



Randomized trial comparing a stent-avoiding with a stent-preferred strategy in complex femoropopliteal lesions

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In the article entitled ‘Randomized Trial Comparing a Stent-Avoiding With a Stent-Preferred Strategy in Complex Femoropopliteal Lesions’, recently published in *JACC: Cardiovascular Interventions*, Wittig and colleagues report the results of the BEST-SFA (Best Endovascular Strategy for Complex Lesions of the Superficial Femoral Artery) study. BEST-SFA is a prospective, multicenter, pilot study randomizing patients with peripheral arterial disease (PAD) that undergo an endovascular intervention for long [mean lesion length 187.7±78.3 mm, 79.2% chronic total occlusions (CTOs)] complex femoropopliteal lesions (1). One-hundred-twenty patients were randomized (60 *vs.* 60), after successful crossing of the lesion of interest, to either endovascular treatment using drug-eluting balloons [DEB; stent-avoiding (SA) group] with provisional stenting or drug-eluting stents [DES; stent-preferred (SP) group]. Vessel preparation prior to the application of the drug-eluting devices was considered in all patients and the use and specific type of vessel preparation were at the discretion of the interventionalist in both arms. Primary patency [78.2% SA (43/55) *vs.* 78.6% SP (44/56); $P>0.99$] and clinically driven target lesion revascularization [CD-TLR; 6.9% SA (4/58) *vs.* 5.1% SP (3/59); $P=0.71$] at 12 months were comparable in both groups.

Studies often focus on the ultimate treatment of the

lesion of interest. However, after crossing a lesion of interest, which is often also a delicate process, the treatment phase can be separated in two important steps. These steps are (I) the vessel preparation step, and (II) the ultimate treatment of the lesion (2). BEST-SFA is different from the majority of studies by taking into account both these steps (1). Vessel preparation aims at minimizing risk of dissection, maximizing luminal gain and making the vessel more amenable for the treatment phase with stents or drug delivery. Currently, we have extensive options for vessel preparation and lesion treatment. For vessel preparation we can use undersized balloons, atherectomy devices, scoring, chocolate or cutting balloons, intravascular laser, or intravascular lithotripsy (IVL). None of the vessel preparation techniques has proven its superiority (3), however some have shown promising results for specific indications (4). These existing vessel preparation options are part of the real-world treatment of femoropopliteal lesions in PAD and should therefore be considered in clinical studies that focus on outcomes after treatment of these lesions. The BEST-SFA indeed considers the vessel preparation without differentiating for the type of technology nor for the specific device or whether recanalization was achieved intraluminal or subintimal. It is likely that these aspects have an impact on the outcome and

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therefore deserve to be further analyzed.

The efficacy of drug-eluting technologies regarding patency and TLR in the endovascular treatment of femoropopliteal lesions in PAD patients has been shown in a wide range of studies (5-8), both in primary interventions as well as re-interventions, such as in-stent restenosis (ISR) (9). A network meta-analysis (5) and a comprehensive literature review on contemporary endovascular devices including over 25,000 patients (8) showed higher patency and lower TLR at one year for both DEB and DES compared to plain balloon angioplasty and bare metal stenting (BMS). Although the results of the studies confirm the improved outcomes with the use of drug-eluting devices in the treatment of femoropopliteal lesions, most of them have important limitations that impede translation towards daily clinical practice. Studies often lack long-term follow-up, include a minority of CTOs, include relatively short-lesions, exclude patients with chronic limb-threatening ischemia (CLTI), and thereby include only a very selected group of mainly non-complex femoropopliteal lesions. Furthermore, most studies limit or do not adequately report the use of additional interventions, such as vessel preparation, and well-accepted reporting standards are often lacking. All these limitations hamper comparability and generalizability of these studies.

BEST-SFA tried to address part of the abovementioned limitations by including long complex femoropopliteal lesions and allow a variety of vessel preparation techniques at the operator's discretion (1). This led to the inclusion of patients with lesions >15 cm in more than 50% of the cases in both groups and roughly 80% of CTOs. In 71.2% of the cases lesions were classified as grade 3 or 4 according to the peripheral arterial calcification scoring system (PACSS), without significant difference between the SA and SP groups ($P=0.733$). Vessel preparation additional to simple predilatation, mainly atherectomy, was performed in 71.3% and 51.7% of the cases in the SA and SP groups, respectively. Adopting this strategy showed similar results for DEB and DES in these complex femoropopliteal lesions, with comparable procedural success (residual stenosis <50% and absence of procedural complications) and outcomes at 12 months. These results are somewhat different from a large retrospective Vascular Quality Initiative (VQI) database study, which showed longer time to TLR for DES [mean time for TLR 1,277 days (SD 546)] than DEB [904 days (SD 330)] in femoropopliteal lesions (10). But this study included mainly lesions <15 cm and reported limited data on other lesion characteristics and did not

report on vessel preparation prior to DEB or DES. Furthermore, this was a retrospective study and inherently affected by confounding and bias. Another propensity score matching study of Nagatomi and colleagues also reported a higher primary patency rate for DES than DEB at 1 and 2 years (84.4% and 71.1% vs. 81.3% and 66.6%, $P=0.043$), without a significant difference in freedom from TLR (11). However, when patency was lost, the rate of occlusion, length of occlusion and severity of symptoms appeared worse in the DES group. Without underappreciating the importance of patency, we should keep in mind other important long-term outcomes.

Appreciating literature on endovascular interventions in (femoropopliteal lesions) PAD becomes more and more complex, due to the increasing amount of options we have for vessel preparation and lesion treatment. Moreover, these studies are influenced by the baseline characteristics of the patients and the vascular lesions. These factors increase the importance of standardizing the reporting framework of endovascular interventions in PAD. The Endo-STAR Framework is an important initiative to develop such a system (<https://endo-star.com/>). The complex interplay between lesion characteristics (location, length, calcification, stenosis vs. occlusion) and all the available devices should be carefully considered and together determine the technical, but especially the long-term, success rate of endovascular interventions. Along with standardized reporting systems, the use of contemporary, pragmatic, overall accepted and also patient-centered outcome reporting are paramount (12,13). A well-designed evidence- and lesion-based treatment algorithm is paramount to the success and standardization of peripheral vascular interventions. The development and validation of such a generally accepted treatment algorithm should be an important future aim, for which a potential role of Artificial Intelligence could be considered (14). Such a generally accepted algorithm supports comparability, standardization and research of treatment strategies within the field of endovascular surgery.

BEST-SFA has a lot of strengths, including the option for vessel preparation in its design, focus on complex femoropopliteal lesions with high rate of CTOs, and trying to mimic the real-world situation. Some of the treatment characteristics and differences in approaches between the SA and SP groups are a reflection of this real-world situation, such as the high rate of bailout stenting in the SA group (48.3%), higher rate of vessel preparation and higher rate of dissections in the SA group. Although this reflects the real-world practice it hampers the direct comparison of effects of

DEB *vs.* DES, but this study aimed to compare the SA and SP strategies rather than effect of devices per se. However, we should also take into account some limitations, such as the higher rate of TASC II B lesions in the SA group, the low sample size and inherent risk of type II statistical error, the very low rate of CLTI patients (3.3% both in SA and SP groups and exclusion of Rutherford 5 and 6 patients) and lack of use of IVL and intravascular ultrasound (IVUS), which were also mentioned by the authors themselves. Despite some limitations BEST-SFA enriches the existing evidence on treatment of complex femoropopliteal lesions and we are looking forward to the long-term results and a future larger trial, including more balanced representation of both claudicants and CLTI patients, to help guide future evidence- and lesion-based endovascular treatment algorithms. However, vessel preparation devices have limited availability in many centers, due to the lack of reimbursement (15) and this should be considered while designing randomized trials and elaborating an algorithm for endovascular treatment.

Finally, the most promising finding of the study of Wittig and colleagues (1) is the excellent clinical outcome at 12 months, with most of the patients in Rutherford category 0 or 1 regardless of the study arm. Since the vessel preparation was performed significantly more often in the SA group ($P=0.038$), it is possible that the drug-eluted technology itself plays the crucial role in the achievement of these good results in both arms. However, these findings need to be confirmed at a long-term follow-up. PAD is characterized by a high variability in morphology, location and extension of the disease. In addition to this, a wide range of devices is available for each treatment phase. As abovementioned this should translate into future treatment algorithms depending on the patient, lesion characteristics and the specific vessel of interest. Hence, we will still have a long way to go before, such a generally accepted and evidence supported endovascular treatment algorithm will be available.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

1. Wittig T, Schmidt A, Fuß T, et al. Randomized Trial Comparing a Stent-Avoiding With a Stent-Preferred Strategy in Complex Femoropopliteal Lesions. *JACC Cardiovasc Interv* 2024;17:1134-44.
2. Dubosq M, Raux M, Nasr B, et al. Algorithm of Femoropopliteal Endovascular Treatment. *Medicina (Kaunas)* 2022;58:1293.
3. Nugteren MJ, Welling RHA, Bakker OJ, et al. Vessel Preparation in Infrapopliteal Arterial Disease: A Systematic Review and Meta-Analysis. *J Endovasc Ther* 2024;31:191-202.
4. Nugteren MJ, Hazenberg CEVB, Akkersdijk GP, et al. Twelve-Month Outcomes of Intravascular Lithotripsy for Treatment of Calcified Popliteal and Infrapopliteal Lesions in Patients With Chronic Limb-Threatening Ischemia. *J Endovasc Ther* 2023. [Epub ahead of print]. doi: 10.1177/15266028231205421.
5. Koifman E, Lipinski MJ, Buchanan K, et al. Comparison

- of treatment strategies for femoro-popliteal disease: A network meta-analysis. *Catheter Cardiovasc Interv* 2018;91:1320-8.
6. Kayssi A, Al-Atassi T, Oreopoulos G, et al. Drug-eluting balloon angioplasty versus uncoated balloon angioplasty for peripheral arterial disease of the lower limbs. *Cochrane Database Syst Rev* 2016;2016:CD011319.
 7. Dake MD, Ansel GM, Jaff MR, et al. Durable Clinical Effectiveness With Paclitaxel-Eluting Stents in the Femoropopliteal Artery: 5-Year Results of the Zilver PTX Randomized Trial. *Circulation* 2016;133:1472-83; discussion 1483.
 8. Marmagkiolis K, Kilic ID, Inanc IH, et al. Superficial Femoral Artery Endovascular Therapy: 12-Month Primary Patency Rates of Contemporary Endovascular Devices from 25,051 Patients. *J Invasive Cardiol* 2022;34:E784-92.
 9. Aru RG, Tyagi SC. Endovascular treatment of femoropopliteal arterial occlusive disease: Current techniques and limitations. *Semin Vasc Surg* 2022;35:180-9.
 10. Marzlin N, Jan MF, Kostopoulos L, et al. Peripheral Artery Disease Intervention: Drug-Coated Balloon vs Drug-Eluting Stent, A Long-Term Comparison. *J Interv Cardiol* 2022;2022:5175607.
 11. Nagatomi S, Takahara M, Nakai T, et al. Comparing the impact of the loss of patency between treatment with drug-coated balloon angioplasty and drug-eluting stent placement. *J Vasc Surg* 2023;77:1751-9.
 12. Gaudino M, Braunwald E, Stone GW. Beyond the classic major cardiovascular event outcome for cardiovascular trials. *Eur Heart J* 2024;45:4700-3.
 13. Jansen S, Teraa M, Chan N, et al. Assessing Limb Outcomes in Drug Trials in Peripheral Artery Disease: The Need for a Universal and Pragmatic Definition. *Eur J Vasc Endovasc Surg* 2023;66:442-3.
 14. Lareyre F, Chaudhuri A, Behrendt CA, et al. Artificial intelligence-based predictive models in vascular diseases. *Semin Vasc Surg*. 2023;36:440-7.
 15. Jones WS, Mi X, Qualls LG, et al. Trends in settings for peripheral vascular intervention and the effect of changes in the outpatient prospective payment system. *J Am Coll Cardiol* 2015;65:920-7.

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