

## Meta-analysis: Single-stent vs. Two-stent

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## **1 vs 2 stents metaanalysis**

EBC

	Year	Studies/Patients N=	Randomized studies	Non- randomized	Clinical endpoints	Angio endpoints
Biondi-Zoccai	2008	5/1141	4	1	Х	X
Brar	2009	6/1641	6	0	Х	
Kastritsis	2009	6/1642	6	0	Х	
Zhang	2009	5/1550	5	0	Х	Х
Hakeem	2009	6/1641	6	0	Х	Х
Athappan	2010	5/1145	3	2	Х	Х
Niccoli	2010	6/962	3	3	Х	X
Zamani	2011	42/6825	6	36	Х	
Behan	2011	2/913	2	0	Х	
Zimarino	2013	12/7041	5	7	Х	

Superiority of A Simple Stenting Strategy For Coronary Bifurcation EBC Lesions In The DES Era (Meta-Analysis Of 1141 Patients)

#### **Included studies**

		Pts on simple	Pts on complex	Specific
Study	Year	strategy	strategy	strategy
BBK	2007	101	101	Т
<b>Bifurcation Sirius</b>	2004	22	63	Crushing
CACTUS	2008	173	177	Crushing
NORDIC	2004	207	206	Т
Pan et al	2004	47	44	Т

G. Biondi-Zoccai ESC 2008

# Superiority of A Simple Stenting Strategy For Coronary Bifurcation EBC Lesions In The DES Era (Meta-Analysis Of 1141 Patients)

#### **Risk of binary restenosis – main branch**



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Superiority of A Simple Stenting Strategy For Coronary Bifurcation EBC Lesions In The DES Era (Meta-Analysis Of 1141 Patients)

#### **Risk of binary restenosis – side branch**



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## Superiority of A Simple Stenting Strategy For Coronary Bifurcation EBC Lesions In The DES Era (Meta-Analysis Of 1141 Patients)

#### **Risk of MACE**

Study	Simple strategy	Complex strategy	Peto OR	Peto OR
or sub-category	n/N	n/N	95% CI	95% CI
BIFURCATION	3/22	12/63		0.69 [0.20, 2.45]
Pan et al	2/47	3/44		0.61 [0.10, 3.69]
NORDIC	6/207	7/206		0.85 [0.28, 2.56]
BBK	14/101	12/101		1.19 [0.52, 2.71]
CACTUS	15/173	21/177		0.71 [0.36, 1.41]
Total (95% CI)	550	591		0.83 [0.54, 1.28]
Total events: 40 (Simple	strategy), 55 (Complex str	ategy)		
Test for heterogeneity: C	chi² = 1.14, df = 4 (P = 0.89)	), l <sup>2</sup> = 0%		
Test for overall effect: Z	= 0.83 (P = 0.40)			
		0.1	0.2 0.5 1 2 5	10

Favours simple Favours complex

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# Superiority of A Simple Stenting Strategy For Coronary Bifurcation EBC Lesions In The DES Era (Meta-Analysis Of 1141 Patients)

#### **Risk of death**

Study	Simple strategy	Complex strategy	Peto OR	Peto OR
or sub-category	n/N	n/N	95% CI	95% CI
BIFURCATION	0/22	1/63	<b>_</b>	0.26 [0.00, 22.78]
Pan et al	1/47	1/44		0.94 [0.06, 15.21]
NORDIC	2/207	3/206	<b>_</b>	0.66 [0.11, 3.87]
BBK	3/101	1/101	<b>_</b>	2.76 [0.38, 19.88]
CACTUS	1/173	0/177		7.56 [0.15, 381.19]
Total (95% CI)	550	591	•	1.25 [0.42, 3.77]
Total events: 7 (Simple	strategy), 6 (Complex strat	egy)		
Test for heterogeneity:	Chi <sup>2</sup> = 2.44, df = 4 (P = 0.66)	), l² = 0%		
Test for overall effect: 2	Z = 0.40 (P = 0.69)			
		0.001 0	0.01 0.1 1 10 100	1000
		Fav	ours simple Favours com	nlex

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## Superiority of A Simple Stenting Strategy For Coronary Bifurcation EBC Lesions In The DES Era (Meta-Analysis Of 1141 Patients)

#### **Risk of MI**

Study	Simple strategy	Complex strategy	Peto OR	Peto OR
or sub-category	n/N	n/N	95% CI	95% CI
BIFURCATION	2/22	7/63		0.81 [0.17, 3.89]
Pan et al	2/47	1/44		1.85 [0.19, 18.27]
NORDIC	8/153	18/126	-	0.34 [0.15, 0.77]
ВВК	1/101	2/101		0.51 [0.05, 4.96]
CACTUS	13/173	16/177	+	0.82 [0.38, 1.75]
Total (95% CI)	496	511		0.60 [0.36, 0.98]
Total events: 26 (Simple	e strategy), 44 (Complex sti	rategy)	•	
Test for heterogeneity:	Chi² = 3.55, df = 4 (P = 0.47)	), l <sup>2</sup> = 0%		
Test for overall effect: Z	Z = 2.02 ( <b>P</b> = 0.04)			
		0.001 0	0.01 0.1 1 10 100	1000

Favours simple Favours complex

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#### **Risk of TLR – any branch**

Study	Simple strategy	Complex strategy		Peto	OR		Peto OR
or sub-category	n/N	n/N		95% Cl			95% CI
BIFURCATION	1/22	7/63	•	•			0.47 [0.09, 2.44]
Pan et al	1/47	3/44	←				0.33 [0.05, 2.44]
NORDIC	4/207	2/206					1.95 [0.39, 9.78]
BBK	11/101	9/101					1.25 [0.50, 3.13]
CACTUS	10/173	10/177					1.02 [0.42, 2.52]
Total (95% CI)	550	591					1.00 [0.58, 1.71]
Total events: 27 (Simple	e strategy), 31 (Complex str	rategy)					
Test for heterogeneity:	Chi² = 2.88, df = 4 (P = 0.58)	), l² = 0%					
Test for overall effect: Z	Z = 0.01 (P = 0.99)						
			0.1 0.2	0.5 1	1 2	5 10	
			Favours	simple	Favour	s complex	

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## Superiority of A Simple Stenting Strategy For Coronary Bifurcation EBC Lesions In The DES Era (Meta-Analysis Of 1141 Patients)

#### **Risk of stent thrombosis**



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No Detiente

## Double Vs Single Stenting for Coronary Bifurcation Lesions, a Meta-EBC Analysis: Procedural Characteristics

	Crossed Over		Truo			CD IIb/IIIa	Final "Kissing	Angiographic
Study	To Simple Strategy	To Complex Strategy	Bifurcation Lesions, n (%)	Stenting Technique* (MV+SB)	Type of DES	Inhibitors (MV; MV+SB)	Balloon" Inflation, n (%) (MV; MV+SB)	Follow-Up (MV; MV+SB)
BBC ONE	4	7	415 (83)	Crush technique (169), culotte technique (75), T-stenting (7), other (4)	PES	70; 110	73 (29); 189 (76)	ND
CACTUS	ND	54	328 (94)	Crush technique (231)	SES	30; 40	156 (90); 163 (92)	302 (150; 152)
Colombo et al	2	22	ND	T-stenting (60), V-stenting (1), Y-stenting (2)	SES	8; 27	19 (86); 60 (95)	ND
Ferenc et al	3	19	138 (68)	T-stenting (120)	SES	0; 0	101 (100); 101 (100)	192 (96; 96)
NORDIC	10	9	ND	Crush technique (103), culotte technique (43), other (69)	SES	106; 105	65 (31); 152 (74)	307 (151; 156)
Pan et al	4	1	78 (86)	T-stenting (45)	SES	29; 25	28 (56); 34 (77)	80

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Kastritsis, Circ Cardiovasc Interv\_2009 Oct;2(5):409-15.

### **O INSTITUT CARDIDVASCULAIRE PARIS SUD** Double Vs Single Stenting for Coronary Bifurcation Lesions



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Kastritsis, Circ Cardiovasc Interv\_2009 Oct;2(5):409-15.

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VINSTITUT CARDIDVASCULAIRE PARIS SUD Provisional vs. complex stenting strategy for coronary bifurcation lesions: meta-analysis of randomized trials



### **Main Branch Restenosis**



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Hakeem, J Invasive Cardiol. 2009 Nov;21(11):589-95.

### VINSTITUT CARDIDVASCULAIRE PARIS SUD Provisional vs. complex stenting strategy for coronary bifurcation lesions: meta-analysis of randomized trials



## **Side Branch Restenosis**

		CS	F	s		Risk Ratio			Risk Rati	0	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H,	Random, I	95% CI	
BBC ONE <sup>16</sup>	0	0	0	0		Not estimable					
CACTUS"	20	152	22	150	30.5%	0.90 [0.51, 1.57]		13	•		
Colombo <sup>12</sup>	12	55	3	21	11.2%	1.53 [0.48, 4.88]				-	
Ferenc <sup>13</sup>	13	96	10	96	20.7%	0.30 [0.60, 2.82]					
Nordic <sup>14</sup>	18	206	29	207	30.8%	0.62 0.36, 1.09		7			
Pan <sup>16</sup>	6	44	2	47	6.8%	3.20 [0.68, 15.05]			+		
Total (95% CI)		553		521	100.0%	1.00 [0.65, 1.54]			•		
Total events	69	2020	66	1000	seasones.				T		
Heterogeneity: Tau <sup>2</sup> = 1	0.07; Chi# :	5.89; d	f=4(p=1	0.21); }	= 32%		-	-	_	-	-
Test for overall effect:	Z = 0.01 (p	= 0.99)			9227		0.01	0.1 Favors CS	1	10 Favors PS	100

CI = confidence interval

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Hakeem, J Invasive Cardiol. 2009 Nov;21(11):589-95.

## True coronary bifurcation lesions: meta-analysis and review of literature

#### Postprocedural minimal luminal diameter of the side branch



Overall estimate of the postprocedural minimal luminal diameter of the side branch in patients treated with the single-stent strategy compared with patients receiving the two-stent strategy. IV, Inverse variance.

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Athappan, J Cardiovasc Med 2010 Feb;11(2):103-10

FBC

## True coronary bifurcation lesions: meta-analysis and review of literature

#### Follow-up minimal luminal diameter of the side branch



Overall estimate of the follow-up minimal luminal diameter of the side branch in patients treated with the single-stent strategy compared with patients receiving the two-stent strategy. IV, Inverse variance.

www.icps.com.fr

Athappan, J Cardiovasc Med 2010 Feb;11(2):103-10

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Long-term risk of clinical events from stenting SB of coronary bifurcation lesions with DES / BMS: meta-analysis

EBC

6825 subjects from 42 studies

MACE

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Zamani,\_Catheter Cardiovasc Interv.\_2011 Feb 1;77(2):202-12.



### Simple or Complex Stenting for Bifurcation Coronary Lesions AB Patient-Level Pooled-Analysis of Nordic 1 and BBC

#### **Trial End Points Simple vs Complex Total**

	Simple ( $n=457$ )	Complex (n=456)	HR (95% CI)	P Value
All-cause death, myocardial infarction (periprocedural and subsequent) or target vessel revascularization at 9 months	46 (10.1%)	79 (17.3%)	1.84 (1.28–2.66)	<i>P</i> =0.001
All-cause death, myocardial infarction (subsequent alone) or target vessel revascularization at 9 months	32 (7.0%)	41 (9.0%)	1.38 (0.87–2.20)	0.168
All-cause death	5 (1.0%)	5 (1.0%)		0.99
Periprocedural	2 (0.4%)	3 (0.6%)		
Subsequent	3 (0.6%)	2 (0.4%)		
Myocardial infarction	22 (4.8%)	56 (12.3%)		< 0.001
Periprocedural	16 (3.5%)	45 (9.9%)		< 0.001
Subsequent	6 (1.3%)	11 (2.4%)		0.22
Target vessel revascularization	26 (5.7%)	33 (7.2%)		0.34
PCI	24 (5.3%)	20 (4.4%)		0.54
CABG	2 (0.4%)	13 (2.9%)		0.004
Stent thrombosis (ARC definite)	3 (0.7%)	6 (1.3%)		0.31
In-hospital				
Death	2 (0.4%)	3 (0.6%)		0.65
Myocardial infarction	17 (3.7%)	45 (9.9%)		< 0.001
CABG	0 (0%)	4 (0.8%)		0.04

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### Simple or Complex Stenting for Bifurcation Coronary Lesions ABC Patient-Level Pooled-Analysis of Nordic 1 and BBC

Kaplan-Meier freedom from the composite event



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### Simple or Complex Stenting for Bifurcation Coronary Lesions ABC Patient-Level Pooled-Analysis of Nordic 1 and BBC



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### Simple or Complex Stenting for Bifurcation Coronary Lesions ABC Patient-Level Pooled-Analysis of Nordic 1 and BBC

Kaplan-Meier freedom from TVR



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### Simple or Complex Stenting for Bifurcation Coronary Lesions ABC Patient-Level Pooled-Analysis of Nordic 1 and BBC

Primary outcome for individual subgroups



Favours Simple Favours Complex

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## Simple or Complex Stenting for Bifurcation Coronary Lesions : EBC A Patient-Level Pooled-Analysis of Nordic 1 and BBC

#### Simple Complex (n = 457)(n = 456)P Value Side branch stented, n (%) 16 (3.5%) 421 (92.3%) < 0.001272 (59.6%) Crush technique, n (%) Culotte technique, n (%) 118 (25.9%) . . . 16 (3.5%) 59 (12.9%) Other complex technique n (%) Final kissing balloons, n (%) 129 (28.3%) 342 (75.3%) < 0.001 Procedural success, n (%) 435 (95.4%) 429 (94.5%) 0.430 Procedural time (min, SD) 0.001 57 78 Fluoroscopy time (min, SD) 15.1 (11.1) 21.5 (11.4) < 0.001 243.2 (108.1) 297.9 (129.3) < 0.001Contrast volume (mL, SD)

#### **Procedure Characteristics**

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### **O** INSTITUT CARDIDVASCULAIRE PARIS SUD Late thrombosis after 2 versus 1 DES in the treatment of coronary EBC bifurcations. Meta-analysis of randomized and observational studies

Summary of the Characteristics of the Included Studies

	Nordic	BBK	CACTUS	BBC-ONE	DK-CRUSH-II	Ge et al.	Di Mario et al.	ARTS-II	COBIS Registry	J CYPHER Registry	JPMS Registry	Assali et al.
Type of study	RCT	RCT	RCT	RCT	RCT	nROS	nROS	nROS	nROS	nROS	nROS	nROS
Year of publication	2006	2008	2009	2010	2011	2005	2007	2007	2010	2011	2011	2012
No. of patients	413	202	350	500	390	174	150	324	1,691	2,122	324	401
Patient treatment (SDS/DDS)	199/196	101/101	173/177	248/249	185/185	117/57	38/109	263/61	1,376/292	1,870/263	263/37	260/141
Follow-up, mo	14	9	6	6	12	9	12	12	22	36	36	24
Type of DES	Sirolimus	Sirolimus	Sirolimus	Paclitaxel	Sirolimus	Sirolimus	Paclitaxel	Sirolimus	Operator discretion	Sirolimus	Sirolimus	Operator discretion
DDS technique	Crush	T stenting	Crush	Crush	Crush	Crush	Crush	Crush	Crush	Crush	Crush	Mini-Crush
	Culotte			Culotte		V stenting	T stenting	V stenting	V stenting	T stenting	T stenting	T stenting
	Other			T stenting		T stenting	Culotte	T stenting	T stenting	Culotte	Culotte	V stenting
				Other		Culotte	Kissing stents	Culotte	Culotte	Kissing stents	Kissing stents	Culotte
True bifurcations*, no. (%)	NA	138 (68)	328 (94)	415 (83)	390 (100)	NA	NA	200 (62)	1,170 (69)	1,181 (56)	NA	NA
Use of glycoprotein Ib/IIa, no. (%)	211 (51)	0	70 (20)	180 (36)	10 (3)	82 (47)	35 (23)	119 (37)	NA	NA	NA	235 (58)
Final kissing balloon, no. (%)	217 (52)	202 (100)	319 (91)	262 (52)	332 (85)	103 (59)	112 (75)	40 (12)	686 (41)	1,254 (59)	97 (30)	318 (79)
Duration of DAPT, mo	14	6	6	>9	>12	>3	>3	2	3-6 (recommended)	3 (recommended)	3 (recommended)	6 (recommended)
Crossover rate from provisional to double stenting. %	430	19	31	-	-	-	-	-	-	-	-	-

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## Late thrombosis after 2 versus 1 DES in the treatment of coronary EBC bifurcations. Meta-analysis of randomized and observational studies

Study	Year	DDS	SDS	DDS better	SDS better	Weight*	RR (random) 95% Cl
RANDOMIZE	, CON	ROLLED	TRIALS				
NORDIC	2008	1/196	2/199		++-	5.37%	0.50 (0.04-5.55)
Ferenc et al.	2008	2/101	1/101	82		5.40%	2.00 (0.18-21.71)
CACTUS	2009	3/177	2/173			9.73%	1.46 (0.24-8.66)
BBC-ONE	2010	5/249	1/248			6.71%	4.97 (0.58-42.31)
DK-CRUSH-II	2011	4/185	1/185	-	┼┼┳───	6.45%	4.00 (0.45-35.44)
META-ANALY	SIS	15/908	7/906		-		2.01 (0.77-5.23)
Cochrane Q: 2.4	46 (p: 0.6	51) I²: 0%					
NONRANDON	IZED, O	DBSERVA	TIONAL S	TUDIES			
Ge et al.	2007	3/57	0/117		-	3.54%	14.24 (0.74-271.13)
Di Mario et al.	2007	4/109	0/38		• • •	3.66%	3.19 (0.17-57.92)
ARTS II	2007	1/61	4/263		╞┼─	6.50%	1.07 (0.12-9.47)
COBIS	2010	2/292	9/1376			13.17%	1.04 (0.22-4.82)
J-CYPHER	2011	3/263	10/1870			18.64%	2.13 (0.59-7.70)
J-PMS	2011	4/37	2/263			11.12%	14.21 (2.69-74.92)
Assali et al.	2011	2/141	3/260			9.72%	1.23 (0.21-7.27)
META-ANALY	SIS	19/960	27/4187		+		2.55 (1.13-5.78)
Cochrane Q: 8.0	06 (p: 0.2	34) I <sup>2</sup> : 25.5	7%		120 21		
META-ANALY	SIS	34/1868	35/5093		•	100%	2.31 (1.33-4.03)
Cochrane Q: 10	.65 (p: 0	473) 12: 0%					

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## Late thrombosis after 2 versus 1 DES in the treatment of coronary EBC bifurcations. Meta-analysis of randomized and observational studies



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## Late thrombosis after 2 versus 1 DES in the treatment of coronary EBC bifurcations. Meta-analysis of randomized and observational studies

Association Between Log-Transformed Risk of DES Thrombosis and Myocardial Infarction



The size of each circle represents the precision of each estimate (the inverse variance of the log RR in the trial), and the line is the best fit for the meta-regression model. Randomized, controlled trials (filled circles); nonrandomized observational studies (open circles).

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**WINSTITUT CARDIDVASCULAIRE PARIS SUD** Randomized study comparing DK Crush with Provisional Stenting for treatment of coronary bifurcation lesions: DK-CRUSH-II

Clinical autoama (9)

Clinical Oulcome (2)										
	DK Group (n = 185)	PS Group (n =185)	p Value							
Procedural success	179 (96.8)	173 (93.5)	0.217							
At 6-month										
Cardlac death	1 (0.5)	2 (1.1)	1.000							
MI	6 (3.2)	4 (2.2)	0.751							
CABG	0 (0)	1 (0.5)	0.500							
TLR	2 (1.1)	6 (3.2)	0.284							
TVR	3 (1.6)	8 (4.3)	0.220							
MACE	6 (3.2)	11 (5.9)	0.321							
Stent thrombosis definite	4 (2.2)	1 (0.5)	0.372							
At 12-month										
Cardlac death	2 (1.1)	2 (1.1)	1.000							
мі	6 (3.2)	4 (2.2)	0.751							
CABG	0 (0)	1 (0.5)	0.500							
TLR	8 (4.3)	24 (13.0)	0.005							
TVR	12 (6.5)	27 (14.6)	0.017							
MACE	19 (10.3)	32 (17.3)	0.070							
Stent thrombosis	5 (2.7)	2 (1.1)	0.449							
Definite	4 (2.2)	1 (0.5)	0.372							
Possible	1 (0.5)	1 (0.5)	1.000							

Follow-up coronary angiography at 8 months / Endpoint at 12-months

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SL Chen J. Am. Coll. Cardiol. 2011;57;914-920

## Incomplete and Inappropriate Coronary Bifurcation Classification

« The use of incomplete and inappropriate Medina coronary bifurcation classification has led to major flaws in randomized clinical trials of coronary bifurcation interventions »

« The authors did not realize that all of the randomized clinical studies in their meta-analysis:

- did not separate so called "true bifurcation lesions" from other less relevant lesions

- failed to include bifurcation angle in their analysis (more / less than 70°: T or V).

- B2 type of the Movahed classification are the only relevant lesions at high risk of SB occlusion using a single stent

- the risk of a side or main branch occlusion in 1m or 1s lesions using single stent technique is very low

- we recommend that the most appropriate and complete Movahed coronary bifurcation classification »



Suffix 1 Suffix 2 Suffix 3 Suffix 4 Prefix B XX) CA С ۱M Ν LM 1<sub>s</sub> S Suffix 1: C = Close to bifurcation N = Non-significant sidebranch S = Small proximal segment L = Large proximal segment Suffix 2: 1M = Only main branch ostium diseased 1S = Only sidebranch ostium diseased 2 = Both main and sidebranch ostia diseased Suffix 3: V = Angle between branch vessels less than 70 degrees T = Angle between branch vessels more than 70 degrees Suffix 4: CA = Calcified LM = Left main involved in bifurcation

Figure 2. Movahed's classification. Originally published in the Journal of Invasive Cardiology 2006;18:199–204.

www.icps.com.fr

Movahed, J Invasive Cardiol. 2010 Mar;22(3):148-9

## A new proposed <u>simplified</u> classification of coronary artery bifurcation lesions



www.icps.com.fr

Movahed. J Invasive Cardiol. 2006 May;18(5):199-204

-BC

## Exhaustive ? Simple ?

## OST OST KST SBT CRT TST CUT

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Schematic description of interventional bifurcation techniques:

OST = one stent technique; SBT = stent with balloon technique; KST= kissing stent technique; TST = "T" stenting technique; CRT = crush stenting technique; CUT = culotte stenting technique

#### Movahed. J Invasive Cardiol. 2006 May;18(5):199-204

## **Bifurcation Lesion Intervention Algorithm**

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## **Conclusions (1)**

Solid datas coming from meta-analysis of randomized and non randomized trials regarding Provisional vs complex strategies for non-LM bifurcation stenting:

- 1. No difference in total / cardiac mortality acutely and at FU
- 2. No difference in TLR
- 3. Less MI
  - in-hospital / 30 days depending of definition (BBC one)
  - at FU
  - linked to stent thrombosis (Zimarino)
- 4. Less stent thrombosis
- 5. No difference in restenosis rate for MV and SB
- 6. Smaller acute gain and late loss in SB ostium
- 7. Less time, X-Ray, contrast medium, wires, balloons, stents, GPIIbIIIa ...

## **Conclusions (2)**



Medina classification is a research instrument completed by other Classifications (stent thrombosis...), dedicated QCA softwares (3 segments references and MLD, 3D angle, lesion length), and Intraluminal online guidance (IVUS and OCT) used to make possible new randomized trials on last technical aspects (POT), DAPT duration, new stents (BVS)...