

Alfredo Augusto Eyer Rodrigues<sup>1</sup> and  
Erlon Oliveira de Abreu-Silva<sup>2\*</sup>

<sup>1</sup>Division of Cardiovascular Imaging and Post-graduation Program in Cardiology, Federal University of Sao Paulo, Sao Paulo, Brazil

<sup>2</sup>Division of Interventional Cardiology and Post-graduation Program in Cardiology, Federal University of Sao Paulo, Sao Paulo, Brazil

**Dates:** Received: 25 July, 2015; Accepted: 25 July, 2015; Published: 27 July, 2015

**\*Corresponding author:** Erlon Oliveira de Abreu-Silva, 715 Napoleao de Barros Street, Division of Interventional, Cardiology, Vila Clementino, Sao Paulo-SP, Brazil Zip code 04024-002, Tel: +55 11 55764000; E-mail: erlon@terra.com.br

[www.peertechz.com](http://www.peertechz.com)

ISSN: 2455-5452

**Keywords:** Inflammation; Peripheral arterial disease; Bare metal stents; Drug-eluting stents; Percutaneous transluminal angioplasty; Drug-eluting balloon

## Editorial

# Endovascular Interventions for Infra-Inguinal Arterial Disease: Collecting Evidence to Expand Indications

In their paper, the authors followed a highly refined algorithm in order to obtain methodological robustness. This is made clear when one pays attention to the presence of 1) a priori inclusion criteria, limiting the analysis to randomized controlled trials (RCTs) where DEB and DES were evaluated for femoro-popliteal and/or infrapopliteal PAD treatment in humans with, at least, one of the following outcomes: binary restenosis (reduction in percent diameter of 50% or greater), target lesion revascularization (TLR; repeat percutaneous or surgical revascularization), late lumen loss (LLL; difference in minimum lumen diameter at procedure completion and at follow-up), amputation rates, or mortality rates; 2) a thorough assessment of possible biases, including publication bias and possible interference from industries (the so-called corporative bias); and 3) a complex, yet elegant, statistical analysis of the selected data. Noteworthy to mention that no study evaluating DEB or DES in the treatment of restenosis was included in this analysis.

After evaluating the available trials, eight randomized trials were found for DEB angioplasty in the treatment of PAD. Analyzing the compelled data, the authors demonstrated statistically significant superiority of DEB over non-pharmacological balloon angioplasty of femoral-popliteal disease for LLL, restenosis, and TLR, without benefit in major amputation or mortality. For infrapopliteal disease, superiority of DEB over percutaneous transluminal angioplasty (PTA) was statistically significant for restenosis and TLR. Twelve trials evaluating the use of DES implantation in peripheral arterial disease were included in this meta-analysis. Drug-eluting stents were significantly superior over bare metal stents (BMSs) for late lumen loss and restenosis in femoral-popliteal disease, with no benefit in mortality or amputation. Evaluating the use of DES for infrapopliteal PAD, DES showed statistically significant superiority over BMSs for both restenosis and TLR; again, no benefit in amputation or mortality was seen.

According to recent AHA/ACC Guidelines for management of patients with PAD [13], the following interventions received a Class I recommendation: use of statins, use of antihypertensive medications - including beta-blockers - to achieve BP control, proper foot care in diabetic patients, smoking cessation - with the use of specific medications, if no contraindication -, use of aspirin (or clopidogrel, as an alternative to it), use of exercise as an initial treatment and use of cilostazol in patients without heart failure. The same guidelines also give a Class I recommendation for endovascular procedures in the following circumstances: 1) those who have lifestyle-limiting claudication with reasonable likelihood of improvement and, at least, 1 of these: inadequate response to exercise/medical therapy and/or

## Editorial

Peripheral arterial disease (PAD) is a common manifestation of atherosclerosis, with a prevalence of 29% in those older than 70 years or aged 50-70 years who are either smokers or diabetic [1,2]. The majority of persons with this condition are asymptomatic, and less a fifth report typical intermittent claudication [3]. The literature shows us that the risk of limb loss for those who do not have diabetes is 2% or less [4] and, also, that this risk increases three-fold in patients with diabetes requiring pharmacological therapy (oral or insulin) [5].

Among the various therapeutically strategies, endovascular procedures are an option for patients with symptoms and short-segment stenosis or occlusions involving the iliac, femoropopliteal and infrapopliteal arteries and for those who do not qualify for surgical bypass. There is still discussion regarding the best treatment option (primary balloon angioplasty with "bail-out" stent placement - ie, emergent stent placement for a procedure-induced flow-limiting dissection - or primary stenting), and this is highly dependent on anatomic location; but one aspect is clear: endovascular revascularization is relatively safe compared with the surgical option and its restenosis rates remains high [6-9]. The use of drug-eluting devices (drug-eluting stents - DES- and drug-eluting balloons - DEB -) have been tested and evaluated in the treatment of coronary artery disease (CAD) [10,11] As a matter of fact, the use of DES is preferred in a number of situations involving CAD patients, according to recent guidelines [11].

As a result, there has been increasing interest in their application for the treatment of PAD. To date, the available evidence is scarce. In an attempt to bring more elements to the discussion, Barlocher et al. recently published a meta-analysis of the outcomes of endovascular procedures involving the use of DEB and DES in the treatment of femoral-popliteal and infrapopliteal PAD [12].

a very favorable risk-benefit ratio (eg. focal aortoiliac disease); 2) it is the preferred technique for TASC (Transatlantic Intersociety Consensus) type A iliac and femoropopliteal lesions; 3) provisional stent is indicated as salvage therapy in the iliac arteries; 4) stenting as the primary therapy for common and external iliac artery stenosis and occlusions. When one takes a look into the recommendations for stenting in femoral, popliteal and tibial arteries, it is seen that the guidelines go with a Class IIa for stenting as salvage therapy, and a III for stenting as primary therapy. On the other hand, surgical interventions received a Class I recommendation, regardless of arterial territory.

In summary, endovascular interventions are an option in the treatment of PAD as long as an adequate evaluation regarding location and extent of disease is performed. Direct stenting is still a class III recommendation for treatment of infra-inguinal PAD, and no statement is made in favor of DES over BMS. The same guidelines do not explicit any preference for DEB over plain angioplasty with non-pharmacological balloons in any arterial territory. Although more randomized trials are needed to better evaluate the role of these new technologies in the treatment of PAD in a broader range, their safety (compared to surgery) and benefits (compared to BMS ou PTA) are being demonstrated and, hopefully, in the future we will have a larger number of class I recommendations for endovascular interventions.

## References

1. Selvin E, Erlinger TP (2004) Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999-2000. *Circulation* 110: 738-743.
2. Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, et al. (2001) Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA* 286: 1317-1324.
3. McDermott MM, Liu K, Greenland P, Guralnik JM, Criqui MH, et al. (2004) Functional decline in peripheral arterial disease: associations with the ankle brachial index and leg symptoms. *JAMA* 292: 453-461.
4. Kannel WB, Skinner JJ Jr, Schwartz MJ, Shurtleff D (1970) Intermittent claudication: incidence in the Framingham Study. *Circulation* 41: 875-883.
5. Muluk SC1, Muluk VS, Kelley ME, Whittle JC, Tierney JA, et al. (2001) Outcome events in patients with claudication: a 15-year study in 2777 patients. *J Vasc Surg* 33: 251-257.
6. Jens S, Conijn A, Koelemay M, Bipat S, Reekers J (2014) Randomized trials for endovascular treatment of infrainguinal arterial disease: systematic review and meta-analysis (part 1: above the knee). *Eur J Vasc Endovasc Surg* 47: 524-535.
7. Romiti M, Albers M, Brochado-Neto FC, Durazzo AE, Pereira CA, et al. (2008) Meta-analysis of infrapopliteal angioplasty for chronic limb ischemia. *J Vasc Surg* 47: 975-981.
8. E Y, He N, Wang Y, Fan H (2008) Percutaneous transluminal angioplasty (PTA) alone versus PTA with balloon-expandable stent placement for short-segment femoropopliteal disease: a metaanalysis of randomized trials. *J Vasc Interv Radiol* 19: 499-503.
9. Katsanos K, Spiliopoulos S, Karunanithy N, Krokidis M, Sabharwal T, et al. (2014) Bayesian network meta-analysis of nitinol stents, covered stents, drug-eluting stents, and drug-coated balloons in the femoropopliteal artery. *J Vasc Surg* 59: 1123-1133.
10. Yu CM, Kwong J, Sanderson J (2008) Drug-eluting balloons for coronary artery disease: a meta-analysis of randomized controlled trials. *Int J Cardiol* 168: 197-206.
11. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, et al. (2011) ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *J Am Coll Cardiol* 58: e44-122.
12. Baerlocher MO, Kennedy SA, Rajebi MR, Baerlocher FJ, Misra S, et al. (2015) Meta-Analysis of Drug-Eluting Balloon Angioplasty and Drug-Eluting Stent Placement for Infrainguinal Peripheral Arterial Disease. *J Vasc Interv Radiol* 2015; 26:459-473.
13. Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, et al. (2013) Management of patients with peripheral artery disease (compilation of 2005 and 2011 ACCF/AHA guideline recommendations): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 127: 1425-1443.

**Copyright:** © 2015 Eyer Rodrigues AA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Citation:** Eyer Rodrigues AA, de Abreu-Silva EO (2015) Endovascular Interventions for Infra-Inguinal Arterial Disease: Collecting Evidence to Expand Indications. *Int J Vasc Surg Med* 1(1): 007-008. DOI: 10.17352/2455-5452.000003