ASK THE EXPERTS

Perfect Pairing: Which Stent Properties Are the Best Match for Drug-Coated Balloons?

Experts weigh in on properties of available stent technology and which combinations could be used to improve femoropopliteal disease outcomes.

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In the era of the "leave nothing behind" concept, in which the trend is to minimize stent use, the combination of drug-coated balloons (DCBs) with stents in the femoropopliteal arteries is a challenging topic. In fact, these two apparently competing technologies demonstrate properties that, when combined, could enhance outcomes of endovascular treatment for femoropopliteal disease. Compared to balloon angioplasty, the main advantage of stent deployment is the achievement of maximum acute luminal gain. On the other hand, DCBs have the advantage of delivering an efficient antirestenotic drug dose within the vessel wall and inhibiting neointimal hyperplasia, without the need of a metallic scaffold. These two properties could be complementary in selected cases.

For example, elastic recoil or dissection persisting after DCB angioplasty and prolonged postdilation should currently be treated with a bare nitinol stent. But why not use a drug-eluting stent (DES)? Concomitant use of DCBs and DESs could lead to critical local paclitaxel concentration levels, and the effect of such a high dose on the vessel wall remains unknown. Moreover, the combination of a bare nitinol stent after DCB angioplasty could enhance outcomes in cases of long, severely calcified lesions, in which the use of DCBs alone appears to produce suboptimal results, not only because the presence of calcium can limit drug diffusion, but also because such hard atherosclerotic lesions are usually resistant to angioplasty.[1]

An ongoing, prospective, single-arm, multicenter, postmarket study sponsored by Bard Peripheral Vascular, Inc. is investigating the concomitant use of DCBs with nitinol stents in long, complex, femoropopliteal lesions. Currently, recruitment has been completed, and results are awaited.[2] On the other hand, the solution in such lesions could be DESs. However, certain hard, severely calcified, eccentric lesions require strong scaffolding to obtain adequate luminal gain and avoid short-term reocclusion, and currently available nitinol DESs lack such radial force. Therefore, it would be interesting to combine the Supera interwoven nitinol stents (Abbott Vascular) with DCB technology, given that a Supera drug-eluting stent is not currently available. Lesion preparation

with atherectomy could limit stent use, but this is true only in cases of intraluminal lesion crossing, and some lesions will still finally require a stent. Stenting and DCB angioplasty is a fast and safe way to improve outcomes after subintimal crossing.

Finally, according to the FAIR randomized controlled trial, DCBs provide superior patency outcomes compared to percutaneous transluminal angioplasty (PTA) for the treatment of in-stent restenosis in the superficial femoral artery,[3] and these data are in line with those reported from large coronary trials.[4] As the perfect device for all different kinds of femoropopliteal artery lesions is unlikely to be discovered, the combination of existing technologies such as self-expandable stents and DCBs could improve endovascular treatment outcomes in selected cases.

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DCBs transfer a reservoir of paclitaxel into the blood vessel wall to prevent the proliferation and migration of smooth muscle cells, which are known to contribute to the development of neointimal hyperplasia and result in patency-threatening negative remodeling. However, DCBs are unable to provide mechanical scaffolding to overcome elastic recoil and treat dissection. This has led to the use of a combination of DCBs and bare-metal stents (BMSs) for their respective antirestenotic and scaffolding properties.

Unfortunately, we don't really know which stents are best suited to combination therapy with DCBs. However, it's an interesting exercise to speculate based on the little evidence that does exist. Three trials have investigated combination therapy with low-profile, self-expanding, 4-F–compatible stents, all with similar rates of success. The first was the DEBATE SFA trial, a single-center, randomized controlled trial that compared the use of the In.Pact Admiral DCB (Medtronic) with PTA, each in combination with the Maris stent (Medtronic).[1] Mean lesion length was 94 and 96 mm in the DCB/BMS and PTA/BMS groups with 12-month patency rates of 83% versus 52.7% (P = .008), favoring the DCB/BMS combination, respectively. The second was the DEBAS trial, a single-arm study that investigated the use of the Passeo-18 Lux DCB (Biotronik) in combination with the Pulsar-18 stent (Biotronik).[2] Investigators evaluated complex lesions (mean length, 187.6 mm) and found an astounding 12-month primary patency of 94.1%. The final study was the BIOLUX 4EVER trial, which looked at the same DCB/BMS combination as the DEBAS trial, again using a single-arm trial design but in somewhat shorter lesions (mean length, 83.3 mm).[3]

Results presented in April 2017 demonstrated a 12-month primary patency rate of 89.9%. There is certainly a school of thought that lower-profile stents have advantages when used in combination with DCBs, particularly if the DCB is used after the implantation of the stent, as was the case in the DEBAS study. This is because a stent with a thin strut and narrow width is thought to allow more complete transfer of drug into the vessel wall, particularly adjacent to the stent itself. Although it is true that these results with low-profile stents are encouraging, we have no way of making a comparison, as there are no studies that have evaluated standard-profile, laser-cut, nitinol stents in combination with DCBs.

The only other trial to evaluate combination therapy in the periphery used both a different stent and DCB compared to the aforementioned studies. The RAPID randomized controlled trial was a Dutch trial that compared pretreatment with the Legflow DCB (Cardionovum), coated in nanocrystalline paclitaxel particles, or PTA in combination with the interwoven Supera stent.[4] Treated lesions had mean lengths of 156 and 155 mm, respectively, and there were no significant differences in primary patency rates (72% vs 61%) at 12 months. Although this study has not yet

been published, questions have arisen regarding the effectiveness of this particular DCB in the superficial femoral artery as well as the stent deployment technique. This is because the 12-month primary patency rate of 61% is inferior to that observed in the published literature, and the Supera device is known to require fastidious vessel preparation and be sensitive to elongation/compression.

So, what do we really know about the BMS attributes that work best in combination with DCBs?

- We need much more data to make any conclusions about which BMSs are best suited to combination therapy.
- Stents with thin struts and narrow width seem well placed to achieve good patency rates, whether DCBs are used before or after stent implantation.
- We lack data on combining standard strut–width BMSs with DCBs, but there is no reason they couldn't be as effective.
- We have no data to support the use of combining DCBs with the interwoven Supera stent.

It is my view that in the absence of meaningful comparative data, the interventionalist should use their better judgment. Combination therapy provides us with the opportunity to use stents selectively, in sections of the artery where mechanical support is needed after DCB predilatation, thus individualizing the application of scaffold technology. The choice of stent should be determined by the desirable mechanical properties of the device regardless of using DCBs, with stents chosen based on attributes such as radial strength, deployment accuracy, flexibility, and fracture resistance.

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DCBs have certainly been proven to be a disruptive technology in the treatment of femoropopliteal disease. Perhaps more than any other device or treatment approach, the introduction of DCBs has caused physicians to rethink stent utilization strategies. As DCB implementation has become more widespread, there has been a corresponding decrease in the popularity of the "full metal jacket" approach to femoropopliteal disease. This is the result of two major factors: (1) the well-known difficulty and expense associated with treating in-stent restenosis, and (2) the significant and well-substantiated decrease in target lesion revascularization rates seen with DCBs.

It has become appropriate to trust that any reasonably acceptable angiographic appearance after DCB treatment would lead to long-term patency. Thus, a "spot-stenting" model of correcting only the most significant dissections and recoil has become popular.

What does this mean for stent selection? Clearly, stents that can be deployed with great accuracy and are short in length hold the advantage. This favors nitinol tube stent platforms over woven wire stents, which lack deployment accuracy. Shorter lengths (eg, 20, 30, or 40 mm) often become better choices than the much longer options employed in full metal jacket stenting. The most minimalistic approach is that of supporting vessel segments as short as 6 mm using the lightweight Tack endovascular system (Intact Vascular, Inc.).

In common practice, DCBs are used first, followed by stent placement. In the unique DEBAS trial design, stents were placed first, followed by DCB treatment. Despite a mean lesion length of 18.8 cm and the fact that 96% of lesions were TASC C and D lesions, 24-month target lesion revascularization was only 11.8%. In this model, a stent with thin struts and minimal stent surface area (eg, the Pulsar-18 stent) is ideal to facilitate drug exposure to the vessel wall.

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DCBs have significantly improved the durability of femoropopliteal interventions compared to PTA and seem to perform equivalent to DESs. However, DCBs are limited by the same shortcomings as conventional balloons, such as elastic recoil, dissection, and local thrombus formation.

As such, the following main stent properties are mandatory:

- Fixation of a flow-limiting dissection or local thrombus. For such an indication, compression resistance of the stent is of inferior importance, and stent length could be limited to a few centimeters; short stents or tacks might be appropriate.
- For overcoming plaque recoil, in particular in heavily calcified lesions, stents with a high compression resistance are preferred, such as interwoven nitinol stents (eg, Supera).
- A third theoretically interesting stent property is changing vessel geometry by implanting a stent with three-dimensional helical centerline geometry, such as the BioMimics stent (Veryan Medical). It has been shown that intentionally rendering the vessel to have nonplanar curvature to impart swirling flow improves the outcome of peripheral intervention in the longer term. The combination of such a stent design may offer the option of a combination of acute restenosis prophylaxis by applying an antiproliferative drug to the vessel wall using the DCB, with longer-term restenosis prophylaxis by changing the vessel geometry with an implant. ■