Title: "Indirect meta-analysis of Tryton side branch® stent versus a complex two-stent technique for patients with a bifurcation coronary lesion".

Autor: Luciano Consuegra Sánchez.

Total word count: 1519.

Correspondence to:

Luciano Consuegra Sánchez

Unidad de Hemodinámica,

Servicio de Cardiología,

Hospital Universitario de Santa Lucia,

Calle Mezquita, S/N, Paraje Los Arcos,

30202, Cartagena, Murcia

Tlfno. 658659063

lconsue@gmail.com

Fax. 968523865

Abstract.

Background. Several trials and meta-analysis have addressed whether bifurcations lesions require stenting of both the main vessel and side branch. The Tryton side brach stent is a bifurcation system that secures the side branch and provides ostial protection. Uncertainty remains on the benefits of such Tryton Stent versus double stenting with regards to the occurrence of periprocedural myocardial infarction (periMI).

Methods. Studies treating bifurcation lesions were searched in Pubmed. The primary end-point was the occurrence of peri-MI. Crude and weighted by the inverse of variance method risks (R) and 95% Confidence Intervals (CI) were computed.

Results. Twenty-one studies were included (n=3006) for the comparison of Tryton stent vs. a complex technique. The crude risk of peri-MI among patients treated with a complex stent technique and Tryton Stent were 5.90 % (95% CI 4.93-6.87%) and 3.45 % (95% CI 2.79-4.12%), respectively. The risk estimation weighted by inverse variance yield 1.63% (95%CI 1.12-2.14%) and 2.78% (95% CI 1.61-3.95%), respectively.

Conclusions. Stenting of both the side branch with a Tryton stent and the main vessel in bifurcation lesions may not reduce the rate of periprocedural myocardial infarction as compared to a complex two-stent technique.

Table 1. Studies using a two stent complex technique, included in the meta-analysis.

Studies	Reference	Complex Technique	Periprocedural MI definition: *Laboratory Criterion*	Periprocedural MI definition: *ECG Criterion*	True bifurcation, %	Left Main, %	Periprocedural MI incidence (2 stent technique)
BBC-ONE & NORDIC pooled analysis	Circ Cardiovasc Interv. 2011;4:57-64	Crush/Culotte /T stent	Biomarkers (Troponin/CKMB ≥ 3 fold)	No ECG changes required	74.7	NS	45 / 456
ARTS II	Eur H J 2007;28:433-42	Culotte/V/Crush	CK ≥ 3 fold or ratio CKMB / total CK > 0.1	New abnormal (Minessota code) Q waves required	52.5*	0	2 / 61
DK-CRUSH II	J Am Coll Cardiol 2011;57:914-20	Double Kissing Crush	NORDIC criteria*	Not stated	100	17.8	6 / 185
Pan	Am Heart J 2004;148:857–64	T stent	CK > 3 fold	No ECG changes required	100	5.0	0 / 44
Chen	Chin Med J. 2011;124:1943-50	Culotte	CKMB ≥ 3 fold	No ECG changes required	94.0	24.0	0 / 34
NORDIC II	Circ Cardiovasc Interv. 2009;2:27-34	Crush/Culotte	Biomarkers (Troponin/CKMB ≥ 3 fold)	No ECG changes required	77.8	10.0	36 / 296
Diaz de Llera	Rev Esp Cardiol. 2006;59:458-64	Crush	CKMB ≥ 3 fold	No ECG changes required	100	52.9	2 / 83
Galassi	J Am Coll Cardiol Intv 2009;2:185-94	Mini-Crush	CKMB ≥ 3 fold	No ECG changes required	89.5	0	0 / 199
Adriaenssens	Eur Heart J 2008; 29:2868–2876	Culotte	CK or CK-MB ≥ 3	No ECG changes required	92.5	0	6 / 132
Yang	Catheter Cardiovasc Interv. 2012 Aug 25. (epub ahead of print)	Mini Crush / Classic Crush	CK-MB ≥ 3	New development of pathologic Q wave accepted	99.0	23.2	2 / 178
Al Rashdan	Catheter Cardiovasc Interv 2009;74:683-690	Carina modification	CK-MB ≥ 3	No ECG changes required	NS	10.3	4 / 156
Chue	Catheter Cardiovasc Interv 2010;75:605-613	Crush	CK > 3 fold	No ECG changes required	93.0	6.0	4 / 100
Sharma	Catheter Cardiovasc Interv 2005;65:10-16	SKS	CK-MB ≥ 3	No ECG changes required	100	15.0	3 / 200
SMART-STRATEGY	JACC Cardiovasc Interv. 2012;5:1133-4	T stent	CK-MB ≥ 3	No ECG changes required	68.5	44.0	23 / 130
				Pooled periprocedural MI incidence			133 / 2254 5.90% 95% CI 4.93-6.87 %

ECG= Electrocardiogram; * additionally considers an increase of CKMB > 1 time the prevalue immediately before stenting in MI patients. A true bifurcation was defined as ≥ 50% diameter stenosis in both main vessel and a side branch ≥ 2.25mm diameter. NS = Not stated; SKS = Simultaneous Kissing stent.

Table 2. Studies included in the meta-analysis reporting the incidence of periprocedural myocardial infarction with Tryton stent.

Study	Reference	Periprocedural MI definition: *Laboratory Criterion*	Periprocedural MI definition: *ECG Criterion*	True bifurcation, %	Left Main, %	Periprocedural MI incidence (2 stent technique)
TRYTON	E*tryton Spain: 147 E*Tryton 150-Benelux: 302 Tryton First In Man: 30 Rotterdam-Poznan registry: 43	CK ≥ 3 fold	No ECG changes required	72.9	6.2	21/545
Magro	Catheter Cardiovasc Interv. 2011;77:798-806	Biomarkers (Troponin/CKMB ≥ 3 fold)	No ECG changes required	80.0	8.0	2 / 96
Grundeken	Neth Heart J 2012;20:439-46	Biomarkers (Troponin/CKMB ≥ 3 fold)	No ECG changes required	91.2	3.3	1 / 91
Dubois	Catheter Cardiovasc Interv. 2012 Jun 28. [Epub ahead of print]	CK-MB ≥ 3	No ECG changes required	70.0	0	2 / 20
		Pooled periprocedural MI incidence		26 / 752 3.45 % 95% CI 2.79-4.12		

A true bifurcation was defined as ≥ 50% diameter stenosis in both main vessel and a side branch ≥ 2.25mm diameter. NS = Not stated

Table 3. Excluded studies and reasons for such a decision.

Studies	Reference	Complex Technique	Periprocedural MI definition	Reason for no inclusion
Colombo	Circulation. 2004;109:1244-9	V/Y/Modified T stent	Not specifically stated	Periprocedural MI not stated
Cohen	Ann Cardiol Angeiol 2009;58:208-14.	Crush stent	CK > 2 fold	Deviation of periprocedural MI definition
Collins	Am J Cardiol 2008;102:404–410	Crush/Culotte	CK > 2 fold	Deviation of periprocedural MI definition
Romagnoli	Am Heart J 2010;160:535-542	Crush/Culotte/T/V	Not specifically stated	Periprocedural MI not stated. Data of periprocedural MI incidence in subgroups not reported.
Lansky (SPIRITIII)	EuroIntervention 2010;6:J44-52	Not specified	CK > 2 fold	No specification of interventional technique
Ge	J Am Coll Cardiol 2005;46:613-20 & Heart 2006; 92:371–376.	Crush	Not specifically stated	Periprocedural MI not stated
CACTUS	Circulation 2009;119:71-8	Crush	non Q wave MI: CK > 2 fold CK; Q MI: Q+CK above reference	Deviation of periprocedural MI definition
Al Suwaidi	J Am Coll Cardiol 2000;35:929 –36	Y / T Stent	CK / CKMB > 3 fold + requirement of Q wave, or prolonged angina or regional wall motion abnormalities.	Deviation of periprocedural MI definition
Yamashita	J Am Coll Cardiol 2000;35:1145–51	T/V/Y/Culotte	Not specifically stated	Periprocedural MI not stated
Hoye	J Am Coll Cardiol 2006;47:1949 –58	Crush	CK > 2 & CKMB rise	Deviation of periprocedural MI definition
Dzavic	Am Heart J 2006;152:762-9	Crush	Not specifically stated	Periprocedural MI not stated
Kanei	Angiology 2010;61:633-7	Crush	Not specifically stated	Periprocedural MI not stated
DK-CRUSH I	Eur J Clin Invest 2008; 38: 361–371	Double Kissing Crush	Not specifically stated	Periprocedural MI not stated
Herrador	Catheter Cardiovasc Interv. 2011;78:1086-92	Mainly provisional stent; residual T-stent/crush	Troponin I > 3 fold	Data of periprocedural MI incidence in subgroups not reported
Kaplan	Am Heart J 2007;154:336-43	Culotte/T Stent	Not specifically stated	Periprocedural MI not stated.
Moussa	Am J Cardiol 2006;97:1317-1321.	Crush	Not stated specifically	Periprocedural MI not stated.
Tanabe	Am J Cardiol 2004;91:115-118.	Mainly T stent/Crush/Culotte/SKS	Not stated specifically	Periprocedural MI not stated.
Anzuini	Am J Cardiol 2001;88:1246-50	T stent	Not stated specifically	Periprocedural MI not stated.
Burzotta	Catheter Cardiovasc Interv. 2007;70:75-82	Small protrusion TAP	Not stated specifically	Periprocedural MI not stated.

Table 4. Meta-analysis of studies with complex two stent technique, applying an inverse-variance weighting method and a classical coefficient correction (Ω= 0.5) for studies with zero risk.

Studies	Risk	Variance	W (1/variance)	Risk x w product
BBC-ONE & NORDIC pooled analysis	45 / 456	1.95×10^{-4}	5126.7	505.9
ARTS II	2 / 61	5.20×10^{-4}	1923.6	63.1
DK-CRUSH II	6 / 185	1.70×10^{-4}	5895.4	191.2
Pan	0 / 44	2.50×10^{-4}	4005.5	45.0
Chen	0 / 34	4.14×10^{-4}	2415.5	35.0
NORDIC II	36 / 296	3.61×10^{-4}	2770.8	337.0
Diaz de Llera	2 / 83	2.83×10^{-4}	3529.5	85.0
Galassi	0 / 199	1.25×10^{-5}	79800.5	200.0
Adriaenssens	6 / 132	3.29×10^{-4}	3042.3	138.3
Yang	2 / 178	6.24×10^{-4}	16022,0	180.0
Al Rashdan	4 / 156	1.60×10^{-4}	6244,1	160.1
Chue	4 / 100	3.84×10^{-4}	2604.2	104.2
Sharma	3 / 200	7.39×10^{-5}	13536.4	203.0
SMART-STRATEGY	23 / 130	11.20×10^{-4}	892.7	158.0
			$\sum$=147809.2	$\sum$=2405.3

Risk (weighted by inverse-variance method) = 2405.3/147809.2= 1.63%

Standard error (risk) = √(1/147809,2)= 0.0026010.

1.96 x SE x 100 = 0.51

95% Confidence interval (risk) = 1.12- 2.14 %

Table 5. Meta-analysis of studies with Tryton side branch stent technique, applying an inverse-variance weighting method and a classical coefficient correction (Ω= 0.5) for studies with zero risk.

Studies	Risk	Variance	W (1/variance)	Risk x w product
E*tryton Spain E*Tryton Benelux Tryton First In Man Rotterdam-Poznan registry	21 / 545	6.80×10^{-5}	14711.0	566.8
Magro	2 / 96	2.12×10^{-4}	4706.0	98.0
Grundeken	1 / 91	1.19×10^{-4}	8373.0	92.0
Dubois	2 / 20	45.0×10^{-4}	222.2	22.2
			∑=28012.2	∑=779.1

Risk (weighted by inverse-variance method) = = 2.78%

Standard error (risk) = 0.005974.

1.96 x SE x 100 = 1.17%

95% Confidence interval (risk) = 1.61 – 3.95 %

Tabla 6. Global findings.

Procedural MI	Weighted risk	Weighted 95% Confidence Interval
Complex two stent technique	1.63	1.12 - 2.14
Tryton stent technique	2.78	1.61 - 3.95