Review of The Utility of Drug-Eluting Stents in Peripheral Arterial Disease by Different Vascular Beds

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Introduction

- **Background**

  Endovascular therapy has recently become the first-line treatment for infrapopliteal occlusive disease; however, there are several endovascular therapy options such as, but not limited to, drug coated balloons (DCB), drug-eluting stents (DES), bare metal stents (BMS), and percutaneous transluminal angioplasty (PTA), with the optimal method yet to be determined. Randomized controlled trial (RCT) data in recent years have shown potential in the application of DES that were standardly used for coronary artery disease now for the treatment of peripheral arterial disease (PAD).

- **Objective**

  There are few reviews of the utility of DES organized by vascular beds. Herein, we conduct an up-to-date review of literature on the applications of DES in the treatment of PAD in multiple vascular beds, and provide recommendations for further investigations.

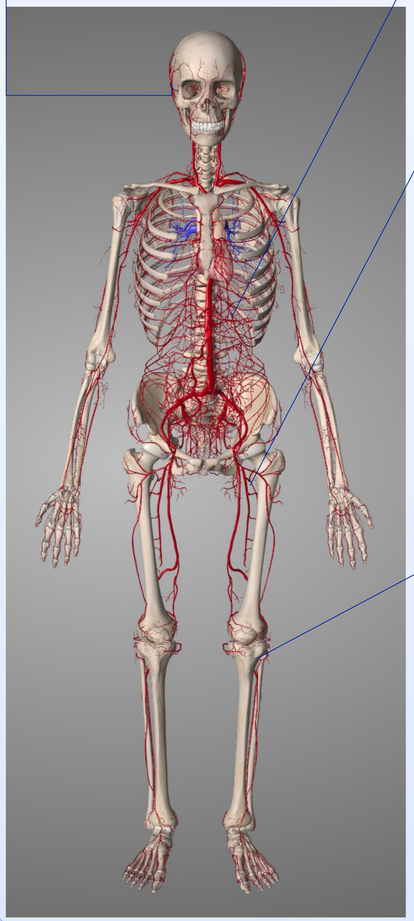
Materials and Methods

- A PubMed search was conducted using relevant search terms to identify randomized controlled trials (RCT) that compared drug-eluting stents to other existing peripheral arterial interventions. Retrospective and cohort studies were also included.
- RCTs were identified and classified based on the vascular bed of interest: femoropopliteal, infrapopliteal, renal, extracranial, or intracranial. Case reports, retrospective studies, and cohort studies were also identified and broken down by vascular beds.
- Data from the trials was organized using a table that compared primary/secondary endpoints and outcomes, comorbidities, lesion length, vessel diameter, and length of follow-up period.

Results

Extra/Intra Cranial Arteries

One RCT compares DES with BMS for intracranial atherosclerotic disease (Jie et al. 2022), which shows DESs comparatively reduce the risk of restenosis and stroke recurrence.



Renal Arteries

The GREAT Trial by Zähringer et al 2007 is the only RCT known to date that compares a sirolimus DES with BMS for the treatment of atherosclerotic renal artery stenosis (RAS). The investigators reported that the DES arm had an absolute reduction in the 6-month angiographic binary restenosis rate, however the small sample size (n=53) prevented the detection of a statistical significance between the two arms. They ultimately concluded that DES may be beneficial for patients with small renal arteries and impaired renal function.

Femoropopliteal Arteries

Trial	DES model, Formulation, n	Control, n	Primary Endpoint	Primary Outcome (DES vs Control)
SIROCCO I & II 2005	SMART, sirolimus, 29	BMS, 28	In-stent mean percent diameter stenosis	22.6% vs 30.9%; (p=0.294)
STRIDES 2011	Dynalink, everolimus, 104	N/A	6-month in-stent binary restenosis rate	14% (95% confidence interval, 7.8%-22.2%).
ZILVER PTX 2011	Polymer free Paclitaxel, 236	PTA (238)	12-month event free survival	90.4% vs 82.6%; P=0.004
IMPERIAL 2018	Eluvia, polymer coated, paclitaxel, 309	Zilver-PTX, polymer free, paclitaxel, 156	12-month primary vessel patency	86.8% vs 81.5%; (p<0.0001)

Infrapopliteal Arteries

Trial	DES model, Formulation, n	Control, n	Primary Endpoint	Primary Outcome (DES vs Control)
DESTINY 2012	Xience V, everolimus, 74	Multi-Link Vision BMS, 66	12-month primary vessel patency	85% vs 54% (p=0.0001)
ACHILLES 2012	Cypher Select, sirolimus, 99	PTA, 101	12-month in-segment binary restenosis	22.4% vs 41.9% (p=0.019)
YUKON-BTK 2012	Polymer free SES, 82	Placebo coated BMS, 79	Event free survival	65.8% vs 44.6% (p = 0.02)
PADI 2016	TAXUS, Paclitaxel, 73	PTA-BMS, 64	6-month primary binary patency	48.0% vs 35.1% (p=0.096)
SAVAL 2019	Saval, paclitaxel, 130	PTA, 71	12-month primary vessel patency	68% vs 71%

Conclusions & Recommendations

- DES are demonstrated by RCTs to be a safe and effective treatment option for patients with PAD of the femoropopliteal or infrapopliteal regions as compared to bare metal stents (BMS), percutaneous transluminal angioplasty (PTA) and drug-coated balloons (DCB). Although there have been many studies comparing DES to BMS, PTA, or DCB, there are few head-to-head comparisons of DES. Additionally, although DES have become a mainstay in treatment of infrapopliteal occlusive disease, studies on the use of DES for superficial femoral, renal, supra-aortic, extracranial, and intracranial arterial disease are sparse.
- Our recommendations are as follows:
  - DES RCT data for the infrapopliteal vascular bed is encouraging, with 4 out of 5 trials noted in this analysis showing superior outcomes for DES as compared to PTA and BMS; however, more RCTs need to be conducted to further determine the safety and efficacy of DES for various lesion lengths and vessel diameters.
  - Head-to-head DES comparison studies with large sample sizes and longer follow-up are recommended to determine the optimal dosing and formulation of DES as well as elucidate the long-term efficacy of DESs.
  - Although there are a few retrospective studies and case studies on the use of DESs in renal and supra-aortic vasculature, further retrospective studies are recommended to elucidate the optimal type of stent to be used In these vascular beds. DES in intracranial and extracranial vasculature is not recommended at this time due to the lack of evidence.

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