

Mechanical Behavior to Overexpansion of Cobalt Chromium Compared with Stainless Steel Stents in the Abdominal Aorta of Hypercholesterolemic Rabbits

Comportamiento mecánico ante la sobreexpansión de stents de cromo-cobalto comparados con stents de acero inoxidable, implantados en la aorta abdominal de conejos hipercolesterolémicos

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ABSTRACT

Objectives: The aim of this study was to analyze the behavior to overexpansion of cobalt chromium stents compared with stainless steel stents.

Methods: Twenty New Zealand rabbits were used, fed with a diet supplemented with 1% cholesterol. Animals were divided into two groups. Group 1 (n=10) received 3.0 mm cobalt chromium stents overexpanded at 20 atmospheres and group 2 (n=10) 3.5 mm stents deployed at 10 atmospheres. These stents were compared with a previous series of 20 animals with stainless steel stents, divided into the same two groups. A third group with conventional diet was used as control. Intravascular ultrasound (IVUS) was performed to assess the degree of elastic recoil and also the degree of symmetry using “intertrust angles”.

Results: In group 1 of cobalt chromium stents, mean elastic recoil was 0.11 ± 0.13 mm, (3.21% recoil) and in group 2 this was 0.3 ± 0.12 mm, (8.26% recoil) ($p=0.002$). In group 1 of stainless steel stents mean elastic recoil was 0.28 ± 0.18 mm (8.21% recoil) and in group 2 this was 0.10 ± 0.11 mm (2.79% recoil) ($p < 0.001$).

Conclusions: In cobalt chromium stents, elastic recoil was lower in overexpanded stents, whereas in stainless steel stents, elastic recoil was higher in overexpanded stents. No differences in symmetry were observed between the different groups.

Key words: Stents - Asymmetry - Elastic recoil - Intravascular ultrasound

RESUMEN

Introducción: Investigar cuál es el comportamiento de los stents de aleación de cromo cobalto ante la sobreexpansión comparados con los stents de acero inoxidable.

Material y Métodos: Se utilizaron 20 conejos neozelandeses que fueron alimentados con colesterol agregado en la dieta al 1%, y divididos en dos grupos. El grupo 1 (n = 10) recibió stents de cromo cobalto de 3 mm sobreexpandidos a 20 atmósferas, y el grupo 2 (n = 10), stents de 3,5 mm implantados a 10 atmósferas. Estos fueron comparados con una serie previa de 20 animales con stents de acero inoxidable, divididos en los mismos dos grupos. Un tercer grupo con dieta convencional fue utilizado como control. Se realizó ultrasonido intravascular (IVUS) para determinar el grado de retracción elástica y se analizó también el grado de simetría por medio de los “ángulos intertrust”.

Resultados: El grupo 1 de stents de cromo cobalto presentó un retroceso elástico de $0,11 \pm 0,13$ mm (3,21% de retracción) y el grupo 2, de $0,3 \pm 0,12$ mm, (8,26% de retracción) ($p = 0,002$). El grupo 1 de stents, de acero inoxidable presentó un retroceso elástico de $0,28 \pm 0,18$ mm, (8,21% de retracción) y el grupo 2, de $0,10 \pm 0,11$ mm, (2,79% de retracción) ($p < 0,001$).

Conclusiones: En los stents de cromo cobalto el retroceso elástico es menor cuando se los sobreexpande, mientras que en los stents de acero inoxidable el retroceso elástico es mayor cuando se los sobreexpande. No se observaron diferencias en términos de simetría entre los diferentes grupos.

Palabras claves: Stents - Stents Metálicos Autoexpandibles - Aorta Abdominal/cirugía - Hipercolesterolemia - Ultrasonografía Intervencional/métodos

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INTRODUCTION

Intravascular bare-metal stent implantation using balloon deployment was introduced in the practice for vascular treatment with catheters in 1985. The first design was developed by the Argentine doctor Julio Palmaz to treat iliac artery occlusions. (1) Shortly after, Dr. Richard Schatz introduced some changes that allowed its use in coronary arteries. (2)

Stents provide a mechanical support which significantly reduces elastic recoil and remodeling of the treated arterial segment. (3) Stent overexpansion is a common practice during implantation, either because an adequate diameter is not attained due to an error in graft selection or because manufacturers have only one graft design mounted on balloons with different diameters. Interestingly, few studies have evaluated and compared in detail the effect of overexpansion on stent elastic recoil. (4, 5)

One of these studies was performed at our institution, using two groups of hypercholesterolemic rabbits with conventional stent implantation in the abdominal aorta, using two implantation techniques. In one group, stents were deployed to a nominal value, whereas the other group received lower diameter stents that were overexpanded. (6) In that study, we demonstrated that overexpanded stainless steel stents experienced greater elastic recoil.

However, it has not been demonstrated whether new drug-eluting cobalt chromium stents have the same behavior to overexpansion. The aim of the present study was thus to compare the mechanical behavior of a series of new cobalt chromium alloy stents implanted in the abdominal aorta of hypercholesterolemic rabbits using two implantation techniques, with that of stainless steel stents of the series corresponding to our previous work "Restenosis and asymmetric expansion of stents in the aorta of hypercholesterolemic rabbits", published in the Argentine Journal of Cardiology (*Revista Argentina de Cardiología*) 2005; 73:174-179, which were implanted using the same technique.

METHODS

Forty New Zealand rabbits were used, weighing 3-4 kg and fed with a diet supplemented with 1% cholesterol during 4 weeks. After this period, experimental procedures for stent implantation were performed, and the outcome was monitored for 8 weeks during which the hypercholesterolemic diet was maintained.

The purpose of this diet was to achieve endothelial dysfunction and incipient atherosclerotic lesions as demonstrated in previous studies from our group, thus resembling as closely as possible what occurs in humans with vascular disease. Stents were implanted in the Experimental Hemodynamics lab of the Basic Sciences and Experimental Medicine Institute (ICBME) at Centro Agustín Rocca de San Justo, belonging to Hospital Italiano de Buenos Aires.

The same aseptic care used for human stent implantation was taken in the experiments to avoid the risk of infection, jeopardizing the life of the animals or the experimental findings. Rabbits were anesthetized with intramuscular in-

jection of 35 mg/kg ketamine and 5 mg/kg xylazine.

A venous catheter was introduced in the marginal vein of the ear through which a blood sample was withdrawn to measure cholesterol level. Then, 5% dextrose was infused to maintain catheter patency. Subsequently, a laryngeal mask was placed and following intubation, anesthesia was maintained with 1-2% isoflurane. Analgesia was supplemented with continuous fentanyl intravenous infusion at a dose of 5 µg/kg/h.

Lead II electrocardiogram was recorded using a cardiograph to obtain heart rate (HR) and determine eventual abnormal cardiac rhythm. Respiratory frequency (RF) was visually controlled by counting thoracic excursions and a pulse oximetry sensor placed on the tongue was used to monitor oxygen saturation.

The groins were shaved and disinfected with povidone-iodine solution before placing the sterile drapes around the surgical field. Once the stage of anesthetic depth was reached, the femoral artery was exposed by plane dissection. After separating the artery from the surrounding tissue with two linen sutures placed around it, an intra-arterial 1.3 mm diameter Teflon cannula (Abbocath 22™) was inserted.

Prior intravenous heparin at a dose of 50 IU/kg was administered. Angiographic control was performed before stent implantation, injecting 5 ml low osmolarity iodine contrast solution through the cannula (Figure 1A). After visualizing the anatomy, a 3-mm diameter abdominal aortic segment was selected, below the origin of the renal arteries. A 0.014" guidewire was inserted and the balloon-stent system was advanced along it (Figure 1B). Twenty stainless steel stents (Multilink Penta-Abbot Vascular™) and 20 everolimus-eluting cobalt chromium stents (XIENCE V-Abbot Vascular™) were implanted in the abdominal aorta of 40 rabbits.

Animals with stents were divided into four experimental groups; two groups corresponded to stainless steel stents and two groups to cobalt-chromium stents. Group 1 with stainless steel stents (overexpanded) (n=10) received 3.0 mm × 18 mm stents deployed at 20 atmospheres to reach a nominal diameter of 3.42 mm and group 2 with stainless steel stents (non overexpanded) (n=10) received 3.5 mm × 18 mm stents deployed at 10 atmospheres to attain a nominal diameter of 3.63 mm. (These two groups correspond to the work: "Restenosis and asymmetric expansion of stents in the aorta of hypercholesterolemic rabbits", published in the Argentine Journal of Cardiology (*Revista Argentina de Cardiología*) 2005; 73:174-179).

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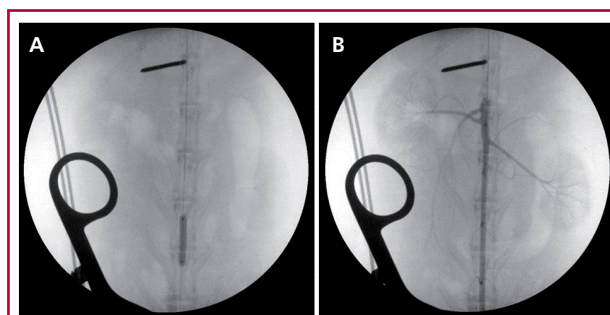


Fig. 1. A: Angiographic image of inflated balloon at the time of stent deployment. **B:** Angiographic image of the abdominal aortogram prior to stent implantation

group 2 with cobalt chromium stents (non overexpanded) (n=10) received 3.5 mm × 18 mm stents deployed at 10 atmospheres to attain a nominal diameter of 3.63 mm.

A fifth group without stent implantation was used as control. In all cases, intravascular ultrasound was performed after implantation using a Galaxy II Boston Scientific™ system to assess stent diameter and area and calculate its elastic recoil based on the ratio between the stent nominal diameter and the ultrasound measured diameter after implantation (Figure 2A).

Also, the intertrust angles were measured in sections every 1 mm to determine in each section if the stent had symmetrical or asymmetrical configuration (8) (Figure 2B). Symmetry was defined using the same criterion of our previous work, describing as “asymmetrical” sections where two or more intertrust angles above 40° were found. (9)

After the end of the procedure, the femoral artery was ligated and the wound was cleansed with povidone-iodine. Suture was performed with separate linen stitches. The cholesterol supplemented diet continued during the follow-up period after stent implantation. Each animal received 5 mg/kg/day aspirin for 8 weeks until follow-up conclusion.

Statistical analysis

Type of distribution was determined for continuous variables, and those with normal distribution were expressed as mean and standard deviation and compared using analysis

of variance (ANOVA) followed by the Bonferroni test. In the case of non-normal distribution, variables were analyzed with non-parametric tests (Kruskal-Wallis). Significance was established at $p < 0.05$.

Ethical considerations

The present study was performed following the guidelines for the Care and Use of Laboratory Animals, published by the US National Institutes of Health (NIH Publication # 85-23, revised in 1996). (7)

RESULTS

Mean blood cholesterol level in group 1 animals was 119.6 ± 18.2 mg, while in group 2 it was 122.4 ± 22.7 mg. In control animals, its value was 61.6 ± 10.8 mg (Figure 3).

For group 1 with stainless steel stents, ultrasound-measured mean stent diameter was 3.41 ± 0.01 mm and mean elastic recoil was 0.28 ± 0.18 mm, corresponding to 8.21% elastic recoil.

For group 2 with stainless steel stents, ultrasound-measured mean stent diameter was 3.58 ± 0.01 mm and mean elastic recoil was 0.10 ± 0.11 mm, corresponding to 2.79% elastic recoil.

For group 1 with cobalt chromium stents, ultra-

Fig. 2. A: Intravascular ultrasound image of an abdominal aortic segment with implanted stent and intertrust angle measurements. **B:** Intravascular ultrasound image of an abdominal aortic segment with implanted stent and diameter and area measurements.

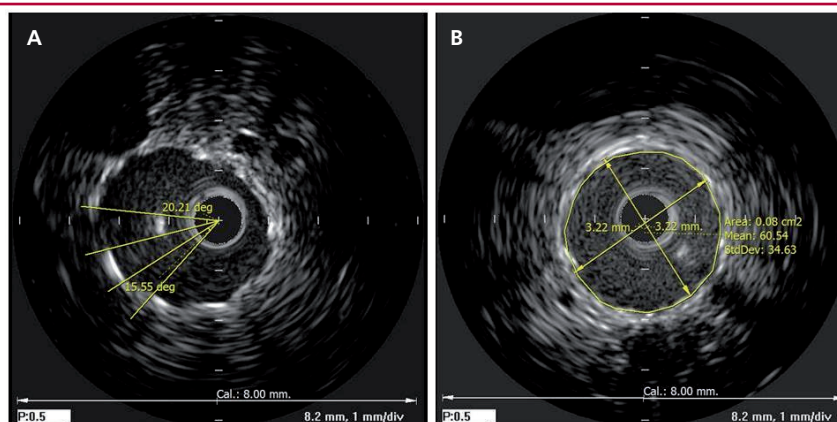
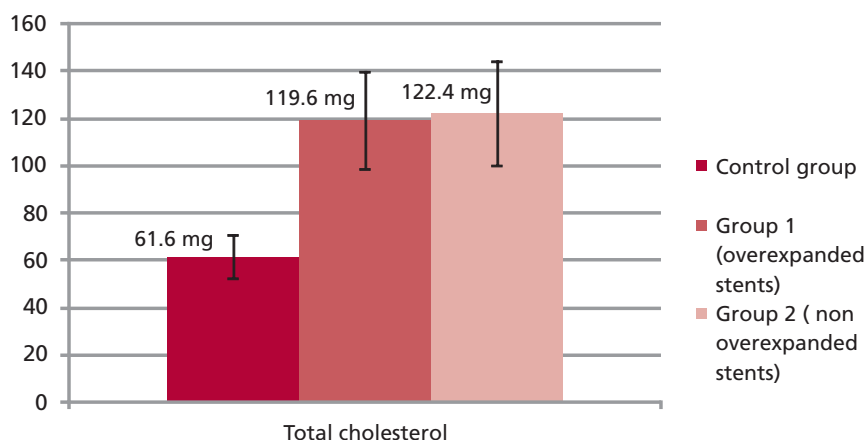


Fig. 3. Mean cholesterol values in the control group and the two groups fed with the cholesterol-supplemented diet.



sound-measured mean stent diameter was 3.31 ± 0.13 mm and mean elastic recoil was 0.11 ± 0.13 mm, corresponding to 3.21% elastic recoil.

For group 2 with cobalt chromium stents, ultrasound-measured mean stent diameter was 3.33 ± 0.12 mm and mean elastic recoil was 0.3 ± 0.12 mm, corresponding to 8.26% elastic recoil (Figures 4 and 5)

No differences in symmetry were found between groups, as in cobalt chromium stents, 70.14% of group 1 sections and 78% of group 2 sections were symmetrical ($p=NS$) and in stainless steel stents 87.6% of group 1 sections and 88.1% of group 2 sections were symmetrical ($p=NS$).

DISCUSSION

Despite the progress in interventional cardiology, bare-metal stent restenosis and late thrombosis of drug-eluting stents are currently the most important limitations of percutaneous coronary intervention. Although numerous predictors for these phenomena have been identified, a common denominator is deficient stent expansion. For this reason, stent overexpansion has become a common practice in interventional cardiology, either for the need of adapting the cylindrical shape of the stents to the conical shape of

the arteries, especially in long segments or bifurcations, or due to the limitations in the availability of certain stent diameters, particularly for large caliber vessels or venous bridges.

Cobalt chromium platforms are characterized by lower strut thickness, making them more flexible, but without compromising stent radial force. Previous studies have shown that cobalt chromium stent platforms have a mechanical behavior similar to those of stainless steel when implanted at nominal diameter; however, no study had evaluated the behavior of these platforms to overexpansion. (10, 11)

Moreover, atherosclerotic disease generated in hypercholesterolemic rabbits is limited to traces of fat deposits which generate minimal resistance to stent expansion and is very distant from the reality of coronary artery disease, where fibrous or fibrocalcific plaques are very common and offer great resistance to expansion. Taking this into account, stent recoil could be even greater in clinical practice.

According to the results of the present study, where cobalt chromium stents present a significantly lower degree of elastic recoil to overexpansion, it could be assumed that these stents would be preferable in case stent overexpansion is required. However, consider-

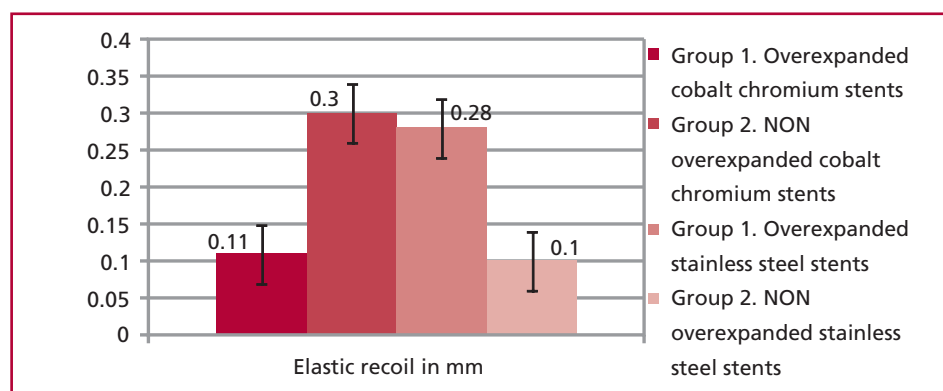


Fig. 4. Elastic recoil (mm) in the two groups of stainless steel and cobalt-chromium stents.

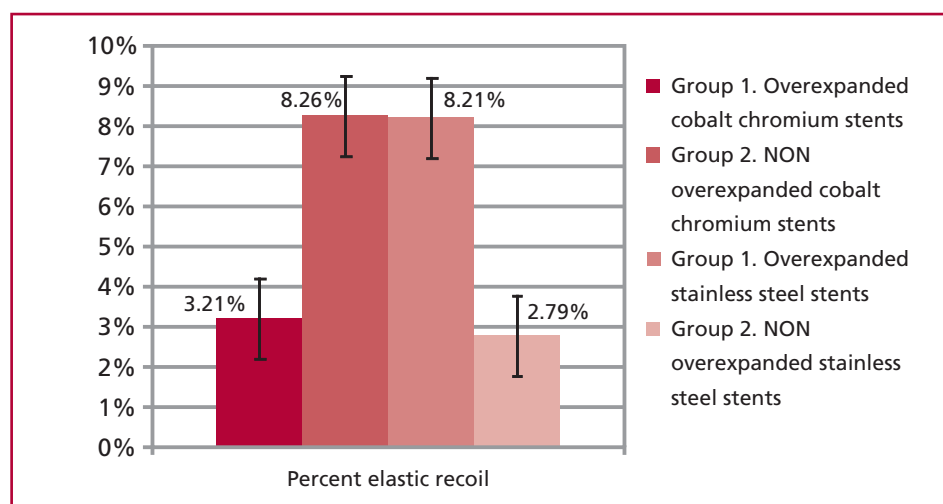


Fig. 5. Percent elastic recoil in the two groups of stainless steel and cobalt-chromium stents.

ing that the mechanical properties of a stent are not only governed by its material, but also by its design, future studies with different designs would be necessary to determine if this behavior to overexpansion is preserved.

Declaration of conflict of interest

None declared.

(See authors' conflict of interests forms on the web/supplementary material.)

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REFERENCES

1. Palmaz JC, Sibbit RR, Reuter SR, Tio FO. Expandable intraluminal graft: A preliminary study. *Radiology* 1985;156:73-7, <http://doi.org/cqk8>
2. Schatz RA, Palmaz JC, Tio FO, García F, García O. Balloon-expandable intracoronary stents in the adult dog. *Circulation* 1987;76:450-7, <http://doi.org/ffjs65>
3. Serruys PW, de Jaegere P, Kiemeneij F, Macaya C, Rutsch W, Heyndrickx G, et al. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. Benestent Study Group. *N Engl J Med* 1994;331:489-95, <http://doi.org/c39m9m>
4. Carrozza JP Jr, Hosley SE, Cohen DJ, Baim DS. In vivo assessment of stent expansion and recoil in normal porcine coronary arteries: differential outcome by stent design. *Circulation* 1999;100:756-60, <http://doi.org/c39m9m>
5. Hong MK, Park SW, Lee CW, Ko JY, Kang DH, Song JK, et al. Intravascular ultrasound comparison of chronic recoil among different stent designs. *Am J Cardiol* 1999;84:1247-50, A8.
6. Fernández AD, Berrocal D, González G, Pérez S, Morales C, y cols. Reestenosis y expansión asimétrica de stents en la aorta de conejos hipercolesterolémicos. *Rev Argent Cardiol* 2005;73:174-9.
7. Guide for the Care and use of Laboratory animal. (7th edition). National Research Council, Institute of Laboratory animal. Resources, Washington DC. National Academy Press; 1996.
8. Schulz C, Herrmann RA, Beilharz C, Pasquantonio J, Alt E. Coronary stent symmetry and vascular injury determine experimental restenosis. *Heart* 2000;83:462-7, <http://doi.org/fn5p8n>
9. Berrocal DH, González GE, Fernández AD, Pérez S, Wilensky L, Morales C, et al. Effects of overexpansion on stents' recoil, symmetry/asymmetry, and neointimal hyperplasia in aortas of hypercholesterolemic rabbits. *Cardiovasc Pathol* 2008;17:289-96, <http://doi.org/dm77h3>
10. He Y, Maehara A, Mintz GS, Bharaj H, Castellanos C, Kesanakurthy S, et al. Intravascular Ultrasound Assessment of Cobalt Chromium Versus Stainless Steel Drug-Eluting Stent Expansion. *Am J Cardiol* 2010;105:1272-5, <http://doi.org/dwx2sg>
11. Kitahara H, Waseda K, Yamada R, Otagiri K, Tanaka S, Kobayashi Y, et al. Acute stent recoil and optimal balloon inflation strategy: an experimental study using real-time optical coherence tomography. *EuroIntervention* 2016;12:e190-e198 published online.
12. Von Degenfeld G, Heinrich D, Giehl W, Boekstegers P. Comparison of Pura-Vario and Palmaz-Schatz stents following implantation using normal and high pressure in pigs: immediate and late results assessed by 3-dimensional IVUS. *Z Kardiol* 1999;88:906-13. <http://doi.org/ct9f3v>