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A Pilot Study of Femoropopliteal Artery Revascularisation with a Low Dose Paclitaxel Coated Balloon: Is Predilatation Necessary?

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WHAT THIS PAPER ADDS

Whether predilatation with an uncoated balloon prior to drug coated balloon (DCB) angioplasty yields superior patient outcomes to direct DCB angioplasty is unproven. This pilot study compared outcomes with or without predilatation prior to DCB in femoropopliteal lesions. Two year outcomes seemed comparable in patients treated with or without predilatation prior to DCB angioplasty, though study groups may not have been powered adequately to detect small differences. Randomised controlled trials of direct DCB use with or without predilatation are required to confirm these preliminary results.

Objective/Background: The objective was to compare 2 year outcomes in patients treated with or without predilatation prior to drug coated balloon (DCB) angioplasty for symptomatic femoropopliteal lesions.

Methods: This prospective multicentre pilot study was conducted at three sites in Germany. It compared claudicants undergoing predilatation with a bare percutaneous transluminal angioplasty (PTA) balloon before DCB (predilatation group) with patients undergoing direct DCB (direct DCB group). Patients were followed for 2 years. Outcomes included late lumen loss at 6 months, and ankle brachial index (ABI), major adverse events, and primary patency at 2 years. A Clinical Events Committee and core laboratories analysed adverse events and angiographic/duplex images, respectively.

Results: Between December 2011 and November 2012, 50 patients were enrolled to the predilatation group (12% total occlusions) and 28 to the direct DCB group (5% total occlusions). Follow-up compliance at the 2 year visit was 88% ($n = 44$) and 86% ($n = 24$), respectively. Late lumen loss at 6 months was lower in the direct DCB group (0.03 ± 0.68 mm vs. 0.54 ± 0.97 mm; $p = .01$). Major adverse events over 2 years occurred in seven (15%) patients who underwent predilatation and in five (19%) after direct DCB. Mean ABI at 2 years was 0.94 ± 0.15 after predilatation and 1.0 ± 0.12 after direct DCB. Over 2 years, primary patency (80.3% vs. 78.2%; $p = .55$) was not statistically different between the groups. After propensity score adjustments, 2 year findings remained unchanged.

Conclusion: Paclitaxel coated PTA, with or without bare predilatation, is effective over 2 years in symptomatic patients with femoropopliteal stenotic lesions. Adequately powered randomised controlled comparisons are required to confirm these preliminary results.

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INTRODUCTION

Endovascular treatment of symptomatic peripheral artery disease has become the primary revascularisation method at most centres.[1,2] However, the optimal endovascular modality for femoropopliteal artery disease has not yet been determined. Standard endovascular treatment options include percutaneous transluminal angioplasty (PTA) and routine stent placement, each with its strengths and limitations. PTA is a simpler and initially less expensive option but is associated with high restenosis rates that require re-intervention in up to 62% of cases within 1 year of initial treatment.[3] Placement of bare metal and drug eluting self expanding stents have emerged as a more durable alternative by providing permanent scaffolding to prevent recoil

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and increase patency rates, particularly in longer lesions.[4,5] Over the long-term, however, the risk of fracture and in-stent restenosis remain important challenges in patients treated with stents.

The use of a drug-coated balloon (DCB) for femoropopliteal lesions is appealing provided acceptable clinical outcomes are achieved, as it fits well into a "leave nothing behind" treatment strategy. Prior to introduction and deployment of a DCB, a lesion is often pre-dilated with an uncoated PTA balloon. This stepwise approach is thought to optimise vessel dilatation while limiting the occurrence of flow-limiting dissections. However, whether predilation improves outcomes versus direct DCB angioplasty is unproven. If a DCB could be inflated directly without the need for predilatation and with comparable outcomes, potential advantages may include shorter procedure times, less device use, and cost savings. The purpose of this pilot study was to compare 2 year outcomes in patients treated with or without predilatation prior to DCB for femoropopliteal lesions.

METHODS

Study design

This prospective pilot study consecutively enrolled 80 patients at three sites in Germany—the first 50 patients underwent predilatation with a bare PTA balloon before DCB (predilatation group) and the last 30 patients underwent DCB without predilatation (direct DCB group). Two year outcomes from the predilatation group have been reported previously.[6,7] The study was conducted in accordance with Good Clinical Practice and the Declaration of Helsinki. Prior to enrollment, the ethics committee at each site reviewed and approved the study protocol and each patient provided signed informed consent. The study included independent oversight of adverse events and independent evaluation of study outcomes. A Clinical Events Committee (CEC) composed of independent physicians adjudicated adverse events. Core laboratories analysed angiographic images (SynvaCor, Springfield, IL, USA) and duplex ultrasound images (VasCore, Massachusetts General Hospital, Boston, MA, USA). All data were monitored for accuracy with 100% source data verification.

Patients

Study entry criteria were consistent for all patients. Eligible patients had symptomatic peripheral arterial disease (Rutherford class 2–4) with *de novo* or restenotic lesions with $>$ 70% stenosis (including total occlusions) located in the superficial femoral artery and/or popliteal artery (P1 segment). Additional inclusion criteria were successful wire crossing of the lesion, lesion length 30–150 mm, ability to treat lesions with no more than two DCBs, target vessel diameter 3–7 mm, and at least one patent tibioperoneal runoff vessel. Main exclusion criteria were acute/subacute thrombus in the target vessel, prior vascular surgery for the target lesion, in-stent restenosis, significant inflow disease, gastrointestinal bleed or coagulopathy contraindicating use of antiplatelet therapy, and use of adjunctive endovascular therapies.

Procedures

All subjects were treated with the Stellarex™ DCB (Spectranetics, Colorado Springs, CO, USA). The DCB is a 0.035″ compatible over-the-wire device with a coating consisting of paclitaxel (2 μg/mm^2 balloon surface) and polyethylene glycol, an excipient that facilitates drug transfer into the vessel wall. Before the procedure, patients were anticoagulated per standard hospital practice. Predilatation balloon diameter was determined at the physician's discretion. The DCBs were sized to ensure the full length of the lesion was treated and the balloon walls apposed the arterial wall without oversizing. Up to two DCBs per lesion were allowed. If two balloons were used, they were overlapped by at least 1 cm. Inflation time was specified for a minimum of 1 minute in all cases. Postdilatation was used to treat residual stenosis $>$ 50% or significant dissection. Postdilatation balloon sizing was at the physician's discretion. Stent placement was used when postdilatation efforts were unsuccessful. Arterial reference vessel diameter measurements were assessed during the procedure by the investigator from the digital subtraction angiogram (DSA). Angiograms of the target vessel were taken at baseline and during the procedure.

Outcomes

Technical success was defined as $<$ 50% diameter stenosis following postdilatation if required and freedom from stent placement by angiographic core laboratory. Lesion success was defined as a final residual diameter stenosis $<$ 50% following treatment, including postdilatation if required, without device malfunction. Procedure success was defined as lesion success without a procedural major adverse event (MAE). MAE included cardiovascular death, index limb amputation, or clinically driven target lesion revascularisation (TLR), as determined by the CEC. Clinically driven TLR was defined as revascularisation associated with $>$ 50% stenosis and worsening Rutherford class in more than one category, or ABI decrease of $>$ 0.15 from the post-procedure value, which was attributable to the target lesion. Primary patency was defined as freedom from clinically driven TLR and Doppler ultrasound stenosis $>$ 50% (peak systolic velocity ratio $\geq$ 2.5). Additional outcomes included late lumen loss (LLL) at 6 months and ABI at 2 years.

Follow-up

Clinical evaluations were performed at baseline, before discharge, and at 1, 6, 12, and 24 months post-procedure. Follow-up evaluations included concomitant medications, ankle brachial index (ABI), Doppler ultrasound of the target lesion(s), angiogram (DSA, 6 months only), and adverse events.

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