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EDITORIAL COMMENT

# Is Paclitaxel-Eluting Stent Use Justified by an Adequate Risk Profile?*

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Peripheral artery disease is a common condition, affecting 1 in 6 elderly Americans by the age of 70 years (1). Current treatment options include a conservative approach, bypass surgery, and endovascular interventions. In recent decades, the latter treatment has been widely used as an alternative to bypass surgery, achieving acceptable patency rates even with more complex TASC II type D occlusive lesions, particularly in patients with critical limb ischemia and at high risk for open surgical procedures (2). Percutaneous therapies continue to evolve, with various options currently available, including balloon angioplasty, stents, and atherectomy devices. For a long time, plain balloon angioplasty and stenting have been considered the standard of practice, but both are limited by high restenosis rates (3) or a not negligible risk for stent fracture, especially for long or distal lesions.

On the basis of the aforementioned clinical needs, drug-coated balloons and drug-eluting stents (DES) were adopted as newer and more sophisticated endovascular therapies. These devices were confirmed in multiple randomized controlled trials demonstrating their superior patency rates compared with other treatment options (2).

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In this issue of *JACC: Cardiovascular Interventions*, Stavroulakis et al. (3) report the 2-year outcomes of a retrospective registry performed in patients with femoropopliteal disease treated with the Eluvia DES (Boston Scientific, Marlborough, Massachusetts). The Eluvia comprises a self-expanding Nitinol stent platform with a coating composed of a polymer system, with paclitaxel eluted over 12 months.

The primary measure outcome of this study was primary patency, defined as freedom from significant restenosis or occlusion without any reintervention. Immediate performance of the device was good, as depicted by an ankle-brachial index of 1.00 (interquartile range: 0.91 to 1.10), and primary patency at 12 and 24 months was 90% and 71%, respectively. Freedom from target lesion revascularization at 24 months was 80%, and freedom from major amputations was 83%.

## THE GOOD NEWS REGARDING THIS STUDY

There are some unique peculiarities regarding this study, which should be recognized: 1) the reason for implanting Eluvia DES was the persistence of flow-limiting dissection after 2 prolonged balloon inflations or impaired angiographic result, thus the study was conducted not in an all-comers population but in a selected group of patients according to a dedicated internal flowchart; 2) the patients enrolled had severe peripheral artery disease, with a median pre-operative ankle-brachial index of 0.4 and a mean lesion length of 19.4 ± 11 cm, >74% of lesions were chronic total occlusions, and 48% of treated vessels were deemed to have moderate or severe calcifications (classified as Peripheral Arterial Calcium Scoring Scale score 3 or 4, indicating circumferential calcification); and 3) the use of duplex ultrasound for the assessment of secondary endpoints is intriguing, and the investigators' suggestion that this method is an improvement over angiography in assessing vessel degeneration seems convincing.

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## CONCERNS REGARDING THIS STUDY DESERVING FURTHER ANALYSIS

The most interesting (and concerning) finding of this study was the observation of vessel wall degeneration in 20% of cases. This finding is alarming considering that patients at high risk for aneurysm formation were already excluded from the study, and another study from the same investigators showed a risk for aneurysms in 8% of patients after 1 year, suggesting a possible increase in this complication over time (from 8% to 20% in 1 year).

The nature and pathogenesis of this phenomenon remain unclear. Some immunohistological assays and imaging studies have revealed excessive inflammation of the vessel wall (vasculitis). Long experience derived from coronary arteries suggests that vessel injury during stent implantation and paclitaxel-associated reduced vascular healing contribute jointly to vessel wall degeneration (4–6).

As a consequence of these findings and a possible long-term prothrombotic effect, paclitaxel-eluting stents have long been abandoned for coronary use. In addition, the application of bare-metal stents after suboptimal results with drug-coated balloons is currently contraindicated (7,8).

Finally, the retrospective nature of this study, the lack of a control group, the limited number of patients and events, the absence of core laboratory adjudication, and the limited follow-up duration are important limitations that could result in underestimation of the clinical occurrence and relevance of this phenomenon.

In conclusion, this study by Stavroulakis et al. (3) underlines the mid-term efficacy of the Eluvia stent in reducing the need for reintervention in the femoropopliteal region in a highly complex population, without signals of increased mortality. However, the late occurring vessel wall degeneration is concerning and calls into question the safety of a paclitaxel-eluting stent implanted to seal vessel dissections after balloon angioplasty.

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## REFERENCES

**1.** Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. Circ Res 2015;116:1509–26.

**2.** Kithcart AP, Beckman JA. ACC/AHA versus ESC guidelines for diagnosis and management of peripheral artery disease: JACC guideline comparison. J Am Coll Cardiol 2018;72:2789–801.

**3.** Stavroulakis K, Torsello G, Bosiers M, Argyriou A, Tsilimparis N, Bisdas T. 2-year outcomes of the Eluvia drug-eluting stent for the treatment of complex femoropopliteal lesions. J Am Coll Cardiol Intv 2021;14:692–701.

**4.** Aoki J, Kirtane A, Leon MB, Dangas G. Coronary artery aneurysms after drug-eluting stent implantation. J Am Coll Cardiol Intv 2008;1:14–21.

**5.** Alfonso F, Pérez-Vizcayno MJ, Ruiz M, et al. Coronary aneurysms after drug-eluting stent implantation: clinical, angiographic, and intravascular ultrasound findings. J Am Coll Cardiol 2009;53:2053–60.

**6.** Ahn CM, Hong BK, Kim JY, et al. Incidence and natural history of coronary artery aneurysm developing after drug eluting stent implantation. Am Heart J 2010;160:987–94.

**7.** Cortese B, Berti S, Biondi-Zoccai G, et al., for the Italian Society of Interventional Cardiology. Drug-coated balloon treatment of coronary artery disease: a position paper of the Italian Society of Interventional Cardiology. Catheter Cardiovasc Interv 2014;83:427–35.

**8.** Cortese B. Paclitaxel-eluting stents and aneurysm formation, a worrisome association. J Am Coll Cardiol Intv 2018;11:967–8.

**KEY WORDS** DCB, DES, paclitaxel, vessel aneurysm, vessel degeneration