JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 7, NO. 9, 2014

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcin.2014.04.015

PERIPHERAL VASCULAR

Paclitaxel-Coated Balloon Angioplasty Versus Drug-Eluting Stenting for the Treatment of Infrapopliteal Long-Segment Arterial Occlusive Disease

The IDEAS Randomized Controlled Trial

Dimitris Siablis, MD, PhD,* Panagiotis M. Kitrou, MD, PhD,* Stavros Spiliopoulos, MD, PhD,* Konstantinos Katsanos, MSc, MD, PhD,† Dimitris Karnabatidis, MD, PhD*

ABSTRACT

OBJECTIVES This study sought to report the results of a prospective randomized controlled trial comparing paclitaxel-coated balloons (PCB) versus drug-eluting stents (DES) in long infrapopliteal lesions.

BACKGROUND DES have an established role in the treatment of short infrapopliteal lesions, whereas there is increasing evidence for the use of PCB in longer below-the-knee lesions.

METHODS Inclusion criteria were patients with Rutherford classes 3 to 6 and angiographically documented infrapopliteal disease with a minimum lesion length of 70 mm. The primary endpoint was target lesion restenosis >50% assessed by digital angiography at 6 months. Secondary endpoints included immediate post-procedure stenosis and target lesion revascularization.

RESULTS Fifty patients were randomized to undergo infrapopliteal PCB angioplasty (25 arteries in 25 limbs; PCB group) or primary DES placement (30 arteries in 27 limbs; DES group). Immediate residual post-procedure stenosis was significantly lower in DES (9.6 ± 2.2% vs. 24.8 ± 3.5% in PCB; $p < 0.0001$). At 6 months, 5 patients died (2 in PCB vs. 3 in DES; $p = 1.00$) and 3 suffered a major amputation (1 in PCB vs. 2 in DES; $p = 1.00$). In total, 44 angiograms were evaluable with quantitative vessel analysis. Binary (>50%) angiographic restenosis rate was significantly lower in DES (7 of 25 [28%] vs. 11 of 19 [57.9%] in PCB; $p = 0.0457$). There were no significant differences with regard to target lesion revascularization (2 of 26 [7.7%] in DES vs. 3 of 22 [13.6%] in PCB; $p = 0.65$). Positive vessel wall remodeling was observed in 3 cases in the PCB arm (3 of 19 [(15.8%)] vs. 0 of 19 [0%] in DES; $p = 0.07$).

CONCLUSIONS Compared with PCB in long infrapopliteal lesions, DES are related with significantly lower residual immediate post-procedure stenosis and have shown significantly reduced vessel restenosis at 6 months. PCB may produce positive vessel remodeling. (Infrapopliteal Drug-Eluting Angioplasty Versus Stenting [IDEAS-I]; NCT01517997) (J Am Coll Cardiol Intv 2014;7:1048–56) © 2014 by the American College of Cardiology Foundation.

From the *Interventional Radiology Department, Patras University Hospital, Patras, Greece; and the †Interventional Radiology Department, Guy's and St. Thomas' Hospitals, NHS Foundation Trust, London, United Kingdom. Dr. Katsanos served as a proctor on paclitaxel-coated balloons for Medtronic Invatec. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received April 9, 2014; accepted April 24, 2014.

Endovascular treatment is increasingly being used as the preferred method of revascularization in patients with infrapopliteal arterial disease suffering from critical limb ischemia (CLI). Compared with surgical bypass, which can be technically challenging or not offered at all because of underlying comorbidities of CLI patients, angioplasty of the crural arteries is able to achieve multivessel recanalization to the foot in a safer and less invasive way (1-3).

Traditional plain balloon angioplasty has long been the gold standard endovascular therapy in the infrapopliteal field, accompanied by bare-metal stents as a bailout choice (4,5). Nearly a decade ago, certain investigators foresaw the advantages of using drug-eluting stents (DES) in the infrapopliteal region (6-9). Since then, 3 multicenter randomized controlled trials and a meta-analysis have confirmed the superiority of DES in terms of inhibiting restenosis, reducing target lesion revascularization (TLR, and improving event-free survival, thereby providing level IA evidence for their use in short infrapopliteal lesions (10-13).

SEE PAGE 1057

On the other hand, paclitaxel-coated balloons (PCB) have already been shown to have superior results with less vascular restenosis and fewer TLR events than with plain balloon angioplasty when used in the superficial femoral artery and in failing arteriovenous fistulas (14,15). Recently, a single-arm and 2 randomized controlled trials provided evidence about improved outcomes with PCB in the treatment of infrapopliteal lesions, at 3, 6, and 12 months, compared with percutaneous transluminal angioplasty (16-18).

CLI cases, especially diabetic ones, are typically characterized by long diffuse atherosclerotic lesions in about one-half of the cases (19). To our knowledge, there is only 1 single-arm study testing plain balloon angioplasty in long infrapopliteal lesions, and evidence on the effectiveness of DES in long these lesions is also very scarce (20,21). On the other hand, the 2 randomized controlled trials reported application of PCB in relatively longer lesions. This trial was designed to explore the effectiveness of PCB versus DES specifically for the treatment of long infrapopliteal lesions that are more representative of routine practice in the treatment of CLI.

METHODS

STUDY DESIGN. The IDEAS (Infrapopliteal Drug-Eluting Angioplasty Versus Stenting) trial was designed to be a single-center randomized (1:1) controlled trial comparing PCB versus DES in long infrapopliteal lesions for the treatment of CLI. It was hypothesized that the 2 competing drug technologies would produce similar inhibition of neointimal hyperplasia (NIH); in other words, the null hypothesis was set at equivalence. The expected angiographic restenosis rate >50% at 6 months was estimated at 10% for both groups and the study was powered to exclude a difference between the 2 treatments of >25% ($\alpha = 0.05$ and statistical power set at 0.80). The number of patients required in each treatment arm was calculated to be 25. No allowance was made for dropouts. One-to-one randomization was computer generated and the method of sealed envelopes was used. The hospital's ethical and scientific committee approved the protocol. Written informed consent was acquired from all recruited subjects. The study was announced on a public database (NCT01517997) and was performed within standards of care without any financial support from industry or research grants.

PATIENT POPULATIONS. From December 1, 2011 to January 1st 2013, 73 patients were referred to our department for percutaneous revascularization of the infrapopliteal vessels due to intermittent claudication or CLI. After screening for potential enrollment in the trial, 23 patients were excluded in total (13 patients did not fulfill the inclusion criteria; 8 patients suffered from distal below-the-ankle disease; and 2 patients did not consent to be included in the study). Overall, 50 patients met the inclusion criteria, provided a signed informed consent form and were randomized to undergo either PCB angioplasty (PCB group) or DES placement (DES group) for the treatment of long infrapopliteal lesions (>70 mm in length, maximum of 2 arteries per limb) (**Figure 1**). In order to be included in the trial, patients had to suffer from severe leg ischemia (Rutherford classes 3- to 6) and to have ≥1 angiographically documented infrapopliteal lesion of >70 mm in length. On the other hand, distal arterial occlusive disease compromising below-the-ankle runoff of the target vessel to be treated (e.g., blocked dorsalis pedis in case of anterior tibial artery treatment or occluded plantar arteries in case of posterior tibial artery treatment) was the most important exclusion criterion (**Table 1**). Inflow iliofemoral occlusive disease was treated as necessary.

BALLOON AND STENT DEVICES. The PCB under investigation was the IN.PACT Amphirion (Medtronic, Brescia, Italy), which was available in sizes with 3 to

ABBREVIATIONS AND ACRONYMS

CLI = critical limb ischemia
CTO = chronic total occlusion(s)
DES = drug-eluting stent(s)
IQR = interquartile range(s)
ITT = intention-to-treat
LLL = late lumen loss
NIH = neointimal hyperplasia
PCB = paclitaxel-coated balloon
QVA = quantitative vessel analysis
TLR = target lesion revascularization