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Identifying the Best Device for Infrapopliteal Revascularization Through Quantitative Evidence Synthesis

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The light is too painful for someone who wants to remain in darkness.

—Eckart Tolle

Our mind always struggles with making sense of apparent confusion in order to eventually bring us some intelligible order.[1] However, a correct conceptual framework cannot always be achieved unless we opt for oversimplification. Endovascular specialists treating patients with infrapopliteal artery disease face the challenge of first safely approaching the below-the-knee district,[2] then successfully and safely recanalizing often challenging lesions,[3,4] and finally the additional hurdle of correctly choosing and employing the most appropriate device to maximize short- and long-term results.[5]

Indeed, a plethora of techniques and devices are already available for infrapopliteal revascularization, from atherectomy to balloon angioplasty (BA),[6] drug-coated balloons (DCB),[7] bare metal stents (BMS), drug-eluting stents (DES),[5] and bioresorbable vascular scaffolds (BVS).[8] All too often, device choice is largely based on the knowledge base of the operator together with his or her own experience and set of skills with the chosen device. While the latter aspects are beyond the scope of our present contribution, it is important to maintain an updated and comprehensive knowledge base on the clinical evidence regarding devices for infrapopliteal revascularization to avoid undermining an apparently successful procedure with a poorly chosen device.

The December 2016 issue of the *JEVT* provides an important adjunct to the biomedical literature focusing on infrapopliteal revascularization, thanks to the original contribution by Katsanos et al.[9] Specifically, they report a systematic review and meta-analysis comparing different devices for infrapopliteal endovascular therapy. They included 16 randomized controlled trials (RCTs) totaling almost 2000 patients and employed state-of-the-art analytical models that can pool head-to-head comparisons, as well as borrow information from indirect comparisons within a network meta-analytic framework.[10] Without focusing on the subtleties of this relatively novel statistical method, we may acknowledge that, providing several important assumptions are met, network meta-analysis is currently considered among the most comprehensive, reliable, and precise approaches for quantitative evidence synthesis.[11]

In order to provide a contemporary synthesis to guide endovascular practice, Katsanos and colleagues focused on RCTs comparing BA, DCB (all paclitaxel-eluting), BMS, and DES to demonstrate a clinical effect on several clinically relevant and objective outcomes, such as restenosis, target lesion revascularization (TLR), wound healing, and limb salvage. They intriguingly found that DES proved most likely to be beneficial for all endpoints, followed by DCB, BA, and BMS, typically (but not invariably) in decreasing order of efficacy. In particular, DES appeared capable of reducing the odds (ie, the number of patients with an event divided by the number of patients without the event, which is considered a reasonable approximation of risk) of restenosis by 56% in comparison

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to DCB, by 74% in comparison with BMS, and by 78% in comparison with BA. Notably, DES also reduced the odds of TLR by 25% in comparison with DCB, by 59% in comparison with BA, and by 74% in comparison with BMS. Accordingly, the odds of wound healing were favorably increased with DES by 50% in comparison with DCB, by 102% in comparison with BA, and by 345% in comparison with BMS. Finally, the odds of amputation were remarkably decreased with DES by 42% in comparison with BA, by 49% in comparison with DCB, and by 62% in comparison with BMS.

Key strengths of the review by Katsanos et al include the careful search, selection, abstraction, and appraisal methods, as well as the reliance on state-of-the-art Bayesian modeling, yielding several inferential estimates such as odds ratios, surface under the cumulative ranking area, and meta-regression coefficients.[10] The main limitations are: (1) the fact that most of the evidence stemmed from studies using BA and BMS as comparators, with quite a few patients randomized to DCB vs DES; (2) that blinding was suboptimal or lacking in several RCTs; and (3) that most studies were funded by device companies. Most importantly, transitivity between patients across RCTs was theoretically incomplete as, for instance, lesion length varied substantially in studies with different devices. In addition, not all DES or DCB included in the review by Katsanos and colleagues can be considered identical, given differences in design, platform, polymer, and anti-restenotic drug.

Another research group has most recently and independently reported a relatively similar network meta-analysis, including 11 RCTs and 1322 patients treated with BA, DCB, BMS, and DES.[12] Specifically, using also a Bayesian approach, albeit implemented in a different statistical package, Xiao et al[12] found that DES were the best choice to reduce the odds of restenosis and amputation in comparison to BA, DCB, and BMS, whereas DCB proved best to reduce the likelihood of target vessel reintervention, and BMS were most likely to achieve acute technical success. Of course, these findings strongly support the results reported by Katsanos et al,[9] which, however, should be considered more precise and valid given the inclusion of more trials and patients and thus the more robust evidence network.

Once we consider this evidence base as established, we can propose a pragmatic approach for device choice for infrapopliteal revascularization, largely based on lesion features.[13] Specifically, short lesions with limited complexity could be safely treated with DCB or DES, whereas more diffuse and complex disease should probably be treated only with DES or a combination of DCB with spot DES implantation. In our opinion, there still remains an elephant in the room, though: the precise role of BVS for infrapopliteal revascularization.[14] Despite some setbacks, these devices have been finally approved by the Food and Drug Administration for coronary procedures, and in light of their remarkable versatility,[15,16] we may envision upcoming trials formally appraising their risk-benefit balance in the infrapopliteal setting. Indeed, by combining the apparently conflicting strengths of DCB and DES in a single device, BVS provides mechanical support and anti-restenotic effect but eventually disappears, thus limiting persistent endothelial injury.[17] In the near future, BVS could become the workhorse tool for infrapopliteal revascularization. Nonetheless, in the meantime, the most favorable data have been accrued for DES and, less consistently or extensively, DCB.

Declaration of Conflicting Interests

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