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Original Article

Performance of the Titanium-Nitride-Oxide Coated Stent in Patients with Multivessel Coronary Artery Disease

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ABSTRACT

Background: To date, there are no studies evaluating the use of the titanium-nitride-oxide coated stent in patients with multivessel coronary artery disease. We have compared the performance of the Titan-2® stent to that of the second generation drug-eluting stents in this scenario. **Methods**: From 2011 to 2012, 284 patients were treated with the Titan-2® stent, of which 100 (35.2%) had multivessel coronary artery disease. This group was compared to 100 patients, of a group of 304 (38.9%) patients with multivessel coronary artery disease treated with second generation drug-eluting stents with durable or biodegradable polymers. The primary endpoint was the occurrence of major adverse cardiovascular events at 1 year. **Results**: Clinical, angiographic and procedure-related characteristics of the patients did not show differences between groups. Most patients in the Titan-2® group were male (70%), mean age was 68.4 ± 12.9 years and 25% were diabetic. Stable symptomatic patients were prevalent (68%), 51% had three-vessel disease and ventricular function was preserved (55.6 ± 12.7%). The incidence of major adverse cardiovascular events at 1 year in the Titan-2® group was 21% (vs. 17%; $p = 0.59$), death was observed in 3% (vs. 2%; $p > 0.99$) of the patients, acute myocardial infarction in 5% (vs. 4%; $p > 0.99$) and a new revascularization procedure in 13% (vs. 11%; $p = 0.83$). Definitive stent thrombosis was not observed in either group. **Conclusions**: The Titan-2® stent showed similar results to those of the second-generation drug-eluting stents, which makes it attractive for use in the complex scenario of patients with multivessel coronary artery disease.

DESCRIPTORS: Percutaneous coronary intervention. Stents. Coated materials, biocompatible. Titanium.

RESUMO

Desempenho do Stent Recoberto por Titânio-Óxido Nítrico em Pacientes com Doença Coronária Multiarterial

Introdução: Até o momento, nenhum estudo avaliou o stent recoberto por titânio-óxido nítrico em pacientes com doença arterial coronariana multiarterial. Comparamos o desempenho do stent Titan-2® ao stents farmacológicos de segunda geração nesse cenário. **Métodos**: No período de 2011 a 2012, 284 pacientes foram tratados com o stent Titan-2®, dos quais 100 (35,2%) eram portadores de doença arterial coronariana multiarterial. Esse grupo foi comparado a 100 pacientes, de um grupo de 304 (38,9%), com doença arterial coronariana multiarterial, tratados com o stent farmacológico de segunda geração com polímeros duráveis ou biodegradáveis. O desfecho primário foi a ocorrência de eventos cardíacos adversos maiores em 1 ano. **Resultados**: Características clínicas, angiográficas e do procedimento não apresentaram diferenças entre os grupos. A maioria dos pacientes do grupo Titan-2® era do sexo masculino (70%), com idade de 68,4 ± 12,9 anos e 25% eram diabéticos. Predominaram os quadros clínicos estáveis (68%), 51% tinham acometimento triarterial e a função ventricular estava preservada. A incidência de eventos cardiovasculares adversos maiores em 1 ano no grupo Titan-2® foi de 21% (vs. 17%; $p = 0,59$), óbito ocorreu em 3% (vs. 2%; $p > 0,99$) dos pacientes, infarto do miocárdio em 5% (vs. 4%; $p > 0,99$) e nova revascularização miocárdica em 13% (vs. 11%; $p = 0,83$). Não foram constatadas tromboses de stent definitivas em nenhum grupo. **Conclusões**: O uso do Titan-2® apresentou resultados similares aos do stent farmacológico de segunda geração, o que o torna atrativo para ser utilizado no complexo cenário de pacientes portadores de doença arterial coronariana multiarterial.

DESCRITORES: Intervenção coronária percutânea. Stents. Materiais revestidos biocompatíveis. Titânio.

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Coronary stent implantation has become the standard percutaneous coronary intervention, with a safer approach and better results than those obtained with balloon angioplasty.[1,2] However, coronary restenosis, although reduced, still remains as a limitation of the procedure, resulting in the need for new procedures and increased costs.[3] Drug-eluting stents (DES) have significantly reduced late luminal loss and angiographic restenosis, as well as the need for repeat revascularization, when compared to bare metal stents (BMS).[4] This reduction has been significant in several clinical and anatomical scenarios,[5-9] especially with second-generation stents.[8]

The Titan-2® bioactive stent (Hexacath – Paris, France) is approved for clinical use in Europe, Asia, and North, Central, and South America, including Brazil, with more than 5,000 units already used worldwide.[10,11] This stent consists of stainless steel coated with titanium-nitride-oxide, which has shown *in vitro* to reduce platelet aggregation and fibrinogen binding when compared to conventional bare metal stents. Preliminary data have shown similar safety and efficacy profiles of first- and second-generation DES in several clinical scenarios.[11-18] However, few studies have addressed the performance of the Titan-2® in the treatment of patients with multivessel coronary artery disease (CAD).

This study aimed to evaluate the performance of the Titan-2® stent in patients with multivessel CAD and compare it to that of second-generation DES.

METHODS

Patients

From January 2011 to December 2012, 284 patients were treated at Hospital Beneficência Portuguesa de São Paulo with the Titan-2® stent, of whom 100 (35.2%) had multivessel CAD and were selected for this analysis. This study excluded cases whose initial clinical presentation was myocardial infarction with ST-segment elevation, and those who had lesions > 50% in the left main coronary artery or when the percutaneous coronary intervention was performed with saphenous vein grafts. This group was compared to 100 patients from a group of 304 (38.9%) patients with multivessel CAD treated with second-generation DES with durable polymers – Endeavor® (Medtronic, Minneapolis, United States) or Xience V® (Abbott Vascular, Santa Clara, United States), and biodegradable polymers – BioMatrix® (Biosensors International, Singapore), in the same period, at the present institution.

The study was conducted in agreement with the Declaration of Helsinki, and all patients signed an informed consent.

The Stents

The Titan-2® balloon-expandable stent combines a stainless steel platform (316 L) of thin struts (0.0040 inch) with open cells and helical connections. It is not coated with polymers or antiproliferative drugs, but rather with a titanium matrix system bound to nitride oxide, applied by vapor deposition on the stent surface.

Stents that were used as controls included the Endeavor®, which releases zotarolimus from a biocompatible phosphorylcholine polymer applied to a cobalt-chromium platform of thin struts; the XienceV®, which releases everolimus from a biocompatible fluorinated acrylic polymer applied to a platform of cobalt-chromium with thin struts; and the BioMatrix®, which releases biolimus A9 from a biodegradable polylactic acid polymer applied to a stainless steel platform with thin struts.

Procedure

Percutaneous coronary interventions were performed according to current guidelines,[19,20] and the final strategy for the procedure was left to the discretion of the surgeon.

During the procedure, unfractionated heparin was administered at a dose of 70-100 IU/kg, and the use of glycoprotein IIb/IIIa inhibitors was at the discretion of the surgeon. Pre-dilation was not compulsory, and post-dilation of stents was recommended in case of residual stenosis > 20% by visual estimation. The administration of dual antiplatelet therapy (acetylsalicylic acid [loading dose 200 mg/100 mg maintenance] and clopidogrel [loading dose 300-600 mg/75 mg maintenance]) should be started at least 24 hours before the procedure. In patients with acute coronary syndromes, a loading dose of 600 mg of clopidogrel, 60 mg of prasugrel, or 180 mg of ticagrelor was recommended. After PCI, therapy with aspirin was maintained indefinitely; clopidogrel, prasugrel (10 mg/day), or ticagrelor (90 mg/day) were maintained for a period of 1 to 3 months for the Titan-2® group, and for at least one year for the DES group.

Outcomes and clinical follow-up

The primary study endpoint was the occurrence of major adverse cardiac events (MACE) during a 12 month follow-up. MACE was defined as death, non-fatal myocardial infarction, and need for repeat revascularization. All deaths were considered cardiac unless a non-cardiac cause could be clearly established by clinical and/or pathological study. The diagnosis of myocardial infarction was based on the development of new pathological Q waves in more than two contiguous ECG leads and/or elevation of creatine kinase MB isoenzyme (CK-MB) greater than three times the upper limit of the normal level after the procedure (during the