

Mariano Larman Tellechea,^{a,b} Miren Telleria Arrieta,^{a,b,*}
Garikoitz Lasa Larraya,^{a,b} Juan Carlos Sanmartin Pena,^{a,b}
and Koldo Gaviria Molinero^{a,b}

^aServicio de Hemodinámica y Cardiología Intervencionista, Policlínica Gipuzkoa, San Sebastián, Guipúzcoa, Spain

^bSección de Hemodinámica y Cardiología Intervencionista, Servicio de Cardiología, Hospital Universitario Donostia, San Sebastián, Guipúzcoa, Spain

* Corresponding author:

E-mail address: mtelarr@gmail.com (M. Telleria Arrieta).

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Mid-term Clinical Outcome of Titanium-nitride-oxide-coated Cobalt-chromium Stents in Patients With de Novo Coronary Lesions: OPTIMAX First-in-man Study



Resultados clínicos a medio plazo de los stents de cobalto-cromo recubiertos de oxinitruro de titanio en pacientes con lesiones coronarias de novo: primer estudio humano de OPTIMAX

To the Editor,

Concerns have been raised about higher rates of late stent thrombosis (ST) following implantation of drug-eluting stents.¹ Localized hypersensitivity reactions were demonstrated in the vessel wall at autopsy in patients with late ST after implantation of first-generation drug-eluting stents. Hence, stents with a biocompatible coating were developed to minimize the vessel wall inflammation responsible for late events.² The safety of titanium-nitride-oxide-coated stents based on a 316L stainless-steel platform has been demonstrated in unselected populations³ and in randomized clinical trials in acute coronary syndrome.⁴ Cobalt-chromium alloy has a superior radial strength that allows the development of ultra-thin struts but preserved radial force. In a prospective first-in-man observational study, we explored the 6-month clinical outcome of a titanium-nitride-oxide-coated stent based on a cobalt-chromium platform in *de novo* coronary lesions.

We enrolled 184 symptomatic patients with significant stenosis of a *de novo* lesion in a native coronary artery or a coronary bypass graft. Clinical presentation included stable angina and acute coronary syndrome. We excluded patients with heart failure, left ventricular ejection fraction < 30%, cardiogenic shock, renal impairment, prior target vessel revascularization, allergy to antithrombotic medications, active bleeding, and life expectancy < 12 months. The study was conducted according to the 1964 Declaration of Helsinki. Informed consent was obtained from all patients. The protocol was approved by our Ethics Committee. The OPTIMAXTM stent (Hexacath, Paris, France) is a thin-strut (81 μm) stent, based on a cobalt-chromium platform with a twin helicoidal design. Titanium-nitride-oxide is coated on all surfaces of the stent. The stent is available in lengths of 7, 10, 13, 16, 19, 22, and 28 mm, and in diameters of 2.25, 2.50, 2.75, 3.0, 3.5,

and 4.0 mm. Procedural success was defined as successful implantation of the stent with residual stenosis < 20% and final TIMI 3 flow, without dissection or thrombosis. Clinical success was defined as procedural success without in-hospital major adverse cardiac events (MACE). The primary endpoint was MACE at 6-months' follow-up, defined as cardiac death, nonfatal myocardial infarction (MI), or ischemia-driven target lesion revascularization (TLR). Cardiac death was defined as death from cardiovascular causes or unknown cause. Myocardial infarction was diagnosed by persistent chest pain with an increase of CK-MB and/or troponin \geq twice the upper reference limit. Target lesion revascularization was defined as a repeat intervention to treat significant (>50%) in-stent restenosis. Secondary endpoints included individual components of the primary endpoint, noncardiac death, ischemia-driven target vessel revascularization, and definite ST at 6-months' follow-up. Stent thrombosis was adjudicated according to the Academic Research Consortium. Patients were prospectively followed up for 6 months. Follow-up coronary angiography was performed in patients developing recurrent symptoms during follow-up. An independent clinical event committee adjudicated all clinical events. Because of the observational design of the current study, no formal power calculation was performed.

The mean age of the cohort was 69 (SD, 9) years; 70.1% were men. Patients presented with acute coronary syndrome in 57.1%, radial access was used in 90.2%, and complex (type B and C) lesions were treated in 80.5%. Baseline clinical and procedural characteristics are shown in Table 1. Procedural and clinical success occurred in 100% of the patients. All patients completed the 6-month clinical follow-up. The mean duration of follow-up was 198 (SD, 18) days. At 6-month follow-up, the primary endpoint of MACE occurred in 4.3%. No ST was observed. Clinical outcome at 6 months is summarized in Table 2.

Over the past decade, titanium-nitride-oxide-coated stents based on 316L stainless-steel platform have shown a satisfactory clinical outcome in observational studies and randomized clinical trials.^{3,4} In a report by Karjalainen et al on 193 patients (212 Titan[®] stents), the 6-month rate of MACE was 6.7%, nonfatal MI 2.1%, and target vessel revascularization 6.2%; the TLR rate was 3.6%.⁵ Nevertheless, 46% of patients had a prior MI (vs 8.5% in the current study). Interestingly, no ST occurred at 6-months' follow-up.⁵ In the TIBET registry, which enrolled 156 diabetic patients (197 Titan[®]

Table 1
Baseline Clinical and Procedural Characteristics (n = 184)

Age, mean (SD), y	69 (9)
Men	129 (70.1)
Diabetes mellitus	28 (15.2)
Insulin-treated	8 (4.3)
Current smoking	35 (19.0)
Hyperlipidemia	92 (50.0)
Hypertension	105 (57.1)
Prior MI	17 (9.2)
Prior PCI	20 (10.9)
Prior CABG	5 (2.7)
Acute STEMI	26 (14.2)
Acute NSTEMI	53 (28.8)
Unstable angina	29 (15.8)
Stable angina	79 (42.9)
Radial access	166 (90.2)
Number of lesions treated per patient, mean (SD)	1.12 (0.37)
Number of stents per lesion, mean (SD)	1.14 (0.33)
Target vessel	
LAD	88 (47.8)
LCx	39 (21.2)
RCA	50 (27.2)
Left main	5 (2.7)
Bypass graft	2 (1.1)
Lesion type	
A	36 (19.6)
B	130 (70.7)
C	18 (9.8)
Thrombus	19 (10.3)
Calcified lesions	64 (34.8)
Bifurcation lesions	33 (17.9)
Reference vessel diameter, mean (mm)	3.03 (0.37)
Lesion length, mean (SD), mm	17.3 (6.4)
Stent diameter, mean (SD) mm	3.10 (0.38)
Stent length, mean (SD), mm	19.5 (5.8)
Total stent length per lesion, mean (SD), mm	21.4 (8.4)
Direct stenting	50 (27.2)
Thrombus aspiration	14 (7.6)
Post-dilatation	140 (76.1)
Low-molecular weight heparin	166 (90.2)
GP IIb/IIIa inhibitor	1 (0.5)
Bivalirudin	22 (12.0)
Clopidogrel	175 (95.1)
Prasugrel	5 (2.7)
Ticagrelol	4 (2.2)
Duration of DAPT, mean (SD), months	4.63 (2.54)

CABG, coronary artery bypass grafting; DAPT, dual antiplatelet therapy; LAD, left anterior artery; LCx, left circumflex artery; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction.

Continuous variables are presented as mean (standard deviation), while categorical variables are presented as frequency (percentage).

Table 2
Clinical Outcome at 6-months' Follow-up (n = 184)

	n (%)
Cardiac death	1 (0.5)
Nonfatal MI	4 (2.2)
Ischemia-driven TLR	5 (2.7)
MACE	8 (4.3)
Ischemia-driven TVR	1 (0.8)
ST	0 (0)
Noncardiac death	1 (0.5)
All-cause death	2 (1.1)

MACE, major adverse cardiac events; MI, myocardial infarction; ST, stent thrombosis; TLR, target lesion revascularization; TVR, target vessel revascularization.

stents), the 6-month rate of MACE was 10.3%, mainly driven by 7.1% TLR.⁶ The high TLR rate is comprehensible, because all patients were diabetic; moreover, 20.3% had a prior MI. Again, no ST occurred at 6 months.⁶ The main limitations of this study include selection bias to a favorable population, which may explain the 100% success rates and low rate of MI. The absence of angiographic follow-up may have contributed to the low TLR rate. We conclude that implantation of the OPTIMAX stent in *de novo* coronary lesions demonstrated excellent 6-month clinical outcomes, with a low rate of MACE and no ST.

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Pasi P. Karjalainen, * Jussi Mikkelsen, Antti Ylitalo, Tuomas Paana, and Wail Nammas

Heart Center, Satakunta Central Hospital, Pori, Finland

* Corresponding author:

E-mail address: pasi.karjalainen@satshp.fi (P.P. Karjalainen).

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