Paclitaxel-coated balloon reduces target lesion revascularization compared with standard balloon angioplasty

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ABSTRACT

Objective: Peripheral arterial disease (PAD) is a highly prevalent condition that contributes significantly to the morbidity and mortality of affected patients. PAD creates a significant economic burden on health care systems around the world. We reviewed all available literature to provide a meta-analysis assessing the outcome of patients treated with drug-eluting balloons (DEBs) compared with percutaneous transluminal balloon angioplasty (PTA) through measuring the rate of target lesion revascularization (TLR).

Methods: An electronic search of the MEDLINE, Scopus, Embase, Web of Science, and Cochrane Library databases was performed. Articles reporting randomized controlled trials that compared treatment with DEBs vs PTA were selected for inclusion. A meta-analysis was performed by pooling data on rates of TLR, binary restenosis (BR), and late lumen loss (LLL).

Results: The 10 included articles comprised a sample size of 1292 patients. Meta-analysis demonstrated the rate of TLR in DEB-treated patients was significantly lower compared with patients treated with PTA at 6 months (odds ratio [OR], 0.24; 95% confidence interval [CI], 0.11-0.53; $P = .0004$), 12 months (OR, 0.28; 95% CI, 0.13-0.62; $P = .002$), and 24 months (OR, 0.25; 95% CI, 0.10-0.61; $P = .002$). Decreased LLL and BR was demonstrated at 6 months in patients treated with DEBs compared with patients treated with PTA (mean difference, −0.74; 95% CI, −0.97 to −0.51; $P = .00001$; OR, 0.34; 95% CI, 0.23-0.49; $P = .00001$).

Conclusions: This meta-analysis demonstrates that treatment with DEBs compared with PTA results in reduced rates of reintervention in patients with PAD. Comparison of DEBs to other emerging treatments to determine which method results in the lowest reintervention rates and in the greatest improvement in quality of life should be the focus of future trials. (J Vasc Surg 2017;65:558-70.)

Peripheral arterial disease (PAD) is a highly prevalent condition affecting the aging population. Several epidemiologic studies have estimated the prevalence of PAD to range from 3% to 10%.[1] This prevalence increases to 15% to 20% in people aged >70 years.[2] There are no national data for PAD prevalence in Australian populations; however, a cross-sectional survey conducted of men from metropolitan Perth found an age standardized prevalence of 15.6%.[3]

PAD contributes significantly to the morbidity and mortality of adults as well as being a significant economic burden.[4] United States data from the REACH (Reduction of Atherothrombosis for Continued Health) registry demonstrated that patients with PAD had the highest rates of fatal myocardial infarction compared with coronary artery disease (CAD) and cerebrovascular disease populations.[5,6] The total annual cost for vascular-related hospitalizations for patients with PAD in the United States is estimated to exceed $21 billion.[6] The average annual cost per patient with diagnosed PAD is estimated to range from 1741 to 3559 in France and from 1005 to 1516 in Germany.[7] This magnitude of expenditure is equal, if not greater, than estimates of annual hospital costs associated with type 2 diabetes mellitus.[8] The high hospitalization costs for patients with PAD are the result of high rates of initial and repeat revascularization procedures.[7]

An endovascular peripheral arterial revascularization procedure is any intervention involving insertion of a guidewire into a peripheral artery. Repeat revascularization procedures are termed target lesion revascularization (TLR). They involve repeat percutaneous intervention of the target lesion or surgical bypass of the target vessel performed for restenosis.[9]

Lesions in the superficial femoral artery and popliteal artery are conventionally treated with percutaneous transluminal balloon angioplasty (PTA).[10] However, this procedure has demonstrated poor efficacy at midterm follow-up, with 40% to 60% of patients requiring reintervention ≤12 months.[10] Stent implantation appears to be an attractive alternative due to the success this method has achieved in reducing rates of reintervention in

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Author conflict of interest: none.

Additional material for this article may be found online at www.jvascsurg.org.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

http://dx.doi.org/10.1016/j.jvs.2016.10.089

patients with CAD.[11] Unfortunately, the use of stents in peripheral arteries leads to an inflammatory response that produces neointimal hyperplasia and results in restenosis. Although the precise mechanism is not known, the metal mesh and polymer coating of the stent are hypothesized to exert an inflammatory stimulus on the vessel.[12]

Drug-eluting balloons (DEBs) are a relatively new treatment option that enables mechanical dilation of the artery as well as delivery of antiproliferative drugs. One notable example is paclitaxel.[12] The presence of paclitaxel inhibits neointimal formation and is hypothesized to maintain artery patency at midterm follow-up. The efficacy and safety of the cytotoxic and antiproliferative effect of paclitaxel has been thoroughly investigated in the literature through in vitro models, animal models, and clinical trials.[13-15]

Previous studies have demonstrated an increased short-term efficacy of DEBs compared with PTA.[16] However, the short follow-up intervals in these studies limited the effect of their results. Currently, the efficacy of DEBs compared with PTA in maintaining patency and reducing reintervention rates in PAD is unknown. As previously mentioned, reducing the reintervention rate in patients with PAD would have substantial implications on hospitalization costs. We conducted a meta-analysis to collate the current evidence investigating the use of DEBs in PAD.

This report reviews all available literature and provides a meta-analysis of all trials involving DEBs. Primarily, this meta-analysis assesses the outcome of patients treated with DEBs compared with PTA through measuring the rate of TLR. Secondary end points include late lumen loss (LLL), BR, primary patency, rates of bailout stenting, death, and amputation.

METHODS

Literature search. A search strategy was devised according to the 2009 Preferred Reporting Items of Systematic Reviews and Meta-Analyses statement. An electronic search of the MEDLINE, Scopus, Embase, Web of Science, and Cochrane Library databases was performed from inception to July 26, 2015, with no language restrictions.

To identify studies investigating the difference in outcomes when comparing DEBs vs PTA, the following search terms were applied: (Arteriosclerosis *or* Peripheral Arterial Disease *or* Peripheral Vascular Disease *or* Arterial Occlusive Disease) *and* (angioplasty *or* balloon angioplasty *or* endovascular procedures) *and* (paclitaxel) with prior checking in the Medical Subject Heading database to include synonyms.

The database search was supplemented by a search of the reference lists of included studies and by using the related-articles function provided in each database. Titles and abstracts were screened to identify potentially relevant studies. If the suitability of an article was uncertain, the full-text article was reviewed. All potentially relevant studies were subsequently assessed by review of the full-text articles.

Eligible studies were those that (1) assessed the outcome of DEB use in patients with PAD in the femoropopliteal arteries (FPA), (2) contained a randomized design where PTA was the control, and (3) reported patient follow-up from at least 6 months. Only publications in English were included.

Studies were excluded when (1) the primary focus was CAD, carotid artery disease, aortic aneurysmal disease, or intracranial vascular disease, (2) patients treated with DEBs were not the primary focus of the report, (3) patients were treated with DEBs combined with other surgical interventions, (4) or the focus of the trial was to assess the efficacy of DEB use in treating in-stent restenosis or graft stenosis.

Data extraction. Data extraction was performed according to a predefined form and recorded in tables. All data were reviewed independently by two authors (N.C., E.N.) and cross-checked in a consensus meeting. Any discrepancies were resolved through discussions.

The following data were obtained from the included studies: study design, sample size, inclusion and exclusion criteria, primary, secondary, and safety end points, follow-up intervals, patient age, sex, and smoking status, comorbidities, such as hypertension, CAD, hyperlipidemia, diabetes, and renal dysfunction, baseline ankle-brachial index (ABI) and Rutherford classification, presence of patent run-off vessels, number of lesions, lesion length, type, and location, degree of calcification, reference vessel diameter, diameter stenosis, total occlusion, bailout stenting, procedural success and at follow-up, rates of death, amputation, TLR, primary patency, BR, minimum lumen diameter, late lumen loss (LLL), change in Rutherford class and ABI, and secondary patency. The end point definitions with type and incidence of events were recorded. The method of statistical analysis and subsequent results were also recorded.

Data were standardized to include event numbers and percentages of the relevant study population, where possible. Potential sources of bias or conflict of interest were recorded. Authors were contacted for additional information when required.[17,18]

Quality assessment. We used a modified quality assessment tool incorporating elements of the Jadad scale and Cochrane Collaboration tool to assess the methodological quality and risk of bias of the included studies.[19,20] The quality assessment tool assessed study design, patients selected, intervention details, follow-up, and outcome measures (Supplementary Table I, online only). The same two independent investigators evaluated the risk of bias in the individual studies using the Cochrane