CLINICAL EFFECTIVENESS OF THE DRUG-ELUTING STENT IN URUGUAY

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Introduction:

- The National Resources Fund (NRF) finances highly specialized medicine in Uruguay.
- Percutaneous coronary interventions (PCI) with stent implantation have been supported since 1993. A regulatory framework, systematic evaluation and national registry were created.
- Coverage with drug eluting stent (DES) began in 2005.
- Randomized clinical trials had shown that DES reduced the risk of restenosis and the need for new vascularization procedures at the target vessel. Observational studies including patients in large registries sugested that DES increased survival, but the residual confounding factors were not adequately controlled (1).

Objective: To assess long-term results of DES and compare them with bare-metal stent (BMS) in patients with PCI in Uruguay.

Methods:

- A national registry of PCI was established at the NRF.
- A historic-cohort of patients undergoing PCI between January 1st 2003 and December 31st 2007 were studied.
- The end point at vessel-treated level was free-survival of target vessel revascularization (TVR).
- At patient level we assessed overall survival, and free-survival of a composite event (CE) of death or TVR.
- The propensity-score (PS) method was used for risk adjustmen (2). We perform one to one matched analysis on the basis of the estimated PS of each treated vessel and patient. Using the probability of the PS, we first randomly selected a case trated with DES and then matched that case with a control treated with BMS with the closest probability at the PS.
- A survival analysis thorough stratified Cox model was performed. A sensitivity analysis according to difference in mortality between both cohorts at day 5 was used to correct the residual confounding for patients survival (3).

Results:

- In this period 11067 patients (16166 vessels) were treated (BMS in 8650, DES in 1458 and both in 959 patients).

VESSELS ANALYSIS

2846 vessels treated with DES were matched (stratified by vessel) with 2846 vessels treated with BMS. Characteristics and standardized differences between groups are shown in Table 1. Groups were well balanced except for myocardial infarction and primary angioplasty.

Free-survivals of TVR at different coronary arteries are shown in Table 2. DES was associated with greater free-survival of TVR (HR 0.78, CI 95% 0.6-0.96). This effect was mainly determined for the results of left anterior descending artery.

PATIENTS ANALYSIS

1458 patients treated with DES were matched with 1458 patients treated with BMS. Characteristics and standardized differences between groups are shown in Table 3. Groups were well balanced.

Overall survival at different quintiles of PS, hazard ratio (HR) and corrected HR are shown in Table 4.

Basal risk was nor completely controlled, at day 5 there was 0.55% of absolute difference (RR=0.5) of mortality in favor of DES cohort. Correcting for this bias, overall survival rate was lower in patients with DES.

CE free-survival was greater in patients with DES (HR 0.7, CI 95% 0.6-0.8), this effect was similar for patients in quintiles 3 to 5.

Table 1. CHARACTERISTICS OF VESSEL GROUPS

Characteristic	BMS %	DES %	Standarized difference
Female	31,5	32,5	2,14
Age (Years)	62,2(11)	62,5 (11)	2,51
Chronic Renal Failure	4,6	5,4	3,67
Hypertension	71,2	72,5	2,89
Diabetes	31,3	32,3	2,15
Current Cardiac Failure	4,6	5,1	2,33
Previous Myocardial Infarction (MI)	17,8	18,7	2,33
Previous Coronary Bypass Surgery	10	11,4	4,53
Previous PCI	20,5	21,4	2,21
Unstable Angina at entrance	61,7	62,6	1,86
Current MI	35,4	26,8	-18,66
Primary Angioplasty	11,1	7,8	-11,30
Hemodynamic Status Stable	97,7	97,8	0,67
Unstable	1,7	1,7	0
CardiogenickShock	0,6	0,5	-4,39
LVEF >30%	96	96	0
20 a 29%	4	3,9	-0,51
>20%	0	0,1	4,47
Two or more vessels - disease	44,1	44,4	0,60
Type treated lesions A	8,3	7,8	-1,84
B	61,9	63,2	2,69
C	29,8	29	-1,76

Table 2. SURVIVAL RATES OF FREE TVR

Treated Vessel	Type of Stent	1 year %	5 years %	p value
Left Coronary Artery	BMS n=58	95,8	-	0,81
	DES n=58	96,2	-	
Proximal Left Anterior Descending Artery	BMS n=805	92,5	90,1	0,02
	DES n=805	95,4	90,7	
Non-Proximal Left Anterior Descending Artery	BMS n=815	94,3	88,6	0,09
	DES n=815	96,5	91,7	
Right Coronary Artery	BMS n=539	96,6	92,1	0,20
	DES n=539	98,3	92,7	
Circumflex Artery	BMS n=346	96,6	95,0	0,41
	DES n=346	98,5	94,5	
Diagonal Branch	BMS n=56	100	96,0	0,70
	DES n=56	96,4	93,8	
Marginal Branch	BMS n=184	98,9	95,7	0,31
	DES n=184	96,6	93,9	
Aortic - Coronary Venous Bypass	BMS n=39	91,8	80,9	0,64
	DES n=39	97,1	86,5	
Total	BMS n=2846	94,9	91,1	0,007
	DES n=2846	96,8	91,6	

Table 3. CHARACTERISTICS OF PATIENT GROUPS

Characteristic	BMS %	DES %	DES %
Female	34	34,4	- 0,84
Age (Years)	62,1 (11,2)	62,4 (11,1)	- 2,819
Chronic Renal Failure	5,2	5,0	0,91
Hypertension	72,6	72,6	0
Diabetes	31,1	32,9	- 3,86
Peripheral Vascular Disease	2,1	2,1	0
Current Cardiac Failure	5,1	5,6	- 2,22
Previous Myocardial Infarction (MI)	14,2	14,9	- 1,99
Previous Coronary Bypass Surgery	11,5	11,9	- 1,24
Previous PCI	10,9	11,3	- 1,27
Unstable Angina at entrance	63,2	62,1	2,27
Current MI	29,3	28,4	1,99
Primary Angioplasty	10,8	10,2	1,96
Hemodynamic Status. Stable	98,0	98,1	-0,72
Unstable	1,2	1,4	-1,77
Cardiogenic Shock	0,8	0,5	3,73
LVEF >30%	96,6	95,9	-3,69
20 a 29%	3,3	4,0	-3,73
>20%	0,1	0,5	0
Number of affected vessels 1	72,1	1033 (70,9)	2,66
2	17,6	275 (18,9)	3,37
3	10,4	150 (10,3)	0,33
Coronary lesion type C	32,3	460 (31,6)	1,50
Number of treated lesions 1	92,2	92,2	0
2	7,5	7,6	-0,38
3	0,2	0,2	0
Lesion of Left Coronary Artery	3,2	3,5	-1,67
Lesion of Anterior Descending Artery	71,4	73,7	-5,16

Table 4. SURVIVAL RATES AND HAZARD RATIOS

Quintile of PS and Type of Stent	1 year %	5 year %	HR	Corrected HR
1 BMS N=34	88,2	85,2	1,22	1,73
DES N=34	91,2	79,8	(0,37 – 4,0)	(1,2 – 2,6)
2 BMS N=81	90,1	80,4	0,77	0,83
DES N=81	93,8	85,0	(0,35 – 1,70)	(0,6 – 1,1)
3 BMS N=188	95,7	82,7	0,78	0,76
DES N=188	94,2	86,1	(0,43 – 1,41)	(0,6 – 0,98)
4 BMS N=349	96,0	88,5	0,80	1,84
DES N=349	95,7	87,9	(0,48 – 1,34)	(1,5 – 2,2)
5 BMS N=806	94,8	86,4	0,58	1,38
DES N=806	98,1	91,7	(0,40 – 0,83)	(1,2 – 1,6)
Total BMS N=1458	89,8	77,4	0,69	1,29
DES N=1458	93,4	80,7	(0,52 – 0,90)	(1,14 - 1,45)

References

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Conclusions:

- DES were effective in Left Anterior Descending Artery but not for other vessels.
- DES were associated with greater overall survival and CE free survival in patients with indication strongly adjusted to the clinical practice that was conducted in Uruguay.
- Once the bias was corrected, the potential benefit of DES on mortality was not confirmed. Sensitivity analysis and bias correction is highly recommended for adequate interpretation of observational studies.