Contemporary Bifurcation PCI: How Advance Over Time?

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Coronary bifurcation lesion

- Approximately 15–20% of all coronary lesion
- One of the most challenging therapeutic procedures.
- Outcomes for bifurcation lesions have steadily improved since last decades
- Controversies about best treatment strategy in bifurcation lesions





Bifurcation PCI What We Know?

Single stent strategy with provisional stenting of SB

2. Two-stents strategy





Meta-Analysis of 12 Major Studies, 6961 Patients (5 RCTs and 7 observational studies) *Provisional Single-Stenting is better than Double-Stenting*

A DES Thrombosis				C Myocardial Infarction											
Study	Year	DDS	SDS	DDS better	SDS better	Weight*	RR (random) 95% CI	Study	Year	DDS	SDS	DDS better	SDS better	Weight*	RR (random) 95% C
RANDOMIZE	, CONT	ROLLED	TRIALS					RANDOMIZER	, CONT	ROLLED	TRIALS				
NORDIC	2008	1/196	2/199			5.37%	0.50 (0.04-5.55)	NORDIC	2008	39/196	20/199		-	16.86%	1.97 (1.19-3.26)
Ferenc et al.	2008	2/101	1/101			5.40%	2.00 (0.18-21.71)	Ferenc et al.	2008	2/101	1/101		-	1.80%	2.00 (0.18-21.71)
CACTUS	2009	3/177	2/173		-	9.73%	1.46 (0.24-8.66)	CACTUS	2009	19/177	15/173			13.48%	1 28 (0.65-2.35)
BC-ONE	2010	5/249	1/248			6.71%	4.97 (0.58-42.31)	BBC-ONE	2010	28/249	9/248		+	11.76%	3.09 (1.49-6.43)
OK-CRUSH-II	2011	4/185	1/185			6.45%	4.00 (0.45-35.44)	DK-CRUSH-II	2011	6/185	4/185		-	5.59%	1 50 (0.43-5.22)
META-ANALY	SIS	15/908	7/906		-		2.01 (0.77-5.23)	META-ANALY	SIS	94/908	49/906		+		1.88 (1.35-2.62)
Cochrane Q: 2.	46 (p: 0.6	151) l [‡] : 0%						Cochrane Q: 3.5	ie (p: 0.4	153) 户: 0%					
ONRANDON	NZED, C	DBSERVA	TIONAL S	TUDIES				NONRANDON	NZED, O	DBSERVA	TIONAL	TUDIES			
Ge et al.	2007	3/57	0/117		· · ·	3.54%	14.24 (0.74-271.13)	Ge et al.	2007	13/57	5/117			8.04%	5.33 (1.99-14.24)
Di Mario et al.	2007	4/109	0/38	(-		3.66%	3.19 (0.17-57.92)	Di Mario et al.	2007	7/109	2/38	100		4.01%	1.22 (0.26-5.62)
ART'S II	2007	1/61	4/263			6.50%	1.07 (0.12-9.47)	ARTS II	2007	3/61	16/263		_	5.94%	0.80 (0.24-2.68)
COBIS	2010	2/292	9/1376	_		13.17%	1.04 (0.22-4.82)	COBIS	2010	5/292	15/1376			7.78%	1.57 (0.57-4.28)
-CYPHER	2011	3/263	10/1870		-	18.64%	2.13 (0.59-7.70)	J-CYPHER	2011	6/263	39/1870			9.77%	1.09 (0.46-2.55)
I-PMS	2011	4/37	2/263			11.12%	14.21 (2.69-74.92)	J-PMS	2011	5/37	6/263			6.48%	5.92 (1.90-18.44)
Assali et al.	2011	2/141	3/260	-	-	9.72%	1.23 (0.21-7.27)	Assail et al.	2011	7/141	10/260			8.49%	1.29 (0.50~3.32)
META-ANALY	SIS	19/960	27/4187		+		2.55 (1.13-5.78)	META-ANALY	SIS	43/960	93/4187		1		1.85 (1.03-3.32)
Cochrane Q: 8.	08 (p: 0.2	34) 19: 25.5	7%					Cochrane Q: 12	79 (p: 0.	041) IP: 53	11%				
META-ANALY Cochrane Q; 10	SIS (65 (p. 0	34/1868 473) P: 0%	35/5093	-	*	100%	2.31 (1.33-4.03)	META-ANALY Cochrane Q: 16	SIS .34 (p: 0	140/1727 129) 1 ² 32	142/5093		•	100%	1.86 (1.34-2.60)
				0.01 0.1 RR (1 10 100 LOG SCALE)	1000						0.01 0.1	1 10 100 00 500 E	1000	
		S	ingle	-stent	Two-s	tent		1			Single	e-stent	Two-	stent	

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Zimarino et al. J Am Coll Cardiol Intv 2013;6:687–95



CENTRAL ILLUSTRATION Simplified Approach to Treatment of Bifurcation Lesions





Sawaya, F.J. et al. J Am Coll Cardiol Intv. 2016;9(18):1861-78.



What Really Matters in Bifurcation PCI; Techniques or Concept?

There has been conceptual changes for bifurcation PCI !!

Functional Concept
Imaging Concept





Functional Concept of Bifurcation PCI To Treat or Not To Treat ?



Side Branch FFR After Main Vessel Stenting (n=232)



Ahn JM et al, JACC Cardiovasc Interv. 2011 Feb;5(2):155-61



Imaging Concept of Bifurcation PCI

Rule of Thumb - Effective Stent Area (Rule of 5,6,7,8 mm²) Restenosis Rate < 5% and TLR < 2%





Kang et al. Circ Cardiovasc Interv 2011;4:1168-74







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Lee, P.H. et al. J Am Coll Cardiol. 2016;68(11):1233-46.

CVRF







Study Population

Study Inclusion Criteria

 Patients with LM and non-LM coronary bifurcation lesions treated with PCI were included from IRIS-DES and IRIS-MAIN registries

Primary Outcome

 Target-vessel failure: a composite of cardiac death, target-vessel MI, clinical driven TVR





Evaluation of Effectiveness and Safety of the First, Second, and New

Drug-Eluting Stents in Routine Clinical Practice;

IRIS-DES Registry



Prospective Enrollment DESSIAN Registry (3,520) IRIS Ultimaster BVS BVS-CILOTAX DEB Xpedition/ DESyne Premier Orsiro Onyx Synergy IRIS-ELMENT (3.000) Registry AMI Registry Registry Alpine Registry Registry Registry Registry Registry Registry Registry Registry IRIS-PRIME (2,000) **K-XIENCE** Registry (2.940) IRIS-NOBORI (2,000) Patients with **IRIS-BIOMATRIX (837)** with IRIS GENOUS Xpedition DXR **BVS** Stent Ultimaster DEB DESyne BVS Synergy Premier Orsiro Onyx **IRIS-INTEGRITY (3,000)** /Alpine (N=300) Stent Stent Stent Stent Stent Stent in AMI Stent STEMI (455) Stent Stent (N=1,000) (N=1,000) (N=1,000) (N=1,000) (N=1,000) (N=1,000) (N=500) (N=1,000) (N=2.000)(N=2,500) 등록완료/ 조기 준비중 등록중 종료 5YrFU중 Clinical follow-up at 1-, 6-, and 12-months, and annually up to 5 years

*Primary end point: Composite of Death, MI, and TVR at 12-months



Park DW al. Circ Cardiovasc Interv. 2012;5:365-371.





A GLOBAL, MULTICENTER, PROSPECTIVE, REAL WORLD OBSERVATIONAL STUDY FOR UNPROTECTEDLEFT MAIN DISEASE



Clinical follow-up at 1-, 6-,12-months, and up to 10 years

*Primary end point: Composite of Death, MI, stroke and TVR at 2Year



Lee PH, et al. JACC 2016;68:1233-46



Flow Diagram of Study Population







Baseline characteristics

	Non-LM B (N =	ifurcations 5050)		LM Bifurcations (N = 2232)			
Characteristic	1 st -generation DES (N=929)	2 nd -generation DES (N=4121)	Р	1 st -generation DES (N=451)	2 nd -generation DES (N=1781)	Р	
Age, years	62.9 ± 10.5	63.6 ± 10.7	0.050	62.6 ± 10.5	64.9 ± 10.2	<0.001	
Male sex	636 (68.5)	2935 (71.2)	0.100	355 (78.7)	1390 (78.0%)	0.810	
BMI, kg/m ²	24.7 ± 2.9	24.7 ± 3.1	0.630	24.6 ± 2.7	24.4 ± 3.1	0.300	
HTN	564 (60.7)	2523 (61.2)	0.800	265 (58.8)	1149 (64.5)	0.030	
DM	306 (32.9)	1315 (31.9)	0.570	178 (39.5)	643 (36.1)	0.200	
Requiring insulin	56 (6.0)	165 (4.0)	0.010	24 (5.3)	103 (5.8)	0.790	
Current smoking	254 (27.3)	1219 (29.6)	0.190	125 (27.7)	436 (24.5)	0.180	
Hyperlipidemia	402 (43.3)	1837 (44.6)	0.490	55 (53.4)	299 (57.2)	0.550	
Previous MI	54 (5.8)	178 (4.3)	0.060	40 (8.9)	125 (7.0)	0.220	
Previous PCI	130 (14.0)	353 (8.6)	<0.001	94 (20.8)	301 (16.9)	0.060	
Previous stroke	74 (8.0)	293 (7.1)	0.400	34 (7.5)	142 (8.0)	0.840	
Previous CHF	22 (2.4)	94 (2.3)	0.970	8 (1.8)	50 (2.8)	0.290	

Baseline characteristics

	Non-LM B (N =	ifurcations 5050)		LM Bifu (N =		
Characteristic	1 st -generation DES (N=929)	2 nd -generation DES (N=4121)	Р	1 st -generation DES (N=451)	2 nd -generation DES (N=1781)	Ρ
Atrial fibrillation	36 (3.9)	125 (3.0)	0.220	12 (2.7)	46 (2.6)	>0.99
Family hx. of CAD	42 (4.5)	296 (7.2)	0.004	47 (10.4)	161 (9.1)	0.420
Chronic lung disease	22 (2.4)	99 (2.4)	>0.99	11 (2.4)	48 (2.7)	0.890
Chronic renal failure	35 (3.8)	143 (3.5)	0.730	11 (2.4)	81 (4.5)	0.060
Peripheral v. disease	7 (0.8)	106 (2.6)	0.001	9 (2.0)	75 (4.2)	0.040
Clinical presentation			<0.001			0.009
Stable angina	459 (49.4)	1715 (41.6)		243 (53.9)	820 (46.0)	
Unstable angina	283 (30.5)	1335 (32.4)		147 (32.6)	654 (36.7)	
MI	187 (20.1)	1071 (26.0)		61 (13.5)	307 (17.2)	
Ejection fraction						
Mean, %	58.6 ± 9.5	58.5 ± 9.9	0.910	60.4 ± 8.6	58.8 ± 10.3	0.002



Angiographic characteristics

	Non-LM E (N =	Bifurcations		LM Bifu (N =		
Characteristic	1 st -generation DES (N=929)	2 nd -generation DES (N=4121)	Р	1 st -generation DES (N=451)	2 nd -generation DES (N=1781)	Р
Bifurcation lesion			0.09			NA
LM	0	0		451 (100.0)	1781 (100.0)	
LAD	729 (78.5)	3099 (75.2)		0	0	
LCX	152 (16.4)	796 (19.3)		0	0	
RCA	48 (5.2)	226 (5.5)		0	0	
Disease extent			0.01			0.11
1-VD	585 (63.0)	2808 (68.1)		0	0	
2-VD	290 (31.2)	1113 (27.0)		334 (74.1)	1383 (77.7)	
3-VD	54 (5.8)	200 (4.9)		117 (25.9)	398 (22.3)	
Stenting strategy			<0.001			<0.001
Simple-crossover	624 (67.2)	3755 (91.1)		278 (61.6)	1335 (75.0)	
2-stent strategy	305 (32.8)	366 (8.9)		173 (38.4)	446 (25.0)	

Arzui.

Simple vs. complex stent strategy Over time from 1st-DES to 2nd-DES



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Primary Outcome (Target-Vessel Failure) Over time from 1st-DES to 2nd-DES



TVR: composite of cardiac death, target-vessel MI, clinical driven TVR





Clinical outcomes according to stent generation

	Non-LM Bifurcat	tions (N = 5050)	LM Bifurcations (N = 2232)			
Characteristic	1 st -generation DES (N=929)	2 nd -generation DES (N=4121)	Р	1 st -generation DES (N=451)	2 nd -generation DES (N=1781)	Р
Primary outcome						
Target-vessel failure	16.5 (14.1–18.9)	14.7 (13.5–15.8)	0.11	25.3 (21.2–29.3)	23.0 (19.3–26.7)	0.30
Secondary outcomes						
Death from any cause	5.4 (3.9–6.8)	4.6 (3.9–5.3)	0.37	4.7 (2.8–6.7)	7.9 (6.5–9.4)	0.02
Cardiac	3.7 (2.5–5.0)	3.3 (2.7–3.9)	0.55	3.4 (1.7–5.1)	6.1 (4.8–7.4)	0.03
Non-cardiac	1.7 (0.8–2.5)	1.4 (1.0–1.7)	0.46	1.4 (0.3–2.5)	2.0 (1.2–2.7)	0.38
MI	11.3 (9.3–13.3)	8.9 (8–9.8)	0.02	19.2 (15.5–22.8)	15.0 (13.3–16.7)	0.04
Any revascularization	8.1 (6.3–9.9)	9.3 (8.3–10.2)	0.32	13.7 (10.5–16.9)	9.6 (8.0–11.1)	0.02
Stent thrombosis	0.2 (-0.1–0.6)	0.4 (0.2–0.6)	0.53	0.7 (-0.1–1.4)	0.4 (0.1–0.6)	0.35

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Primary Outcome (Target-Vessel Failure) According to Stenting Strategy







Clinical outcomes according to stent strategy

	Non-LM Bifurca	tions (N = 5050)	LM Bifurcations (N = 2232)			
	Simple	Complex		Simple	Complex	
Characteristic	Strategy	strategy	Р	Strategy	strategy	Р
	(N=4379)	(N=671)		(N=1613)	(N=619)	
Primary outcome						
TVF	14.8 (13.7–15.9)	16.4 (13.6–19.2)	0.15	21.5 (19.4–23.6)	28.5 (24.7–32.3)	0.001
Secondary outcomes						
Death	5.0 (4.3–5.7)	3.7 (2.2–5.2)	0.17	7.2 (5.8–8.6)	6.7 (4.5–8.9)	0.53
Cardiac	3.6 (3–4.2)	2.3 (1.1–3.5)	0.10	5.5 (4.2–6.8)	5.0 (3.1–6.9)	0.54
Non-cardiac	1.4 (1.0–1.8)	1.4 (0.5–2.3)	0.98	1.9 (1.2–2.6)	1.8 (0.6–3.0)	0.85
MI	12.7 (10.2–15.2)	8.9 (8.0–9.8)	0.001	19.1 (16.0–22.2)	14.6 (12.9–16.3)	0.007
Any revascularization	9.0 (8.0–10.0)	9.2 (6.9–11.5)	0.79	9.2 (7.6–10.8)	14.0 (11.0–17.0)	0.004
Stent thrombosis	0.4 (0.2–0.6)	0.0 (0.0-0.0)	0.12	0.4 (0.1–0.7)	0.5 (-0.1–1.1)	0.79

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Adjusted HR for Target-Vessel Failure According to stent strategy over time



**Multivariable Cox regression models are adjusted for age, sex, diabetes, previous MI, previous PCI, chronic renal failure, clinical presentation, ejection fraction, bifurcation location, disease extent, and use of intravascular ultrasound.

Adjusted HR for Target-Vessel Failure According to stent strategy over time



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In Summary...

- Over the last decade, patients with bifurcation lesions, patient characteristics, stenting strategy, and PCI outcomes have substantially changed.
- Simple stenting strategy has been more frequently used and clinical outcomes have been improved from 1st generation DES to 2nd generation DES.





In Summary...

- Although simple strategy was associated with a lower rate of target-vessel failure, the treatment gap between 1st and 2nd gen-DES has progressively narrowed over time.
- This trend might be due to improved stent device, technique, clinical concept and increasing experience and expertise for bifurcation PCI.



