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Journal of Clinical Cardiology and Cardiovascular Interventions
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Review Article

# Drug Coated Balloon Angioplasty in Peripheral Vasculature: Review of Literature

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**Received date: December 03, 2019; Accepted date: December 11, 2019; Published date: December 16, 2019**

**Citation:** Valerie F. Civelli, Ngo V, Anand M, Sharma O, Singh S, Sharma S. (2019) Drug Coated Balloon Angioplasty in Peripheral Vasculature: Review of Literature. J Clinical Cardiology and Cardiovascular Interventions, 2(4); DOI:10.31579/2641-0419/034



## Abstract

Drug-coated balloons (DCB) are commonly used to treat peripheral artery disease (PAD) and are often used in combination with or in place of a stent or rotational atherectomy. DCB's are manufactured with the drug, Paclitaxel with the first-line indication of preventing restenosis of arteries following an intervention. Recent literature has suggested an increased mortality risk at years 2 and 5 post DCB angioplasty. Inspired by Katsanos et al. and their important work in researching outcomes for DCBs in PAD, we conducted a thorough review of all literature to compile an informed conclusion.

**Key Words:** drug-coated balloon angioplasty; DCB; restenosis; revascularization; atherectomy

## Introduction

Drug-coated balloons (DCB) are commonly used to treat peripheral artery disease (PAD) and are often used in combination with or in place of a stent or rotational atherectomy. DCB's are manufactured with the drug, Paclitaxel with the first-line indication of preventing restenosis of arteries following an intervention.

Restenosis is the proliferation and hyperplasia of cells that results in repeat vessel closures and life-threatening consequences after previous interventions. This occurs when inflammation stimulates cell growth factors, which may go unchecked in diseased peripheral vasculature. Hormones also play a role. Paclitaxel is effective at preventing re-stenosis as it inhibits smooth muscle formation at the tunica intima thus avoiding caliber loss and re-emergence of stenosis.

Paclitaxel, the drug of choice for peripheral DCB's, is attached to the balloon membrane, usually packaged into folds around the shaft, which is pushed into the vessel walls when inflated at the target lesion. Three minutes of contact with arterial endothelial lining are allowed. During this time the drug is absorbed into the tunica media with the assistance of the excipient urea. Paclitaxel, also an oncology medication, blocks the cellular division process by targeting tubulin, the fibers that stretch and physically divide cells, effectively paralyzing the cell. Paclitaxel has been chosen due to its effectiveness at inhibiting smooth muscle formation, low solubility, and high bioavailability. Literature review has also shown no functional or clinical impairment with dose-dependent levels of the drug in circulation after DCB deployment [16]. Paclitaxel formulary can be given locally as with a DCB for prevention of hyperplasia or systemically.

A previous systematic review and meta-analysis by Katsanos et al. encompassing 28 randomized controlled trials (RCTs) noted a significant increase in the rate of all-cause patient deaths at 2 and 5 years as well as a significant increase in absolute risk of death with paclitaxel-coated devices when compared to controls [1]. From this trial, concern for increased mortality with peripheral DCB angioplasty emerged. Inspired by Katsanos et al. and their important work in researching outcomes for DCBs in PAD, we conducted a thorough review of all literature since publication of their article. [1] Clinical trials have been fruitful in comparing outcomes of different types of paclitaxel-coated DCB's with various other procedures, most commonly with plain balloon angioplasty (PBA). The diversity of trials included real-world experiences from single-center studies to large, multi-center efforts. The FAIR trial was a small, industry-sponsored trial that showed decreased in-stent restenosis (ISR) rates at 6 months and better target-lesion revascularization (TLR) rates at 12 months for DCB versus PBA, with comparable safety outcomes [8]. A single-center RCT published in September 2019 comparing Orchid brand DCB versus PBA also showed better ISR rates in the DCB groups, with no apparent differences in safety [9]. An industry-sponsored RCT of the Stellarex brand DCB showed better outcomes in terms of device and procedure-related deaths through 30 days, and freedom from limb amputation and revascularization through 12 months [13]. Contrastingly, two real-world studies were unable to replicate the favorable outcomes seen in industry-sponsored trials: A single-center Lutonix brand DCB study with follow up at 1 and 2 years showed inferior clinical outcomes for DCB angioplasty [2], and another single center study using two types of paclitaxel balloons showed no significant differences between DCB and PBA, with or without stenting [18].

## Results

In summary, many industry-sponsored trials showed better short-term

outcomes for DCB versus PBA in restenosis rates and all-cause mortality, but some real-world trials showed either no significant differences or inferior outcomes between DCB and other groups. Systematic reviews and meta-analyses have also shown a small amount of favorable short-term outcomes for DCB, e.g. in primary patency, target-lesion revascularization, and better composite safety at 12 months when compared to PBA [11, 19], as well as better restenosis rates [4]. Reviews that looked at longer outcomes though, such as 5-year outcomes for patients treated with IN.PACT Admiral brand DCB; 2-year and 5-year outcomes in the three LEVANT trials utilizing Lutonix brand DCB, and 3-year outcomes for patients treated with Stellarex brand DCB on the ILLUMENATE trial showed no significant differences between study groups [5,7, 12]. A large retrospective cohort analysis of more than 80,000 total patients using Medicare data also showed favorable outcomes at the 12-month mark of lowered all-cause mortality, hospitalization, and major amputation, with overall use deemed safe in this patient population [10]. In conclusion, review into the efficacy and outcomes of DCB compared to other methods of PAD treatment shows favorable short-term outcomes within a year, but more research is warranted to further strengthen the data presented by recent small RCTs. There was a consensus of no significant difference found between DCB versus PBA in the current literature for PAD. The majority of studies showed equal outcomes in safety for DCB versus PBA or other treatment methods and the latest mortality association remains in question. Lastly, based on paclitaxel's known mechanism of action and that it can be given locally and systemically, it is difficult to rationalize the claims of Katsanos, et al. [1] As DCB's continue to be used in the treatment of PAD, robust research and rigorous analyses are needed to determine their true impact.

## Acknowledgement

All authors have contributed equally to this manuscript, agree to equal correspondence and there were no conflicts of interest.

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