

## CORRESPONDENCE

**The Use of Drug Coated Balloon in Femoro-popliteal Atherosclerotic Disease**

Recently Katsanos et al. demonstrated increased mortality in patients treated with paclitaxel-coated balloons or stents in the femoro-popliteal artery in a comprehensive systematic review and meta-analysis of 28 randomized controlled trials with over 4600 patients included.<sup>1</sup> The increased mortality after 2 and 5 years of follow-up that was found in the meta-analysis raised doubt on the safety of drug coated technology, especially for those devices using paclitaxel.

There are some unresolved issues when interpreting the data of the cited meta-analysis.<sup>1</sup> For example, only a subset of the included trials reported follow-up beyond 1 year. Moreover, most of the studies that reported increased mortality at 2 and 5 years, already showed this mortality difference at 1 year follow-up. However, when pooling the 1-year data, no significant difference in mortality was found. Furthermore, the reasons for withdrawals and loss-to-follow-up were unknown in many of the included patients. Currently, an explaining mechanism for paclitaxel leading to increased mortality is still lacking. The majority of included studies did not report the actual cause of death, which unfortunately hampers identification of a causal mechanism. Although the meta-analysis definitely raised questions on the safety of drug-coated technology, definitive answers are not available yet and further research, for example on patient-level data, is needed to further establish the significance, size and cause of the effect on mortality that was found.

In the last decade, drug coated balloons (DCB) and stents (DES) gained popularity for application in the femoro-popliteal arteries and these techniques were widely adopted in clinical practice. The improved patency rates for DCB compared to standard PTA in femoro-popliteal lesions was found in trials predominantly including claudicants with relatively short lesions.<sup>2</sup> However, in current daily clinical practice, the majority of patients we treat have many comorbidities, suffer long chronic total occlusions and present with critical limb ischemia. For these patients, next to patency, outcomes such as wound healing, treatment of infections and reduction of ischemic pain are more relevant.

Currently, there are many different DCBs on the market, all with slightly different designs and properties such as dosage of drugs incorporated and the excipients and coatings used. Clinicians may not see the wood for the trees. For example, what is the optimal inflation time and pressure to allow adequate transmission of the drug to the vessel wall? How can we determine the optimal drug transfer during DCB procedures? For devices that are much more expensive than the standard PTA balloons one would expect this information to be available. Moreover, the exact role of

stenting and proper vessel preparation should be further established. Cumulating evidence demonstrates that longer stents lead to higher restenosis rates, compared to spot-stenting, whereas a strategy of leave nothing behind is generally advocated.<sup>3</sup> The use of atherectomy devices in severely calcified vessels to improve drug delivery and patency rates and to reduce the need for provisional stenting is another interesting emerging strategy that deserves further investigation.<sup>4</sup>

To conclude, while drug-coated technology has gained an increasing role in the treatment of femoro-popliteal lesions, despite its significant costs, the first priority now is to further investigate the safety of drug-coated technology and to further elucidate the findings in the meta-analysis by Katsanos et al.<sup>1</sup> If the safety of these devices is re-established, further studies are needed to elaborate the optimal strategy for vessel preparation, balloon inflation technique for drug transfer, and the role and type of provisional stenting or other adjuncts.

## REFERENCES

- 1 Katsanos K, Spiliopoulos S, Kitrou P, Krokidis M, Karnabatidis D. Risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the leg: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc* 2018;7:e011245.
- 2 Giacoppo D, Cassese S, Harada Y, Colleran R, Michel J, Fusaro M, et al. Drug-coated balloon versus plain balloon angioplasty for the treatment of femoropopliteal artery disease: an updated systematic review and meta-analysis of randomized clinical trials. *JACC Cardiovasc Interv* 2016;9:1731–42.
- 3 Deloosse K, Callaert J. Less is more: the "As Less as Reasonably Achievable Stenting" (ALARAS) strategy in the femoropopliteal area. *J Cardiovasc Surg (torino)* 2018;59:495–503.
- 4 Katsanos K, Spiliopoulos S, Reppas L, Karnabatidis D. Debulking atherectomy in the peripheral arteries: is there a role and what is the evidence? *Cardiovasc Interv Radiol* 2017;40:964–77.

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