Pharmacological Stent Deployment in the Left Anterior Descending Artery: Late Event Indicators

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Summary

Background: The efficacy of pharmacological stents in decreasing the incidence of cardiac events is not homogeneous for all lesions or patient subgroups.

Objective: 1) To evaluate the late clinical evolution of patients submitted to pharmacological stent implantation in atherosclerotic lesions of the left anterior descending artery; 2) to identify, among the clinical, angiographic and intravascular ultrasonographic characteristics, the ones predictive of cardiac event risk.

Methods: From May 2002 to August 2005, 205 patients were treated with 236 pharmacological stent implants, guided by the intravascular US (IVUS).

Results: After a mean follow-up period of 711 days, the rate of stent thrombosis was 0.48%, the same observed for acute myocardial infarction or revascularization surgery. The revascularization rate of the treated lesion was 7.31% and the general event rate was 10.24%. The event indicators, according to the multivariate analysis were the implant of more than one stent in the same artery, concentric lesions and the minimal intra-stent area measured by IVUS < 3.88 mm².

Conclusion: Based on the data obtained, we conclude that the revascularization of the left anterior descending artery with pharmacological stent implant, chosen and optimized by IVUS, presents a low incidence of late events. The implant of two pharmacological stents for the treatment of long lesions was the main independent factor for the occurrence of late events. The final luminal area > 3.88 mm² obtained in the small reference-diameter segments is an independent indicator of event-free evolution. (Arq Bras Cardiol 2009;92(1):2-8)

Key words: Angioplasty, balloon; stents; ultrasonics.

Introduction

The pharmacological stents with antiproliferative agents have as target the suppression of neointimal hyperplasia. The pharmacological actions of these agents directly block the cell cycle in its initial phase (cytostatic phase) or in its final phase (cytotoxic phase). The sirolimus-coated (rapamycin) or paclitaxel-coated pharmacological stents - the most extensively studied pharmacological prosthesis with long-term evolution - have presented a significant decrease in late events, especially due to the decrease in the re-stenosis, when compared to non-pharmacological (metallic) stents[1-4].

The good evolution of the anterior descending artery revascularization is an independent indicator of survival in the main comparative surgical studies of patients receiving or not mammary artery grafts.

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This revascularization technique is extensively indicated, mainly in patients with complex lesions in the anterior descending artery – lesions that involve the diagonal branches, long lesions (> 20 mm), thin vessels (< 2.75 mm of diameter) or due to association with diabetes mellitus.

These subgroups were included in many studies that were randomized for the use of pharmacological stents[3,5-7]; however, they were not specific for the anterior descending artery (ADA). The acknowledged benefit of the pharmacological stents in selected groups, in the several aforementioned randomized studies, allows a good evolution of the ADA revascularization, regardless of the complexity of the atherosclerotic lesion or its present clinical characteristic.

Some studies have suggested that the use of IVUS to guide non-pharmacological stent implants could reduce the incidence of late re-stenosis in some subgroups of patients[8]. Regarding the participation of this resource to guide pharmacological stents, however, the published studies have been scarce.

The aims of the present study are:

1) To evaluate the late clinical evolution (cardiac events) of

patients submitted to the treatment of atherosclerotic lesions of the ADA with pharmacological stent implants;

2) To identify, among the clinical, angiographic and intravascular ultrasonographic characteristics, the ones that allow us to predict the risk of cardiac events.

Methods

Pre-procedure assessment

All patients submitted to the intervention procedure had presented a previous diagnostic coronary angiography. On the day before the procedure, following the standard operations of the Service, they were submitted to clinical evaluation, electrocardiographic and laboratory assessment - complete blood count, creatinine and fasting glycemia. The prescribed medication was aspirin 200 mg, clopidogrel 300 mg and the attending physician's statin of choice. The patients' other usual medications were maintained, except anticoagulants and oral hypoglycemic drugs. A six-hour fasting, prior to entering the hemodynamic room, was prescribed.

Before the release of the pharmacological stents, the pre-dilation of the lesions was carried out using the conventional balloons with a diameter between 2.0 mm and 3.5 mm or through atheroabrasive techniques. A direct implant without pre-dilation was performed when conditions favorable for its expansion were seen to be present.

The pharmacological stents were released with a pressure between 4 and 18 ATM and the complementary dilation was carried out with a balloon that was shorter than the stent length, which allows the expansion of the latter without injuring its borders. After the adequate angiographic result of stent release (residual lesion < 10% by the subject analysis of the operator) and based on the measurements obtained post-implant with IVUS, the necessity of new dilations was assessed.

Intravascular ultrasound

A transducer catheter Atlantis of 40 MHz was used, which has a rotating angulated mirror in its extremity that rotates at 1,800 rpm in the front of the sound-wave emitting crystal. The emitted sound waves were received and transformed into images of the interior of the vessel by the Galaxy or Clearview ultrasound device, by Boston Scientific, which projected them on the screen in real-time and stored them in video cassette tapes. The pre-implant analysis of the pharmacological stent aimed at evaluating the proximal and distal reference diameters, as well as the extension of the atherosclerotic plaque in order to select the ideal pharmacological stent (in diameter as well as in extension). In the post-implant control, a good apposition of the stent rods to the vessel walls and a correlation between intra-stent minimal luminal areas and the reference areas were sought.

The calculations of the assessment of the post-implant IVUS were carried out with the Echoplaque 2 program, version 2.5.x, by Indec Systems Inc, California, USA.

Clinical follow-up

The patients were followed by their clinicians throughout the entire process. In May and June 2006, the occurrence of major cardiac events was verified by telephone contact.

The late events that were emphasized were:

- death;

- acute myocardial infarction;

- thrombosis of the pharmacological stent, defined as acute or late angiographic occlusion of the stents;

- target lesion revascularization (TLR), characterized as any new surgical or percutaneous revascularization caused by an angiographic re-stenosis of previously dilated lesions;

- target vessel revascularization (TVR), characterized by any new surgical or percutaneous revascularization caused by a re-stenosis or a new lesion in the previously dilated vessel.

Inclusion criteria

Patients aged 18 years or older, regardless of gender, risk factors and clinical syndrome at the moment of admission; with indication of interventionist treatment only for the ADA, associated or not to the septal or diagonal branches. Left ventricular ejection fraction (EF) was > 30% in all patients and the reference diameter of the ADA was ≥ 2.25 mm. The uniarterial and multiarterial patients were joined, with all types of *de-novo* atherosclerotic lesions (nomenclature by the AHA/ACC task force[9]) and all types of non-pharmacological or pharmacological stent re-stenosis.

Exclusion criteria

To have been submitted to surgical or percutaneous intervention of other vessels other than the ADA system during the prior three months; patients with stent implant in the left coronary trunk or circumflex artery, caused by ostial lesion of the descending artery; pregnant patients those with concomitant severe disease, with high probability of death within 12 months and patients with economic or clinic limitations to receive the association of the platelet antiaggregants clopidogrel and acetylsalicylic acid for at least three months.

Statistical analysis

In the present study, the considered response variable was at least one event (present or not). To evaluate the association between dichotomous variables and the response variable, Fisher exact test was considered. Continuous variables were assessed by the Student's *t* test for independent samples, considering the homogeneity or not of the variances, or by the non-parametric Mann-Whitney test. A multivariate analysis was carried out by adjusting a model of logistic regression that included all variables that had a p value < 0.25[10]. In addition to these variables, others were included, which had clinical relevance (gender, long lesion > 20 mm, smoking and implanted stent diameter).

The continuous variables age, diameter of the balloon used to expand the post-implant stents and minimal intra-stent luminal area were included in the model in the dichotomized form; an acceptable cutoff was found according to the adjustment of the ROC curve (area below the curve significantly > 0.5 mm).

The following cutoffs were considered acceptable:

- age: 57 years;

- minimal intra-stent luminal area: 3.88 mm^2;

- diameter of the balloon used to expand the post-implant stents: 3 mm.

The statistical analysis was carried out using the software SPSS 11.0. Statistical significance was set at $p<0.05$.

Patients

This sample consisted of patients with obstructive atherosclerotic coronary disease of the anterior descending artery (ADA), diagnosed by invasive coronary angiography.

The obstructive lesions presented stenotic involvement of the arterial lumen > 70%, thus the indication of the pharmacological stent implant as the interventionist treatment, based on the clinical and angiographic findings.

The patients were treated with sirolimus-eluting (Cypher™ stent) or paclitaxel-eluting stent implant (Taxus™ stent). All the prostheses were selected through the measurements obtained at the ultrasonographic assessment in the pre-implant phase and optimized in their expansion with post-dilation guided by US. Patient inclusion started in May 2002 and finished in August 2005. The procedures were carried out in *Hospital Cardiológico Costantini*.

Results

Clinical characteristics

A total of 205 patients were treated with pharmacological stent implant, whose clinical characteristics are shown in Table 1.

Table 1 - Initial clinical characteristics

Clinical Characteristics	Patients (%)
Mean age	61.98±12.06 yrs
Male sex	142 (69.26%)
Female sex	63 (30.71%)
Stable angina	41 (20%)
Unstable angina	64 (31.21%)
Acute myocardial infarction	4 (1.95%)
Asymptomatic	74 (36.09%)
Atypical chest pain	22 (10.79%)
Arterial hypertension	132 (64.39%)
Family history	79 (38.53%)
Dyslipidemia	129 (62.92)
Smoking	33 (16.09%)
Diabetes**	45 (21.95%)
Previous myocardial infarction	19 (9.26%)
Previous revascularization surgery	15 (7.31%)
Previous angioplasty	35 (17.07%)

Angiographic characteristics

In 153 individuals (74.63%) the atherosclerotic disease was restricted to the anterior descending artery (ADA), whereas in 52 (23.36%), the disease involved other vessels rather than the ADA (multiarterial patients). The lesions in the ADA involved, in 56.61% of the cases, the origin of the diagonal branches larger than 2.25 mm, bifurcation lesion.

A total of 242 lesions of the ADA were treated in the 205 patients (mean of 1.18 lesions per patient), thus classified according to the AHA/ACC task force[9]:

- type A: 6 lesions (2.47%);

- type B1: 23 lesions (9.50%);

- type B2: 96 lesions (39.66%);

- type C: 80 lesions (33.57%).

Thirty-seven lesions did not follow the classification by the AHA/ACC task force, as they were re-stenotic lesions. The isolated characteristics of the lesions are shown in Table 2. A total of 240 stents were implanted in the ADA, of which 236 were pharmacological ones (1.51 pharmacological stents per artery).

The characteristic differences between the implanted Cypher™ and Taxus™ stents are shown in Table 3.

The mean extension of the pharmacological stents per vessel was 27.74±11.59 mm. In the studied sample, according to the addition of the extensions of the pharmacological stents implanted in a same anterior descending artery (ADA), the following data was observed:

- 67 ADAs (32.6%) received between 8 and 20 mm;

- 55 ADAs (26.8%) received between 21 and 30 mm;

- 57 ADAs (27.8%) received between 31 and 40 mm;

- 10 ADAs (4.8%) received between 41 and 50 mm;

- 16 ADAs (7.8%) received between 51 and 65 mm.

Table 2 - Angiographic characteristics of the 242 treated lesions

Angiographic Characteristics	Number
Eccentric	177 (73.14%)
Concentric	65 (26.85%)
Bifurcations*	137 (56.61%)
Calcified	16 (6.61%)
Ostial	14 (5.78%)
With thrombus	4 (1.65%)
Ulcerated	1 (0.41%)
Lesions with extension <10 mm	46 (19.00%)
Lesions with extension of 10 to 20 mm	108 (44.62%)
Lesions with extension > 20 mm	88 (36.36%)
Angulation of vessel <45º	215 (88.84%)
Angulation of vessel 45º to90º	27 (11.15%)
Angulation of vessel >90º	0 (0.00%)

**Bifurcation - presence of a lateral branch ≥ 2.25 mm involved in the affected segment of the anterior descending artery.*

Table 3 - Characteristics of the cypher™ and taxus™ stents implanted in the anterior descending artery and of the catheters used in the stent post-dilation

	Cypher™ (N=64)	Taxus™ (N=172)
Pre-dilation		
Balloon diameter	2.96±0.29	3.00±0.31
Balloon length	24.25±7.01	24.20±7.21
Administered pressure	11.42±4.20	11.56±3.96
Post-dilation		
Balloon diameter	3.07±0.39	3.04±0.34
Balloon length	17.41±6.70	17.63±6.92
Administered pressure	14.92±3.42	15.40±2.63

These measurements were obtained through the analysis of the intravascular US

In the proximal reference segment, the vessel area was 15.13 ± 4.36 mm², the lumen area was 7.62 ± 2.55mm², the percentage of stenosis was 48.68 ± 11.47% and the reference diameter was 3.10 ± 0.51mm. In the distal reference segment, the vessel area was 9.94 ± 3.51 mm², the lumen area was 6.27 ± 1.98mm², the percentage of stenosis was 35.39 ± 13.31% and the reference diameter was 2.82 ± 0.43mm.

The measurements of the intravascular US of the stent segment were:

- Minimal luminal area (mm²) of 5.13±1.53;
- Minimal luminal diameter (mm) 2.55±0.37;
- Asymmetry 0.86±0.86;
- Volume 190;79±93;14.

Clinical evolution

The mean follow-up period of the 205 patients was 711±306 days (23.3±10 months), more than 8 months of evolution of the last patient in this series. The incidence rates of stent thrombosis, acute myocardial infarction or revascularization surgery or TVR were similar: 1/205 - 0.48% for each outcome. The only patient with thrombosis was a 43 year-old male that had been submitted to one Taxus™ implant 3.0/16 mm (re-stenotic stent lesion). The reintervention with conventional angioplasty occurred 4 months after the pharmacological stent implant and 15 days after clopidogrel withdrawal.

The 1.46% death rate corresponds to three female patients:

- *Patient A* - 76 years old, with re-stenotic lesion of non-pharmacological stent, submitted to the implant of 1 Cypher™ stent, 3.0/18 mm. The procedure was carried out in May 2002 and the death occurred in June 2005. Sudden death occurred at home.

- *Patient B* - 60 years old, diabetic, with re-stenotic lesion of non-pharmacological stent. Submitted to the implant of 2 Cypher™ stents, 2.5/28 mm and 2.5/18 mm. The procedure was carried out in December 2002 and the death occurred in October 2005. Death by acute infarction occurred in her hometown.

- *Patient C* - 78 years old, lesion type B2, submitted to the implant of one Taxus™ stent 2.75/32 mm. The procedure was carried out in February 2004 and the death occurred in August 2005. Sudden death occurred at home, probably due to cerebral ischemic accident.

The incidence of TVR was 7.31% (15 patients), of which 9 received a new pharmacological stent and the others were treated with angioplasty with balloon-catheter with titanium blades.

Univariate analysis

In the present study, the considered response variable was at least 1 cardiac event (present or not, Table 4).

Table 4 - Univariate analysis

Demographic Characteristics	No event [N of patients (%)]	At least 1 event [N of patients (%)]	P value
Sex			
Male	126 (88.73)	16 (11.27)	0.6195
Female	58 (92.06)	5 (7.94)	
Age*			
≤57 yrs	73 (94.81)	4 (5.19)	0.0942
>57 yrs	111 (86.72)	17 (13.28)	
Family History			
No	114 (89.76)	13 (10.24)	1.00
Yes	70 (89.74)	8 (10.26)	
Smoking			
No	150 (90.91)	15 (9.09)	0.2572
Yes	34 (85.00)	6 (15.00)	
Diabetes			
No	147 (91.88)	13 (8.13)	0.0903
Type 1 or 2	37 (82.22)	8 (17.78)	
Dyslipidemia			
No	68 (89.47)	8 (10.53)	1.00
Yes	116 (89.92)	13 (10.08)	
SAH**			
No	66 (90.41)	7 (9.59)	1.00
Yes	118 (89.39)	14 (10.26)	
Vessels with lesions			
Uniarterial	137 (89.54)	16 (10.46)	1.00
Multiarterial	47 (90.38)	5 (9.62)	
Clinical condition***			
ACS	59 (86.76)	9 (13.24)	0.3351
Stable syndrome	125 (91.24)	12 (8.76)	
Type of Lesion			
A or B1	16 (100.00)	0 (0.00)	0.3812
B2. C. RB, RS or RSR	168 (88.89)	21 (11.11)	

Continuation: Table 4 - **Univariate analysis**

Eccentricity			
Concentric	44 (84.62)	8 (15.38)	0.1860
Eccentric	140 (91.50)	13 (8.50)	
Bifurcation			
Absent	70 (89.74)	8 (10.26)	1.00
Present	114 (89.76)	13 (10.24)	
Ostial Lesion			
Absent	174 (89.23)	21(10.77)	0.6032
Present	10 (100.00)	0 (0.00)	
Calcium			
Absent	171(89.53)	20 (10.47)	1.00
Present	13 (92.86)	19 (7.14)	
Thrombus			
Absent	182 (89.66)	21 (10.34)	1.00
Present	2 (100.0)	0 (0.00)	
Extension			
≤20 mm	110 (91.67)	10 (8.33)	0.3512
>20 mm	74 (87.06)	11 (12.94)	
Angulation			
<45°	20 (86.96)	3 (13.04)	0.7087
≥45°	164 (90.11)	18 (9.89)	
Number of stents in the DA			
1 stent	160 (91.95)	14 (8.05)	0.0228
More than 1 stent	24 (77.42)	7 (22.58)	
Type of stent			
Cypher™	50 (87.72)	7 (12.28)	0.6086
Taxus™	134 (90.54)	14 (9.46)	
Bifurcation approach			
Non-treated or treated with balloon in the lateral branch	144 (91.72)	13 (8.28)	0.1060
Treated with 2 stents	40 (83.33)	8 (16.67)	
Pre-dilated vessel			
No	54 (88.52)	7 (11.48)	0.8016
Yes	130 (90.28)	14 (9.72)	
Diameter of stents*			
≥3 mm	131 (90.97)	13 (9.03)	0.4500
<3 mm	53 (86.88)	8 (13.12)	
Diameter of post- dilation balloon *			
>3 mm	49 (96.08)	2 (3.92)	0.1109
≤3 mm	135 (86.54)	19 (12.34)	
Intra-Stent Ultrasound Measurement			
Luminal Area (mm^2)			
>3.88	147 (93.04)	11 (6.96)	0.0107
≤3.88	37 (78.72)	10 (21.28)	
Diameter (mm)	2,39±0.36	2.23±0.34	0.344
Asymmetry	0.86±0.07	0.86±0.05	0.965
Volume	190.81±93.78	190.64±89.55	0.935
Proximal reference			
Luminal Area (mm^2)	7.65±2.58	7.33±2.35	0.5885
Luminal Diameter (mm)	3.10±0.51	3.04±0.48	0.6134
Distal Reference			
Luminal Area (mm^2)	6.28±2.00	6.15±1.82	0.7713
Luminal Diameter (mm)	2.82±0.44	2.79±0.44	0.7807

**age cutoff: 57 years, established by the ROC curve. **Clinical - SCA = unstable angina or acute myocardial infarction, stable syndrome = assymptomatic patients, atypical angina or stable angina.*

Multivariate analysis

Table 5 shows the p values resulting from the adjustment of the logistic regression model, which included the variables considered in the study.

Tabela 5 - **Multivariate analysis**

Variable	P value	Estimated OR	95% Confidence Interval for OR
1 stent	0.0039	0.12	(0.03 – 0.51)
Eccentricity	0.0124	0.20	(0.06 – 0.71)
Minimum area* > 3.88 mm^2	0.0219	0.24	(0.07 – 0.81)
No diabetes	0.0536	0.31	(0.10 – 1.02)
Age <57 yrs	0.0565	0.29	(0.08 – 1.04)
Non-treated or treated with balloon in the lateral branch	0.0721	0.34	(0.11 – 1.10)
Diameter of the stent ≥3	0.1489	0.35	(0.09 – 1.45)
Diameter of the post-implant balloon >3	0.2547	0.38	(0.07 – 2.02)
Male gender	0.5262	0.68	(0.21 – 2.24)
Lesion <20 mm	0.5543	0.73	(0.25 – 2.10)
Non-smoker	0.7187	0.79	(0.22 – 2.82)

** Minimum area of the stent measure by US.*

Discussion

This study aimed the long-term follow-up (mean of 23.3±10 months) of patients submitted to the angioplasty of the anterior descending artery (ADA) with the implant of one or more pharmacological stents guided by intravascular ultrasound (IVUS). The association of the IVUS technique as a guide to implant the non-pharmacological stent allows its optimization, decreasing the late re-stenosis[8]. As for the implant of pharmacological stents, the use of IVUS to select and optimize the stent expansion needs to be validated by scientific studies.

Randomized studies with the implant of pharmacological stents present distinct late outcomes, which are directly related to the characteristics of the treated lesions. The Sirius[3] study allowed the inclusion of long lesions and thin vessels, raising the incidence of late stenosis to 8.9%, located mainly in the stent borders, considering that the incidence of intra-stent re-stenosis was low (3.2%).

The data presented raise some questions: If the selection of the extension of stents were guided by ultrasound, prioritizing the lining of the entire extension of the target plaque, would the rates of stent border re-stenosis be the same? Although the rates of intra-stent re-stenosis of pharmacological stents are known to be low, would the optimization of the stent expansion have a positive late effect?

These are difficult questions to answer, as they involve many biases of the stent implant technique, as well as of the personal interpretation of the IVUS images.

The intravascular ultrasound was used in the pre-implant assessment of the stent to analyze the extension of the obstructive atherosclerotic plaque, which would allow the chosen stent to recover the entire segment of the plaque, with its borders in a segment with a lower plaque load or without atherosclerotic lesion.

All stents implanted in anterior descending artery had their expansion optimized according to the IVUS assessment. Regardless of an optimal angiographic image, if the ultrasound assessment showed that the prostheses were not adequately expanded, the stents were dilated again.

With the development of the pharmacological stents - which allowed a good control of the neointimal proliferation - it was observed that the later loss of the intra-stent luminal diameter was low not only in the short stents (shorter than 20 mm), but was very low in long stents, as well[11]. Due to this action of long pharmacological stents observed in scientific studies and in clinical practice, the importance of the assessment of the atherosclerotic plaque by ultrasound in the selection of the length of the stents, so that the entire injured segment could be covered, increased even more.

In this study, the general rate of (at least one) cardiac events was 10.24%. Events such as death, revascularization surgery and acute myocardial infarction were scarce and among them, the rates of TVR were the highest (7.31%), corresponding to 9 patients that received a new pharmacological stent and other 6 patients submitted to dilation with catheter-balloon with titanium blades.

The incidence of late thrombosis was 0.48% per patient or 0.33% per stent, even when including patients with complex lesions, long stents, multiple stents and bifurcation lesions; this is a very low incidence, similar to the one found in studies with non-pharmacological stents[12].

Thrombosis occurred in only one patient that withdrew the use of clopidogrel in the fourth month, developing an intra-stent thrombosis 15 days later.

In this series, all types of atherosclerotic lesions or clinical syndromes that involved the ADA were treated, and the results show that the survival rate among these patients is high (98.54%). The clinical re-stenosis (target vessel revascularization rate) was the main late event observed in our series (7.31%). However, the TVR rate observed here was lower than the ones described in many clinical studies.

The main factors that indicated late events were the final luminal area evaluated by ultrasound and the number of stents implanted in the ADA. The reference diameter of the vessel, bifurcation lesion, stents implanted in thin vessels (≤ 2.75) or the type of stent implanted (Cypher™ or Taxus™) did not show any statistical difference at the uni- or multivariate analysis.

The univariate analysis carried out in the present study showed that the intra-stent luminal area < 3.88 mm² was an event predictor, with a significant p value (p=0.0107). The patients with an intra-stent luminal area < 3.88 mm² at the final ultrasound assessment presented a higher incidence of events when compared to patients with intra-stent luminal area > 3.88 mm² (21.28 % *vs* 6.96%, respectively, with p= 0.01). The treatment of long lesions implies in the implant of stents in the most distal segments of the vessel, consequently obtaining a luminal area that is quite smaller than the areas obtained in the most proximal segment. When these stents are well-implanted, it is verified if there is a good apposition of all the stent rods to the vessel wall and if the final luminal area corresponds to the reference luminal area. We observed that the stents with final luminal area > 3.88 mm² at the ultrasound presented a better late evolution (this luminal area corresponds to the minimal wanted luminal area in the segments considered to be thin vessels). However, the finding of a final luminal area of 3.88 mm² in a segment of a large-caliber vessel implicates in a hypo-expanded prosthesis, with loose rods inside the lumen of the vessel, which can interfere in the late outcome. This hypothesis was not analyzed in this series, as all the stents were hyper-expanded, with areas that were adequate to the proximal an distal reference luminal areas.

Thirty-one patients had more than 1 pharmacological stent implanted in the ADA; of these, 7 (22.58%) presented at least one event. The implant of long stents (mean length of stents implanted in this series: 24.11) was not a late event risk increase factor; however, the implant of two prostheses was an independent event factor. This finding supports the importance of the availability of long stents, with more 30 mm of length, indicating to the interventionist the use of these stents, instead of the implant of two prostheses for the treatment of long lesions.

A noteworthy fact observed herein was that the only angiographic characteristic with a p value < 0.25 was lesion eccentricity (p=0.18). The concentric lesions were independent predictors of events, similarly to the eccentric

lesions that had an OR = 0.24 (95%CI: 0.07-0.81). The fact might be related to the distribution of the stent rods, which usually separate close to the wall with less resistance, i.e., with less plaque, and gather on the side with lower expansion, which is the segment with more plaque.

The multivariate analysis showed a statistical tendency of diabetes to be an independent indicator of cardiac events; non-diabetic individuals presented an odds ratio of 0.31 (95%CI: 0.10-1.02; p=0.0536), thus diabetes was not a strong predictor of events as shown in the literature; this fact might be related to the characteristic of the group of non-diabetic patients that also received long stents, equaling the extension of the metallic net per vessel between the groups. The advent of pharmacological stents showed that the protective effects of the drugs also extend to the diabetic patients, who present evolution that is very similar to that of non-diabetic patients. However, one cannot affirm that it is possible to fully control late events in diabetic patients.

Many clinical studies have demonstrated the good evolution with pharmacological stents in vessels < 2.75 mm (thin vessels). In this series, the rate of events was 13.12% with the use of stents < 3mm and 9.03% (p=0.45) with longer stents. This variable was studied in the logistic regression due to its relevance as an indicative factor in studies with metallic stents. The multivariate analysis showed a non-significant p (p=0.14).

The studied series represents the experience of a single group that has as its characteristic, the routine use of intracoronary ultrasound to guide the implant of pharmacological stents. This study shows mainly which patients are event-free (percentage of exactness of 99.5% by the adjusted model of logistic regression).

Conclusion

Based on the obtained data, we conclude that the revascularization of the anterior descending artery with the implant of pharmacological stents chosen and optimized by the use of intravascular ultrasound presents a low incidence of late events. The implant of pharmacological stents for the treatment of long lesions was the main independent factor for the occurrence of late events. The final luminal area > 3.88 mm^2, obtained in segments of small reference diameters is an independent indicator of event-free evolution.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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References

1. Morice MC, Serruys PW, Sousa JE, Fajadet J, Hayashi EB, Perin M, et al. [for The Ravel Study Group]. A randomized comparison of a sirolimus: eluting stent with a standard stent for coronary revascularization. N Engl J Med. 2002; 346 (23): 1773-80.
2. Fajadet J, Morice MC, Bode C, Barragan P, Serruys PW, Wijns W, et al. Maintenance of long-term clinical benefit with sirolimus-eluting coronary stents: three-year results of the Ravel trial. Circulation. 2005; 111 (8): 1040-4.
3. Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, et al. [for the Sirius Investigators]. Sirolimus: eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med. 2003; 349 (14): 1315-23.
4. Holmes DR Jr, Leon MB, Moses JW, Popma JJ, Cutlip D, Fitzgerald PJ, et al. Analysis of 1-year clinical outcomes in the Sirius trial: a randomized trial of a sirolimus-eluting stent versus a standard stent in patients at high risk for coronary restenosis. Circulation. 2004; 109 (5): 634-40.
5. Schofer J, Schlüter M, Gershlick AH, Wijns W, Garcia E, Schampaert E, et al. [for the E-Sirius Investigators]. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-Sirius). Lancet. 2003; 362 (9390): 1093-9.
6. Schlüter M, Schofer J, Gershlick AH, Schampaert E, Wijns W, Breithardt G, et al. [for the E- and C-SIRIUS Investigators]. Direct stenting of native de novo coronary artery lesions with the sirolimus: eluting stent a post hoc subanalysis of the pooled E- and C- Sirius trials. J Am Coll Cardiol. 2005; 45 (1): 10-3.
7. Colombo A, Moses JW, Morice MC, Ludwig J, Holmes DR Jr, Spanos V, et al. Randomized study to evaluate sirolimus-eluting stents implanted at coronary bifurcation lesions. Circulation. 2004; 109 (10): 1244-9.
8. Casella G, Klauss V, Ottani F, Siebert U, Sangiorgio P, Bracchetti D. Impact of intravascular ultrasound-guided stenting on long-term clinical outcome: a meta-analysis of available studies comparing intravascular ultrasound-guided and angiographically guided stenting. Cathet Cardiovasc Intervent. 2003; 59 (3): 314-21.
9. Ryan TJ, Faxon DP, Gunnar RM, Kennedy JW, King SB 3rd, Loop FD, et al. Guidelines for percutaneous transluminal coronary angioplasty: a report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Transluminal Coronary Angioplasty). Circulation. 1988; 78 (2): 486-502.
10. Hosmer DW, Lemeshow S. Applied logistic regression. New York: Wiley; 1989.
11. Cardiovascular Research Foundation. Drug-eluting stent: clinical trials. CD9. In: 2004 TCT Meeting (Transcatheter Cardiovascular Tehrapeutics). Washington; 2004.
12. Colombo A, Hall P, Nakamura S, Almagor Y, Maiello L, Martini G, et al. Intracoronary stenting without anticoagulation accomplished with intravascular ultrasound guidance. Circulation. 1995; 91 (6): 1676-88.