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EDITORIAL COMMENT

Treatment Paradigms for the Superficial Femoral Artery

Are They A-Changin?*

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The main limitation of endovascular treatment modalities in the femoropopliteal tract is the high rate of recurrent lesions necessitating repeat interventions. Although 1-year patency rates of plain balloon angioplasty might be as low as 30% to 40% (1), improved results have been reported with a primary stenting approach. Nevertheless, depending on the lesion length, in-stent-restenosis rates at 1 year are still in the range of 20% to 40% (2–5). Particularly in longer lesions, the occurrence of stent fractures seems to contribute to the development of in-stent-restenosis and has the potential to further complicate subsequent endovascular procedures (6).

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Due to the chronic nature of peripheral arterial disease and the high restenosis rate, in many patients with femoropopliteal obstructions repeat interventions are an essential part of the long-term treatment strategy. The concept of saving more options for the future is an important consideration favoring nonstent-based treatment modalities in an attempt to limit the problem of in-stent-restenosis treatment. From that perspective a treatment alternative that effectively inhibits the restenosis process after balloon angioplasty, achieving an improved clinical outcome with minimal need for stent implantation, would be an important step forward.

In this issue of *JACC: Cardiovascular Interventions*, Micari et al. (7) report the first single-arm study results with a drug-coated balloon (DCB) catheter with urea as drug carrier and dissolvent and paclitaxel as the active substance. Their data are generally in line with the already published THUNDER (Local Taxane with Short Exposure for Reduction of Restenosis in Distal Arteries) and FEMPAC (Femoral Paclitaxel) trials, where paclitaxel-coated balloons with the contrast agent iopromide as an additive resulted in a significantly reduced neointimal proliferation as measured by late lumen loss at 6-month angiographic follow-up (8,9). Beyond this technical proof of concept, the paper by Micari et al. (7) reports on the currently largest cohort in the published data with DCB for femoropopliteal disease. A total of 105 patients have been successfully treated, with only 12.3% of lesions requiring stenting. Ninety-two patients have completed the 12-month follow-up, demonstrating a primary patency rate of 83.7% and a reintervention rate as low as 7.6%.

Despite the obvious study limitations inherent in the single-arm design and the lack of independent data adjudication, the authors have to be congratulated for these outstanding results, which strongly support the concept that DCB might be a powerful treatment alternative for femoropopliteal disease. It has to be noted that these results were achieved in a cohort of patients with a mean lesion length of 76.3 mm and almost two-thirds of patients were classified as moderately or severely calcified. In that context the bailout stent rate of only 12.3% is remarkably low—probably achieved by a very high dedication of the investigators to an optimized PTA technique using prolonged balloon inflations (mean inflation time 181 s). Although the obvious reluctance of the investigators to implant stents resulted in a somewhat higher rate of patients with residual stenoses >30% (technical success rate 89.6%), this does not seem to interfere negatively with the outcome at 12 months. This is reassuring for the concept of limiting the use of stents after DCB treatment as much as possible.

Are DCBs going to shift treatment paradigms for the SFA away from stenting to nonstent-based treatments? It is certainly too early to draw final conclusions from the available published data. Although the report by Micari et al. (7) might be an important piece in the puzzle, we have to face the fact that the total reported experience of DCB-treated patients in the SFA is on <200 patients so far. Clearly, the primary patency rate of 83.7% in a patient cohort with a mean lesion length of 76.3 mm compares very favorably with reported results on primary stenting. Nevertheless, direct randomized head-to-head comparisons will be necessary to ensure comparability of the treatment groups. Only this approach will allow investigators to obtain reliable data that might eventually guide us in these important treatment decisions.

The real challenge and "unmet clinical need" for interventional treatment of femoropopliteal lesions are clearly long lesions and chronic total occlusions of the SFA. This is the specific subcategory of lesions that continues to represent a major challenge for currently available endovascular treatment approaches. In particular, primary stenting with conventional nitinol stents did not show convincing patency rates, and stent fractures have been most prevalent in long

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stented segments (6). This might indicate that nonstent-based solutions would be particularly desirable for long lesions. However, will DCB have the potential to be a primary choice treatment for such lesions? For the moment we have to admit that almost nothing is known to date about the potential of DCB treatment for those complex lesions. In that regard, it will be very important that future studies will specifically address this complex subgroup of patients.

In particular, the effectiveness of the combination of DCB with stenting is currently unclear. At least theoretically, there are concerns that the biological effect of the single drug delivery by the DCB might be outweighed by the chronic proliferation stimulus induced by the implanted stent. This results in the current paradigm to avoid stenting as much as possible after DCB treatment. In fact, the study by Micari et al. (7) has shown that this approach can give excellent results for short- to intermediate-length lesions. However, on the basis of experience with conventional balloon treatment, it is likely that with increasing complexity of the lesion the need for a mechanical stabilization of at least part of the treated segment might become necessary. Therefore, the combination of DCB with spot stenting might be an important concept to explore as a treatment modality for long segment disease. Alternatively, other combination therapies like atherectomy followed by DCB might be viable options and need further evaluation. Last but not least, with the paclitaxel-coated Zilver PTX stent (Cook Medical, Bloomington, Indiana), there is a drug-eluting stent becoming available that has not only been proven to have significantly better patency rates than PTA and the bare Zilver stent (10) but has also shown very encouraging results in long lesions (11). Particularly for complex lesions, this technology might be a strong competitor to DCB.

Yes, paradigms for interventional treatment of the SFA are changing—away from a primarily mechanical approach with ballooning and stenting, toward a more differentiated physiological treatment. Likely, antiproliferative drug delivery will have an important role in the future to optimize long-term outcomes. To what extent such treatment algorithms will still rely on mechanical treatment modalities, including stent placement as a bailout or as a drug delivery platform, remains to be determined. It is time for more good clinical research!

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