, the entire CCTA dataset was split into training and validation sets (4:1). To build a decision tree model, the training and validation sets were used for ***recursive partitioning*** *with* ***10-fold cross-validation****.* ***Information gain*** *was used to selected attributes for* ***higher nodes****……..*



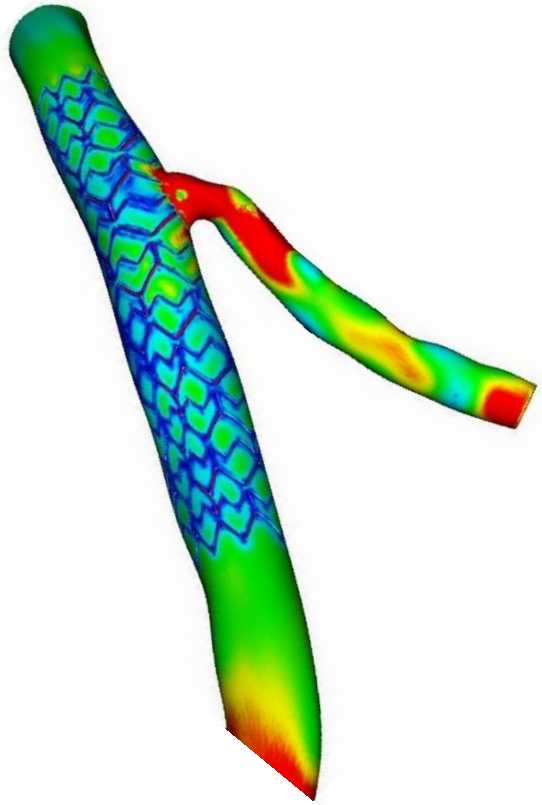
Jeon WK, Koo BK, et al. Eurointervention, In press

Decision Tree for % FMM ≥ 10%



Jeon WK, Koo BK, et al. Eurointervention, In press

Are you (un)happy with this?



Koo BK, LaDisa J, 2009

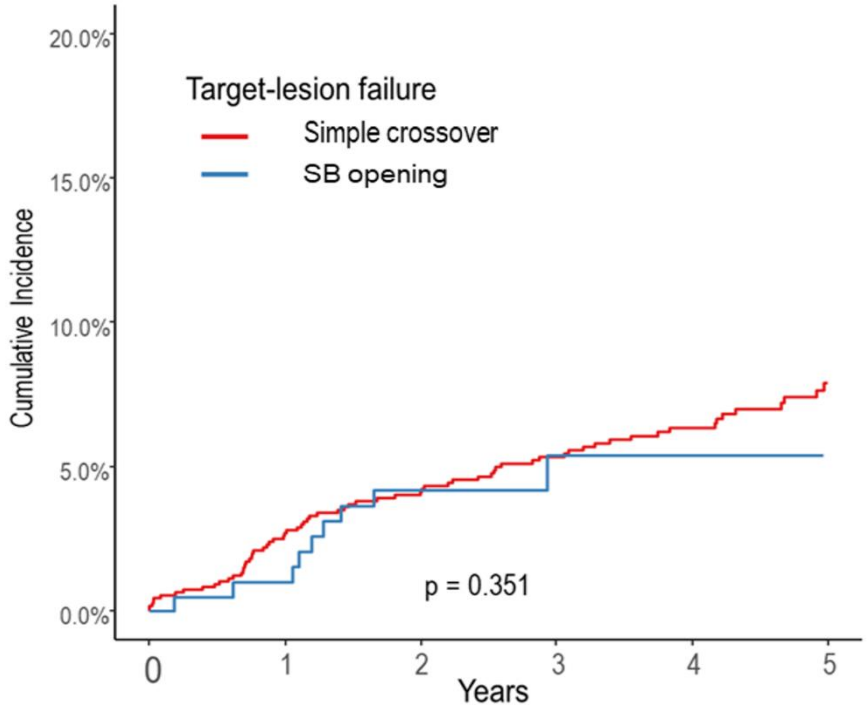
OCT: 18 mo after Cypher

Courtesy of Dr Otake

COBIS III Registry

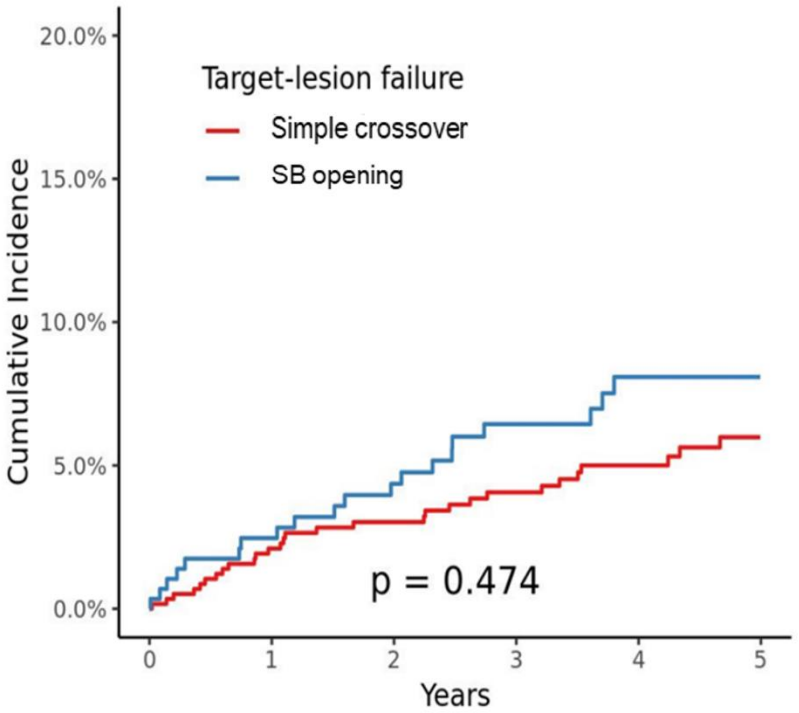
Clinical relevance of SB opening

Non-True Bifurcation



Leave alone	1085	979	909	808	619	372
SB opening	212	191	175	151	118	69

True Bifurcation



Leave alone	600	549	495	434	332	230
SB opening	297	267	244	207	146	90

Nam CW, et al. Preliminary data from COBIS 3 registry

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How to avoid SB compromise after MV stenting?

- **How to protect SB?**
  - Jailed wire technique
  - SB predilation
  - Optimal stent sizing, ……

Predictors of SB occlusion from COBIS II

Variables	OR [95% CI]	p Value
SB DS ≥50%	2.3 [1.59-3.43]	<0.001
SB lesion length (by 1 mm)	1.0[1.003-1.06]	<0.001
Proximal MV DS ≥50%	2.3 [1.57-3.50]	0.03
Acute coronary syndrome	1.5 [1.06-2.19]	0.02
Left main lesions	0.3 [0.16-0.72]	0.005

Hahn JY, et al. JACC 2013

Korean Bifurcation Pooled Cohorts

Predictors of TVF in 2-stent strategy

- Treated with 2-stent strategy: N=951

	Adjusted HR*	95% CI	p Value
Treated bifurcation in LM	2.09	1.43 – 3.03	<0.001
High SYNTAX score >32	2.00	1.28 – 3.14	0.002
Diabetes mellitus	1.41	1.00 – 1.99	0.05
Second-generation DES	0.26	0.12 – 0.57	0.001
Non-compliant balloon	0.53	0.36 – 0.79	0.002
Final kissing ballooning	0.44	0.29 – 0.68	<0.001

*Adjusted for age (continuous), acute coronary syndrome as presentation, preprocedural hemoglobin level, pre-procedural creatinine level, bifurcation angle (continuous), multi-vessel coronary disease, transradial approach, intravascular ultrasound, provisional approach, stenting techniques, total stent length in side branch (continuous).

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Conclusion

- COBIS registry started with bifurcation PCI patients since 2004 are still ongoing with dedicated QCA core laboratory/CRO, independent statistical analysis team and event adjudication committee.
- Results of COBIS studies expanded our knowledge on bifurcation treatment and improved the patients' clinical outcomes.
- Ongoing COBIS III study will provide more insights on coronary bifurcation lesions and their treatment.