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EDITORIAL COMMENT

Vascular Scaffold for Below-the-Knee Vascular Disease

Have We Got a New Challenger?*

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Critical limb ischemia (CLI) is the most challenging setting for peripheral arteries interventions. Below-the-knee (BTK) vascular interventions are experiencing a dramatic increase compared to surgery (1), which makes mandatory to find effective and durable solutions to prevent early restenosis and recurrent hospitalizations. In a previous paper (2), we identified this scenario as the potential 'battlefield' of an ongoing challenge between the novel drug-coated balloon technology (that we identified as David) and the drug-eluting stents, a class of mature and established devices already tested in BTK interventions (that we identified as Goliath). Actually, the time has come to introduce a new challenger in the competition.

The use of drug-eluting stents for CLI has gained popularity for its ability of reducing restenosis in the long-term follow-up of patients treated with peripheral angioplasty (3). In fact, the use of stents in this setting (compared with standard balloon angioplasty) offers some advantages. First, all endovascular procedures determine profound and circumferential stretch injuries to the target artery. This direct vascular injury and inflammatory response with smooth muscle cell activation and proliferation could be blocked by a slow (more than a periprocedural) release of an antiproliferative drug. Second, during the early weeks after revascularization, the artery is susceptible to mechanical recoil from energy stored in the stretched external elastic lamina. Maintaining scaffolding and support to deal with this elastic recoil for a sufficient duration could definitely help in preventing an early restenosis for mechanical shrinking. That is why stents work.

In contrast, conventional stents have undeniable limitations in treating BTK vessels: the extension of the disease, together with the peculiar nature of BTK atherosclerotic disease, which is often characterized by a large intimal lipid burden and a severe medial calcification, make questionable the use of permanent stents and raises issues about the potential risk of rupture. For these reasons, a drug-coated technology that requires no implant to be left behind has been claimed as the potential solution to reduce the risk of restenosis after BTK interventions. To this aim, bioresorbable scaffolds have then been tested in this setting, with the first data about dedicated peripheral vascular scaffolds being not satisfactory due to the lack of a sustained antiproliferative drug release and to poor scaffolding properties of the devices (4).

The Absorb drug-eluting bioresorbable vascular scaffold (BVS) (Abbott Vascular, Santa Clara, California), which is composed of a PLLA polymer scaffold and the antiproliferative drug everolimus, can probably overcome the 2 problems. Everolimus effectively inhibits neointimal hyperplasia, enhances remodeling, and has been shown to be safe. The Absorb BVS was designed effectively to maintain its structure and strength for the full 6-month post-implantation period, with full preservation of the scaffold area, as confirmed in coronary studies (5-7). This translated into striking clinical results for coronary interventions, as confirmed by the large-scale, multicenter ABSORB (A bioabsorbable everolimus-eluting coronary stent system for patients with single de-novo coronary artery lesions) III trial (8).

In the this issue of *JACC: Cardiovascular Interventions*, Varcoe et al. (9) describe their experience with Absorb coronary scaffolds with BTK TASC-A lesions.

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They report a rate of freedom from both binary restenosis and target lesion revascularization of 96.0% at a follow-up of 12 months. Target vessel patency was also associated with a limb salvage rate of 100%.

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We congratulate the authors for reporting the long-term clinical outcome of their experience with coronary scaffolds in BTK interventions; their restenosis rate, together with the appropriate duration of clinical follow-up, actually represent a proof of concept of the great potential of vascular scaffolds in peripheral interventions. Their results are in line with other recently reported experiences comparing BVS and drug-eluting stent results in BTK interventions in a retrospective series and showing a substantial equivalence between the 2 approaches (10). Such a finding should certainly be considered as the starting gate toward a wider and more specific assessment of these technologies in BTK setting.

Nevertheless, being their first experience with these devices in BTK vessels, the authors selected a population with very focal lesions: mean lesion length of the target vessel was 19.2 mm, which reminds us of the coronary setting the scaffolds were planned for. This makes it impossible to derive reliable considerations about the usefulness and the real impact (in clinical practice) of these devices on BTK procedures, given that infrapopliteal disease is known to be more diffuse and complex in a real-world setting.

A number of further limitations of the present study should be acknowledged. First, although a purely lesion-related primary efficacy endpoint supports the inclusion of patients with both CLI and intermittent claudication, such a mixed population makes the interpretation of major amputation difficult and potentially misleading. Second, it would have been interesting to consider the relation between vessel calcification and BVS deployment. The authors do not mention any issue in stent deployment, but vessel calcification, which is common in BTK disease, is often challenging for scaffold tracking and proper expansion. To this aim, the use of intravascular imaging for the future assessment of these devices in peripheral angioplasty should be encouraged to better explore their scaffolding properties in such an aggressive disease. And last, but not least, intravascular imaging could give information about the risk of device rupture, which could lead to unpredictable outcomes if scaffolds are deployed in severely calcified lesions.

In conclusion, the reported results are not enough to justify an enthusiastic conversion to bioresorbable scaffolds for treatment of CLI, especially because of the number of limitations and the carefully selected population, but they should be considered as pilot and idea-generating data to assess the role of BVS in this setting. Of note, they confirm the idea that a sustained scaffolding effect, together with a prolonged antiproliferative drug release, are able to significantly reduce restenosis in BTK interventions. Whether this effect would be confirmed for longer and more complex lesions is now to be explored. New studies and technology developments (i.e., longer BVS) will need to clarify if bioresorbable devices could offer a reliable and, in perspective, safer solution for CLI patients requiring stent implantation in BTK vessels by having a wider and less selected indication. This would definitely tell us if there is a new contender in the ongoing BTK challenge.

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