

Preclinical Study of a Biodegradable Polymer-based Stent with Abluminal Sirolimus Release

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Abstract

Background: Bioabsorbable polymer stents with drug elution only on the abluminal surface may be safer than durable polymer drug-eluting stents.

Objective: To report the experimental findings with the Inspiron™ stent – a bioabsorbable polymer-coated stent with sirolimus release from the abluminal surface only, recently approved for clinical use.

Methods: 45 stents were implanted in the coronary arteries of 15 pigs. On day 28 after implantation, angiographic, intracoronary ultrasonographic and histomorphological data were collected. Five groups were analyzed: Group I (nine bare-metal stents); Group II (nine coated with bioabsorbable polymer on the luminal and abluminal surfaces); Group III (eight stents coated with bioabsorbable polymer on the abluminal surface); Group IV (nine stents with bioabsorbable polymer and sirolimus on the luminal and abluminal surfaces); and Group V (ten stents with bioabsorbable polymer and sirolimus only on the abluminal surface).

Results: The following results were observed for Groups I, II, III, IV and V, respectively: percentage stenosis of 29 ± 20 ; 36 ± 14 ; 33 ± 19 ; 22 ± 13 and 26 ± 15 ($p = 0.443$); late lumen loss (in mm) of 1.02 ± 0.60 ; 1.24 ± 0.48 ; 1.11 ± 0.54 ; 0.72 ± 0.44 and 0.78 ± 0.39 ($p = 0.253$); neointimal area (in mm²) of 2.60 ± 1.99 ; 2.74 ± 1.51 ; 2.74 ± 1.30 ; 1.30 ± 1.14 and 0.97 ± 0.84 ($p = 0.001$; Groups IV and V versus Groups I, II and III); and percentage neointimal area of 35 ± 25 ; 38 ± 18 ; 39 ± 19 ; 19 ± 18 and 15 ± 12 ($p = 0.001$; Groups IV and V versus Groups I, II and III). Injury and inflammation scores were low and with no differences between the groups.

Conclusion: The Inspiron™ stent proved to be safe and was able to significantly inhibit the neointimal hyperplasia observed on day 28 after implantation in porcine coronary arteries. (Arq Bras Cardiol. 2014; 102(5):432-440)

Keywords: Drug-Eluting Stents; Sirolimus; Epidemiology, Experimental.

Introduction

In the years of 2002 and 2003, the Cypher™ (Cordis Corp, Miami Lakes, USA) and Taxus™ (Boston Scientific, Natick, USA) drug-eluting coronary stents were approved for clinical use and provided a major breakthrough in the percutaneous treatment of coronary stenoses, thanks to a significant reduction of the incidence of in-stent restenosis and of the need for a new target-vessel revascularization^{1,2}. However, the occurrence of cases of late and very late thrombosis^{3,4} after implantation was an alert for the safety of these drug-eluting stents.

Among the multiple pathophysiological processes pointed as predisposing factors for late and very late thrombosis are: delayed strut endothelialization; positive remodeling with acquired poor apposition; endothelial dysfunction; and inflammatory reaction due to the presence of a durable polymer⁵.

With the purpose of overcoming the limitations and adverse events related to first-generation stents, several new drug-eluting stents have been developed. These new stents show variations either in the composition of the alloy, in the strut thickness, in the mesh design, in the drug-carrying polymer, in the drug class and dosage, or in the place on the stent surface from which the drug is released.

We hypothesized that, after drug release and degradation of the biodegradable polymer, only the metallic platform would remain in the arterial wall (like in a bare-metal stent), thus reducing the late and very late thrombosis rates of these stents, without compromising the anti-restenotic efficacy. Drug release from the abluminal surface only (stent surface in contact with the vessel wall) could also prevent delayed endothelialization of the stent struts, which is another mechanism pointed as responsible for thrombosis.

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This study presents preclinical data on the Inspiron™ stent (Scitech® Medical Products Inc., Goiânia, Goiás, Brazil) – a stent composed of a chromium-cobalt L605 alloy, which is coated with a sirolimus and biodegradable polymer mixture only on its abluminal surface, and was recently approved for clinical use.

In this experimental study, the results observed in porcine coronary arteries by means of angiographic, intracoronary ultrasonographic, and histomorphological assessment on day 28 after implantation of the Inspiron™ stent versus stents with polymer and sirolimus on the luminal and abluminal surfaces, and bare-metal stents were compared.

Methods

Ethical Aspects

The study protocol was approved by the Institutional Research Ethics Committee and was carried out according to the Good Laboratory Practices guidelines.

Animal species

A total of 15 non-atherosclerotic juvenile pigs from a commercial farm were used. Their mean weight was 28.9 kg (26 to 31.5 kg), and they received oral acetylsalicylic acid (200 mg) and clopidogrel (300 mg) one day prior to stent implantation.

Stents

Forty five pre-assembled stents manufactured by Scitech™ Medical Products, Inc., with 2.5, 3.0 and 3.5-mm diameters and 19-mm length were used. These stents are made of a chromium-cobalt L605 alloy, and have a thin strut (75- μ m thickness), forming rings with short cells (1.1 mm) linked to each other by 65- μ m struts⁶.

Except for 9 stents with no polymer or drug coating, the other stents were coated with biodegradable polymer, a mixture of poly (lactic acid) and poly (lactic acid-co-glycolic acid); this layer was 5- μ m thick, and water- and CO₂ degradable within 6 to 9 months (Figure 1).

The drug used in the drug-eluting stents was sirolimus, with 60% release in the first week and 90% within up to 4 weeks. The sirolimus dose used was 8.8 μ g per mm of stent in the sirolimus-releasing stent from the luminal and abluminal stent surfaces; or 4.4 μ g per mm of stent, on the sirolimus-releasing stent only from the abluminal surface (Inspiron™ stent).

Thus, five types of stents were assessed: nine stents without polymer or antiproliferative drug coating (Group I, bare-metal stent); nine bioabsorbable polymer-coated stents on the luminal and abluminal surfaces (Group II); eight bioabsorbable polymer-coated stents on the abluminal surface (Group III); nine bioabsorbable polymer and sirolimus coated stents on the luminal and abluminal surfaces (Group IV) and ten bioabsorbable polymer- and sirolimus-coated stents only on the abluminal surface (Group V, Inspiron™ stent).

Stent implantation procedure

Intramuscular preanesthetic medications were administered (ketamine 3 mg/kg and midazolam 0.5 mg/kg). Then, after intravenous infusion of thiopental, the animals underwent endotracheal intubation, mechanical ventilation, maintenance of the anesthetic plan with isoflurane and monitoring of their heart rhythms, heart rates, and oxygen saturation.

An arterial line for the stent implantation procedure was obtained by dissecting the common femoral artery, with arterial puncture under direct visualization and insertion of a 6-French valved introducer. Under fluoroscopy (Phillips BV – The Netherlands), a 6-French Judkins Right therapeutic catheter was manipulated for selective catheterization of the coronary arteries; next, intracoronary nitroglycerin (200 μ g) was administered and coronary angiography was performed in the left anterior oblique view at 45 degrees.

Then, a 0.014-inch Choice PR™ guidewire (Boston Scientific, Natick, USA) was inserted with its distal tip positioned in the target-coronary artery. Following a previous raffle, one stent per artery was implanted, preferably in an arterial segment with few lateral branches and without significant lumen reduction and deployment pressure enough to reach a stent deployment balloon diameter: artery rate of 1.1:1 (Table 1).

Post-Procedure follow-up

After the procedure, the animals were observed regarding their anesthetic recovery and were given prophylactic intramuscular antibiotic therapy with benzyl penicillin 1,200,000 units and gentamicin 40 mg. They were extubated when well awake, and sent to individual pens. They later received commercial feed for growing pigs (Cooper™, São José dos Campos, São Paulo, Brazil) and water *ad libitum*. For 28 days, oral antiplatelet agents were administered (acetylsalicylic acid 100 mg a day and clopidogrel 75 mg a day); the animals were seen daily by veterinarians, who observed them and made notes on their general status, level of physical activity, feed intake, and presence of fever; they also diagnosed and treated occasional surgical wound infections.

On day 28 after stent implantation, the animals were sent back to the animal experimentation laboratory and underwent control coronary angiography with quantitative coronary angiography and intracoronary ultrasonography. They were euthanized by deepening the level of anesthesia and administration of a lethal intravenous injection of potassium chloride (30 to 40 mL).

Histological processing

After euthanasia and left paramedian thoracotomy, the heart of each animal was carefully removed, with minimal handling, to prevent external stent compression; the blood in the cardiac chambers was washed out with drinking water and 0.9% saline solution. A 10% formaldehyde solution was then infused in the aortic root at a 100-mmHg pressure for 30 minutes. The arterial segments containing the stents were dissected from the adjacent tissues, removed, and placed in a 10% formaldehyde solution for 24 hours, and later, in

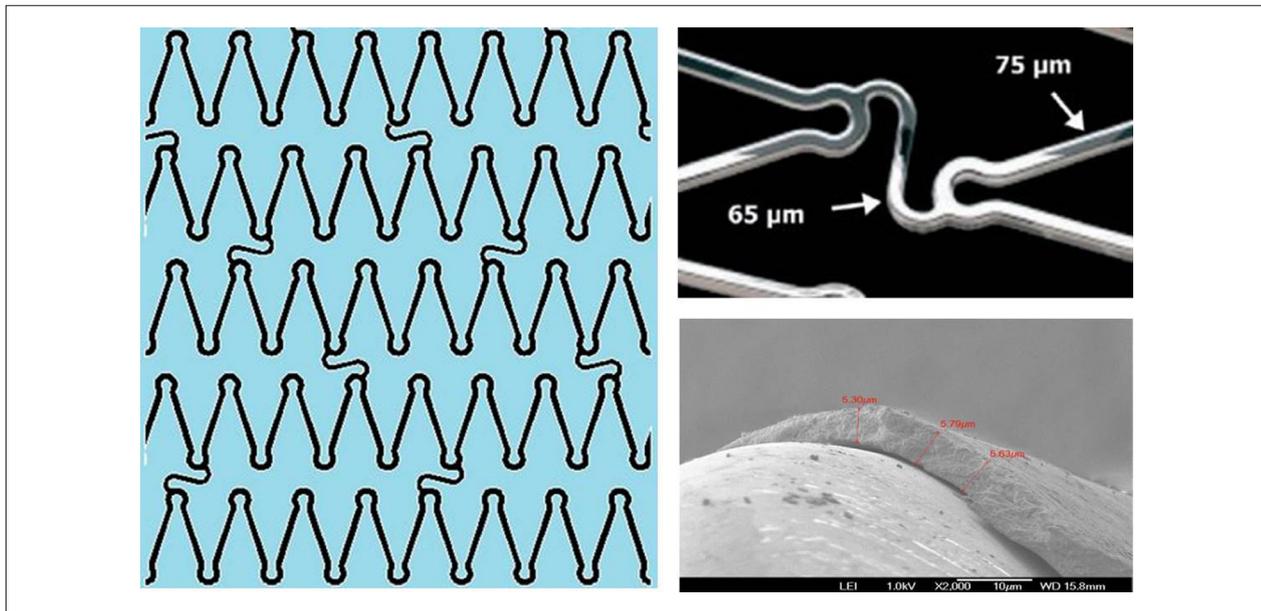


Figure 1 – Detail of the metal mesh (left), strut thickness (top right), and polymer (bottom right) of the chromium-cobalt L605 coronary stent (Scitech® Medical Products Inc., Goiânia, Goiás, Brazil).

70% absolute alcohol. These arterial segments containing the stents were desiccated in alcohol solutions, embedded in methacrylate plastic resins, and subsequently subjected to cross sections (mean thickness of $3.5 \mu\text{m}$), with a tungsten knife in a proper microtome (RM 2265, Leica, Germany).

Quantitative Coronary Angiography

All angiographies of the stent implants and the control studies performed at day 28 were analyzed by means of off-line quantitative coronary angiography using the CASS II software (Pie Medical, Maastrich, The Netherlands). The minimum lumen diameter (MLD, in mm), reference diameters (RD, in mm), percentage angiographic stenosis (%), and late lumen losses (in mm) were determined.

Intracoronary ultrasonography

40-MHZ Atlantis™ SR Pro (Boston Scientific, Natick, MA, USA) intracoronary sonography catheters were used, with automatic pull back at 0.5 mm/s . The images acquired were analyzed by the built-in measurement software of the intracoronary ultrasound imaging system (Ilab®, Boston Scientific, Natick, MA, USA); using planimetry, the lumen areas (in mm^2), stent areas (in mm^2), neointimal hyperplasia areas (in mm^2), and percentage neointimal hyperplasia areas (%) were determined.

Histomorphology

Three histological slides were obtained per third of stent segment (proximal, mid-, and distal). These slides were stained with hematoxylin-eosin and Verhoeff's method for elastic fibers; later, they underwent histomorphological analyses. These analyses were blind as regards the type of

stent implanted and semiquantitative scores were used for the assessment of inflammation⁷, fibrin deposits⁸, and degree of injury⁹.

Statistical Analysis

Quantitative data are expressed as mean \pm standard deviation (SD) or median. After verifying that the data were normally distributed, the simple analysis of variance (one-way ANOVA) was calculated for comparison of the means between the groups; post-hoc analysis was carried out when statistically significant differences were observed between these groups. The Statistical Package for the Social Sciences (SPSS) software, version 20.0, was used for data analysis and the significance level was set at 5%.

Financial disclosure

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Results

The stents were successfully implanted in all target coronary arteries, with no complications during the implantation procedures or in the immediate post-procedure period.

One animal (number 10) died on day six after stent implantation. The death cause determined by pathological study of the heart was acute inferior myocardial infarction due to occlusion of the right coronary artery in which a

Table 1 – Individual data on the stent implantation procedure

Animal number	Weight (kg)	Target coronary-artery	Group	Stent size (mm) (diameter x length)	Implantation pressure (ATM)
1	31	RC	I	3.0 x 19	8
		CX	III	3.0 x 19	6
		AD	IV	3.0 x 19	7
2	30	RC	I	3.0 x 19	10
		CX	III	3.5 x 19	8
		AD	II	3.0 x 19	10
3	30	RC	II	3.0 x 19	6
		CX	IV	3.5 x 19	10
		AD	III	3.0 x 19	5
4	31.5	RC	IV	3.0 x 19	8
		CX	I	3.0 x 19	6
		AD	II	3.0 x 19	9
5	28.5	RC	IV	3.0 x 19	10
		CX	II	3.0 x 19	6
		AD	III	3.0 x 19	7
6	30	RC	III	3.0 x 19	10
		CX	V	3.0 x 19	10
		AD	I	3.5 x 19	10
7	30	RC	V	3.0 x 19	10
		CX	I	3.0 x 19	12
		AD	III	3.0 x 19	11
8	26	RC	III	3.0 x 19	10
		CX	V	2.5 x 19	8
		AD	I	2.5 x 19	9
9	31	RC	V	2.5 x 19	6
		CX	II	3.0 x 19	7
		AD	IV	2.5 x 19	10
10	27.5	RC	II	3.0 x 19	8
		CX	I	3.5 x 19	8
		AD	V	2.5 x 19	7
11	26.5	RC	IV	3.0 x 19	12
		CX	IV	3.5 x 19	10
		AD	V	3.0 x 19	10
12	27.5	RC	III	3.5 x 19	7
		CX	V	3.0 x 19	5
		AD	II	3.5 x 19	10
13	27	RC	II	3.5 x 19	8
		CX	IV	3.0 x 19	7
		AD	V	3.0 x 19	11
14	26.5	RC	V	3.0 x 19	11
		CX	III	3.5 x 19	5
		AD	I	3.0 x 19	7
15	31.5	RC	I	3.0 x 19	10
		CX	IV	3.5 x 19	10
		AD	V	3.5 x 19	10

RC: right coronary artery; CX: circumflex artery; AD: anterior descending artery; Group I: bare-metal stents; Group II: stents with bioabsorbable polymer on the luminal and abluminal surfaces; Group III: stents with bioabsorbable polymer on the abluminal surface; Group IV: stents with bioabsorbable polymer and sirolimus on the luminal and abluminal surfaces; Group V: stents with bioabsorbable polymer and sirolimus only on the abluminal surface.

stent coated with biodegradable polymer on the luminal and abluminal surfaces had been implanted (Group II stent). The other arteries – anterior descending and circumflex, and the stents implanted in these arteries, were patent, with no firmly adherent intraluminal thrombi. This early death determined an early mortality rate of 6.6% (one in 15 animals), which, according to an Investigators Consensus, is representative of “good implantation technique and stent technology”¹⁰ (rate should be lower than 10%).

On day 28 after stent implantation, control coronary angiography performed in the surviving animals showed arterial segments with patent stents and no image suggestive of thrombus.

Findings of quantitative coronary angiography, intracoronary ultrasonography and histopathology are described in Table 2.

Quantitative Coronary Angiography

On quantitative coronary angiography, the porcine coronary arteries had a reference diameter of approximately 2.6 mm during the stent implantation procedure. The inflation pressure for stent implantation was, on average, of 8.5 ATM (5 to 12 ATM; $p = 0.348$), reaching a balloon: artery ratio of 1.1:1 to cause moderate injury to the arterial wall.

Control quantitative coronary angiography on day 28 after the procedure did not show any statistically significant difference between the groups.

Intracoronary ultrasonography

On intracoronary ultrasonography, adequate stent strut apposition was observed in all cases on day 28 after implantation. Also, statistically significant larger luminal areas (mm^2) were observed in the drug-eluting stents (Groups IV and V) in relation to control stents (Groups I, II and III) ($p = 0.001$). Likewise, the neointimal area and percentage neointimal area were significantly smaller in these drug-eluting stents in relation to control stents ($p = 0.001$ for comparisons of Groups IV and V individually versus Groups I, II and III), as shown in Figure 2.

The neointimal hyperplasia observed in the stents coated with bioabsorbable polymer and sirolimus only on the abluminal surface (Group V, Inspiron™ stent) was equivalent to that observed in stents with the same coating on the luminal and abluminal surfaces (Group IV), with no statistically significant difference ($p = 0.913$).

Histomorphology

The injury and inflammation scores were low and showed no statistically significant differences between the groups ($p = 0.999$). Figure 3 shows histological images of the neointimal hyperplasia on day 28 after implantation of a bare-metal stent (on the left) and of a drug-eluting stent (on the right) in arteries.

Table 2 – Results of quantitative coronary angiography, intracoronary ultrasonography and histomorphology

	Group					p value
	I (N = 9)	II (N = 9)	III (N = 8)	IV (N = 9)	V (N = 10)	
Baseline RD (mm)	2.59 ± 0.21	2.62 ± 0.20	2.63 ± 0.30	2.61 ± 0.24	2.50 ± 0.43	0.901
Ballon inflation pressure (ATM)	9.0 ± 1.9	8.0 ± 1.7	7.6 ± 2.2	9.3 ± 1.6	9.0 ± 2.1	0.348
Ballon diameter (mm)	2.76 ± 0.27	2.79 ± 0.24	2.89 ± 0.32	2.83 ± 0.19	2.71 ± 0.26	0.716
Ballon/artery ratio	1.06 ± 0.04	1.06 ± 0.08	1.10 ± 0.07	1.09 ± 0.10	1.10 ± 0.10	0.845
MLD at procedure termination (mm)	2.67 ± 0.23	2.74 ± 0.22	2.69 ± 0.21	2.73 ± 0.22	2.59 ± 0.26	0.749
RD on control angiography (mm)	2.30 ± 0.30	2.49 ± 0.32	2.39 ± 0.30	2.48 ± 0.22	2.54 ± 0.30	0.470
MLD on control angiography (mm)	1.64 ± 0.61	1.59 ± 0.45	1.57 ± 0.49	1.95 ± 0.43	1.85 ± 0.36	0.379
Percentage stenosis (%)	29 ± 20	36 ± 14	33 ± 19	22 ± 13	26 ± 15	0.443
Late lumen loss (mm)	1.02 ± 0.60	1.24 ± 0.48	1.11 ± 0.54	0.72 ± 0.44	0.78 ± 0.39	0.253
Luminal area (mm^2)	4.49 ± 2.16	4.29 ± 1.53	4.33 ± 1.40	5.77 ± 3.32	6.03 ± 2.18	0.001*
Vessel area (mm^2)	6.95 ± 1.40	6.90 ± 1.27	6.97 ± 0.87	7.00 ± 1.10	7.00 ± 1.58	0.305
Stent area (mm^2)	7.09 ± 1.40	7.03 ± 1.27	7.07 ± 0.87	7.07 ± 1.10	7.00 ± 1.70	0.676
Neointimal area (mm^2)	2.60 ± 1.99	2.74 ± 1.51	2.74 ± 1.30	1.30 ± 1.14	0.97 ± 0.84	0.001*
Percentage neointimal area (%)	35 ± 25	38 ± 18	39 ± 19	19 ± 18	15 ± 12	0.001*
Inflammation (median) (min-max)	1 (0 - 2)	1 (0 - 2)	1 (0 - 3)	1 (0 - 1)	1 (0 - 1)	0.999
Schwartz injury (median) (min-max)	1 (0 - 3)	1 (0 - 2)	1 (1 - 3)	1 (0 - 2)	1 (0 - 2)	0.999

* Group IV versus Groups I, II, III and Group V versus Groups I, II, III.

Group I: bare-metal stents; Group II: stents with bioabsorbable polymer on the luminal and abluminal surfaces; Group III: stents with bioabsorbable polymer on the abluminal surface; Group IV: stents with bioabsorbable polymer and sirolimus on the luminal and abluminal surfaces; Group V: stents with bioabsorbable polymer and sirolimus only on the abluminal surface; RD: reference diameter; MLD: minimum lumen diameter.

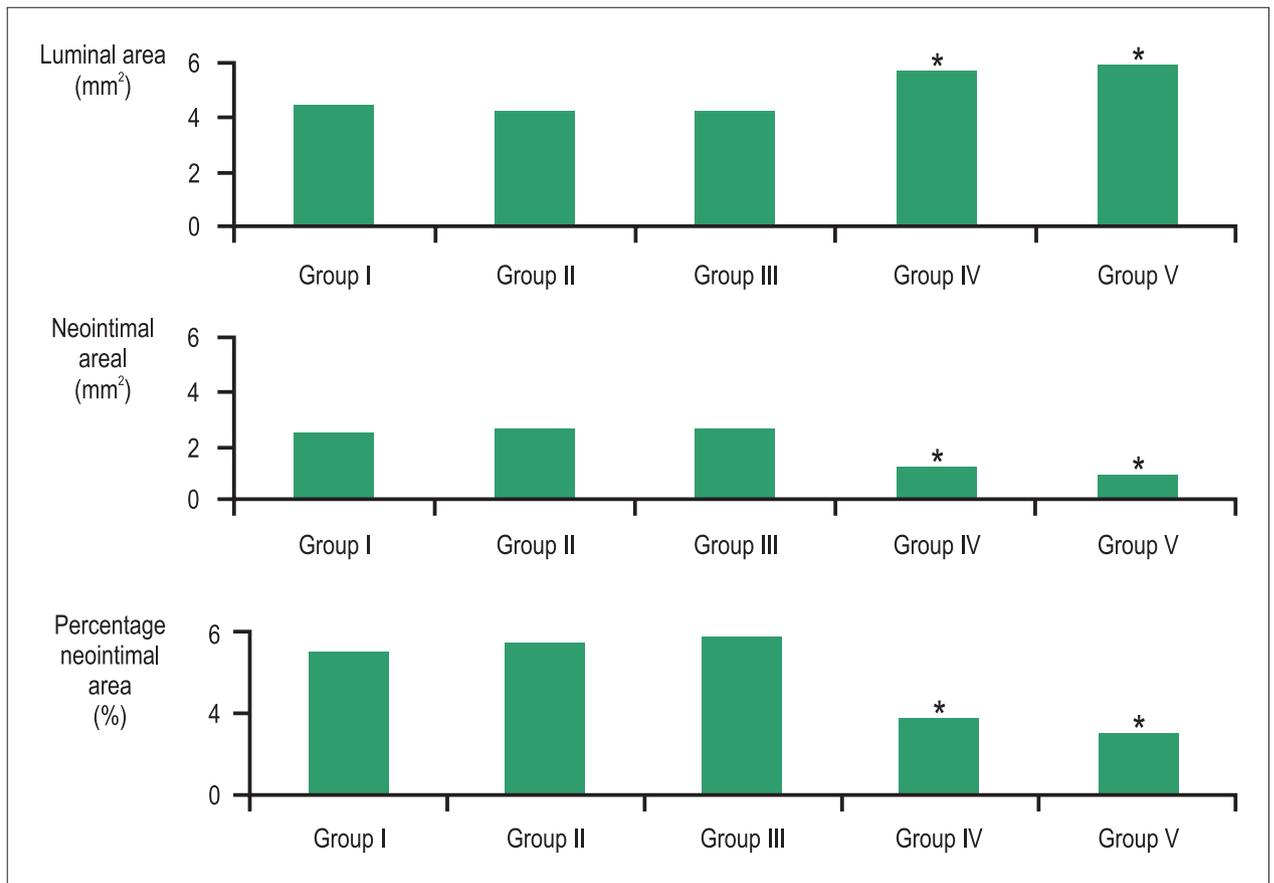


Figure 2 – Luminal area (mm²), neointimal area (mm²), and percentage neointimal area (%) observed in the experimental groups I to V. * p value < 0.05 for Group IV versus Groups I, II and III, and Group V versus Groups I, II and III.

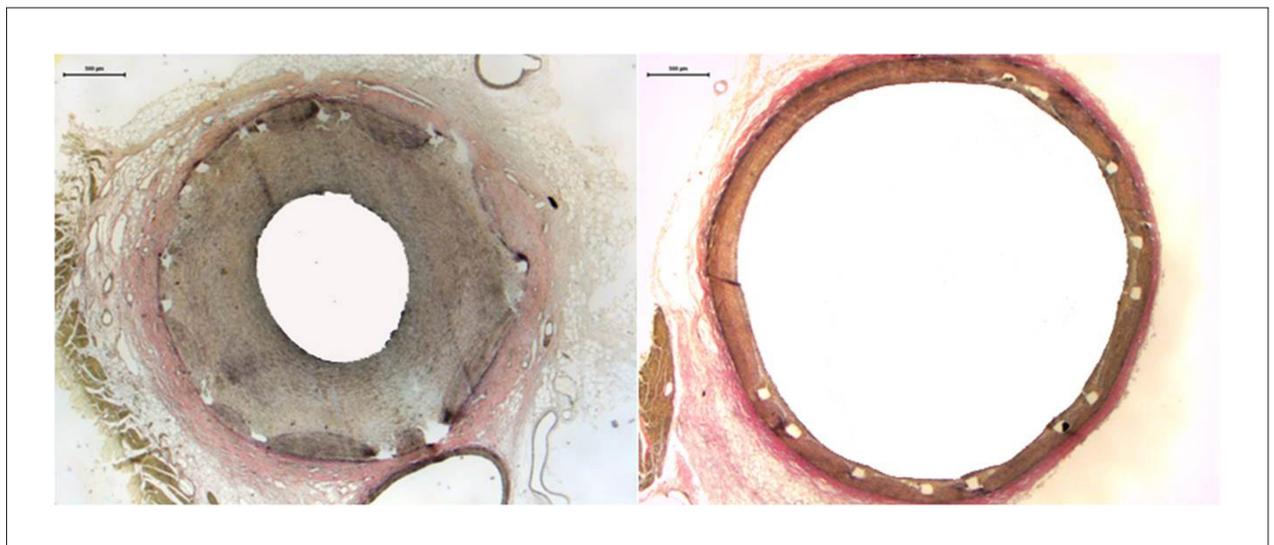


Figure 3 – Cross-sectional views of porcine coronary arteries on day 28 after bare-metal stent implantation (Group I, left) and biodegradable polymer-coated stent with sirolimus elution on the abluminal surface (Group V) (right). Magnification 40X.

Discussion

Preclinical studies in laboratory animals for the development and improvement of coronary stents are important to provide an initial idea of the mechanical performance, safety and efficacy profile of the stents, in addition to being required by regulatory agencies for the approval of these devices for clinical use¹¹.

Despite all the benefits from the first-generation drug-eluting stents which brought a revolution in the treatment of atherosclerotic coronary disease, questions arose on the long-term safety of these devices, especially in relation to late thrombosis¹².

After the initial reduction in the number of drug-eluting stents implantation observed at that time, new efforts have focused on the development of stents with the use of different alloys (chromium-cobalt and platinum-chromium), new biocompatible or biodegradable polymers, and the incorporation of new drugs (everolimus, zotarolimus and biolimus A9), aiming to increase the safety of these devices.

Although the pathophysiology of stent thrombosis is multifactorial, several animal and clinical evidences have pointed to the presence of durable polymers as responsible for inflammation and delayed vascular repair¹³. These evidences have fostered the development of biodegradable polymer-based stents and bioabsorbable stents.

In the present preclinical study on porcine coronary arteries, we observed that biodegradable polymer-coated stents with sirolimus release only from the abluminal surface (Group V, Inspiron™ stent) showed neointimal hyperplasia quantitatively similar to that of polymer and sirolimus-coated stents on the luminal and abluminal surfaces (Group IV). The groups with sirolimus-releasing stents (Groups IV and V) showed lower neointimal area in relation to the bare-metal stents (Groups I, II and III). No difference was observed between the five groups in relation to the injury and inflammation scores, thus showing that both the bioabsorbable polymer and the antiproliferative drug used were safe and effective.

The Inspiron™ eluting-stent is characterized by being composed of a chromium-cobalt L605 alloy, biodegradable polymer coating, and sirolimus elution only on the abluminal surface. Possibly because of being coated with a biodegradable polymer, it is safer than durable-polymer stents. In a meta-analysis of randomized clinical trials comparing stent thrombosis rates up to 4 years after use of the Yukon (Translumina, Hechingen, Germany) and Biomatrix™ Flex (Biosensors International, Singapore) biodegradable polymer-based drug-eluting stents versus the Cypher™ (Cordis Corp, Miami Lakes, FL, USA) durable-polymer stent, the biodegradable polymer-based stents showed less definitive stent thrombosis, less clinical endpoints and less target-lesion revascularization than the Cypher™ durable-polymer stent¹⁴.

An experimental study in a porcine model compared the endothelial activity and inflammation scores in animals undergoing Nobori™ stent implantation – a stent coated with bioabsorbable polymer and biolimus only on its abluminal surface, to that of animals undergoing Cypher™ stent implantation, and found increased endothelial relaxation,

decreased production of superoxide anion, and less inflammation in the coronary segments in the group receiving the Nobori™ stent¹⁵.

Recent findings, however, suggest that the presence of a durable polymer per se does not determine a greater risk of late thrombosis^{16,17}. In an experimental study, Kolandaivelu et al¹⁸ observed that drug-eluting stents with durable polymer (XIENCE) showed less early thrombogenicity than a corresponding bare-metal stent (Multilink Vision), i.e., polymer and drug coating provided a protective effect for acute thrombogenicity. Factors such as the stent design and strut thickness emerged as other important factors predisposing stent thrombosis.

Several other stents using biodegradable polymer and antiproliferative drugs released only from the abluminal surface have been developed. Examples of these stents are the stainless steel biolimus A9-eluting Nobori™ (Terumo Corp., Japan) and Biomatrix™ (Biosensors International, Singapore) stents ; the stainless steel paclitaxel-eluting JACTAX™ stent (Boston Scientific, Natick, USA) , and the chromium-cobalt sirolimus-eluting Firehawk™ stent (MicroPort Medical, Shanghai, China).

The Inspiron™ stent has been extensively studied in experimental animals with results comparable to those of other drug-eluting stents as regards safety, stent-strut endothelialization, and neointimal hyperplasia^{19,20}.

Clinical studies are underway to evaluate the efficacy of this new drug-eluting stent. The preliminary clinical results of the Inspiron™ stent (INSPIRON I) have shown a good angiographic response, with late lumen loss of 0.18 mm; good ultrasonographic response, with percentage neointimal obstruction of 8.2%; and target-vessel revascularization of 0%.

A randomized clinical trial (DESTINY) comparing the Inspiron™ stent with Biomatrix™ stent is currently being conducted, expected to include 165 randomized patients 2:1 (Inspiron™ stent versus Biomatrix™).

Study limitations

The model used in the present study was healthy porcine coronary arteries, which may not represent the progression in a vascular segment with atherosclerotic disease. Atherosclerotic animal models have been developed in rabbits and pigs; however, these models are still uncommonly used in preclinical studies for the development and improvement of coronary stents.

Intracoronary ultrasonography was used only in the control on day 28 after stent implantation with the purpose of assessing in-stent neointimal hyperplasia, and not to guide stent implantation. However, despite the known limitations of quantitative coronary angiography, the findings of this method revealed that the stents were adequately implanted (balloon: artery ratio of 1.1:1) and the intracoronary ultrasonographic findings showed adequate stent strut apposition in all cases.

Optical coherence tomography is a method that has been widely used in preclinical and clinical validation studies of new stents; however, this method was not yet available for experimental animal use in our institution at the time the study was carried out.

Conclusions

In this experimental study, the drug-eluting stents coated with sirolimus and bioabsorbable polymer in porcine coronary arteries showed less neointimal hyperplasia when compared to control bare-metal stents. The bioabsorbable polymer-based stent with sirolimus released only from its abluminal surface (Inspiron™ stent) showed the same neointimal antiproliferative efficacy as the stent with sirolimus released from both the luminal and abluminal surfaces.

Author contributions

Conception and design of the research: Takimura CK, Campos CAH; Acquisition of data: Takimura CK, Campos CAH, Campos JC, Gutierrez PS; Statistical analysis: Takimura CK; Analysis and interpretation of the data: Takimura CK; Writing of the manuscript: Takimura CK, Craveiro PHM; Supervision / as principal investigator: Takimura CK; Critical

revision of the manuscript for intellectual content: Campos CAH, Craveiro PHM, Borges TFC, Curado L, Morato SP, Laurindo FRM, Lemos Neto PA.

Potential Conflict of Interest

The authors Celso Kiyochika Takimura, Francisco Rafael Martins Laurindo Alves and Pedro Lemos Neto are scientific consultants of Scitech Medical Products. The authors Luciano Spero Penha Morato Curado and are employed of Scitech Medical Products.

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Study Association

This study is not associated with any thesis or dissertation work.

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