Bioresorbable Scaffolds: Do Recent Study Results Support Revival for Use in the BTK Arteries?

Emerging platforms, recent study results, and progress in the BTK arteries.

By Marianne Brodmann, MD

Endovascular treatment options for peripheral artery disease have improved tremendously over the last few years. A milestone achievement was the development of drug-coated balloons (DCBs) and drug-eluting stents, and now, with the availability of vessel preparation tools, the current first-line strategy is use of DCBs after optimal vessel preparation and the shortest possible scaffold in cases of mechanical issues (ie, the so-called "leave as little metal behind as possible" strategy).

Mechanical issues such as acute recoil, dissection, or high-grade residual stenosis still need to be addressed despite the technologies that are currently available. The placement of nonresorbable stents (permanent scaffolds) is indicated in these circumstances to improve short- and long-term outcomes, but this remains associated with the problem of stent fractures and difficult-to-treat in-stent restenosis (ISR), especially in the femoropopliteal and below-the-knee (BTK) segment.[1,2]

LESION MORPHOLOGY AND ANGIOGRAPHIC PATTERNS OF ISR

In the femoropopliteal segment, 30% to 40% of patients will present with ISR after initial stent implantation, and of those, 65% will return with recurrent ISR posttreatment.[2] The increased localized inflammatory response and excessive neointimal proliferation seen after stent implantation leading to ISR has not been satisfactorily solved, even with the application of debulking technologies and DCBs.[2]

Microscopically, ISR lesions are heterogeneous, consist primarily of a hydrated collagen matrix (60%-80% of the restenotic volume is aqueous), and present a higher plaque burden. Angiographic characteristics of femoropopliteal ISR lesions are an important predictor of subsequent outcomes. Tosaka et al described angiographic patterns of ISR specific to the femoropopliteal segment: short, focal lesions (class I ≤ 50 mm) and diffuse lesions (class II > 50 mm) are associated with reasonable patency after treatment; in contrast, total in-stent occlusions (class III) often predict recurrent ISR when treated with percutaneous transluminal angioplasty (PTA) (85% recurrence at 2 years).[3]

EFFICACY OF DCBs FOR ISR

DCBs have been evaluated as a treatment option in ISR and have shown benefit in nonocclusive lesions, but results can still be improved.[4] In the BTK space, DCBs, specifically paclitaxel-coated DCBs, have failed to show efficacy, and thus there is currently no effective treatment strategy for ISR. The primary treatment strategy is plain old balloon angioplasty and a scaffold if needed.[5] As mechanical recoil and dissections are problematic due to vessel morphology, the need for a mechanical solution below the knee is even greater than in the above-the-knee space.[6]

USE OF BIORESORBABLE SCAFFOLDS BELOW THE KNEE

Given the lack of effective treatment for ISR, the usage of bioresorbable scaffolds (BRSs) in the BTK space has been evaluated. The approach was thought to be advantageous, as the diameter of the BTK arteries is similar to that of the coronary arteries, where BRSs have demonstrated good outcomes. However, outcomes of various studies have been mixed.

AMS INSIGHT Trial

One of the initial trials evaluating BRS use in BTK arteries was the AMS INSIGHT trial using a first-generation, balloon-expandable, tubular laser–slotted, electropolished stent made of a bioabsorbable magnesium alloy. The mechanical properties of this magnesium stent were similar to those of permanent stainless-steel stents, including a high collapse pressure (0.8 bar), low elastic recoil (< 8%), and minimum amount of shortening after inflation (< 5%).[7] The stents (10, 15, and 20 mm in length; 3 and 3.5 mm in diameter), premounted on a low-compliance, fast-exchange delivery balloon catheter, were deployed after predilatation of the lesion. In this trial, 117 patients with 149 BTK lesions were treated; 57 patients with 75 lesions were assigned to PTA and 60 patients with 74 lesions to absorbable metal stent (AMS). At 6 months, the rate of target lesion revascularization (TLR) was 16% (12/75) in the PTA group and 31.1% (23/74) in the AMS group (P = .052); lesion revascularizations were clinically indicated for eight of 12 (66.7%) lesions in the PTA group and 18 of 23 (78.3%) lesions in the AMS group.[7]

Data from this randomized controlled trial were contrary to positive data showing better efficacy of BRSs in the BTK space in a recent meta-analysis.[8] Ipema et al identified five studies that included 155 patients (160 treated limbs) treated with BRSs in the BTK arteries (two prospective case series, two retrospective case series, and one retrospective registry study).[8] Studies were determined to be of moderate quality per MINORS score. Pooled 12-month primary patency per limb was 90% (143/160), freedom from clinically driven TLR was 96% (124/130), the limb salvage rate was 97% (156/160), survival was 90% (112/125), and amputation-free survival was 89% (110/125). Results were similar in a subgroup analysis of studies of the Absorb BRS (Abbott). Although this meta-analysis demonstrated good 12-month patency and clinical results with BRSs for BTK arterial disease, even in patients with multimorbidity and short but complex lesions, it is important to note that included studies were prospective cases series with a small number of patients, lesion lengths were short, and patients were not randomized to a control arm. Given the positive efficacy and safety outcome, the authors concluded that these results encourage a revival of BRSs.

LIFE-BTK Trial

The positive outcome of the multicenter, randomized controlled LIFE-BTK trial has had a huge impact on the revival of BRSs, especially in the BTK space.[9] A total of 261 patients with chronic limb-threatening ischemia (CLTI) and infrapopliteal artery disease were randomized (2:1) to treatment with an everolimus-eluting resorbable scaffold or angioplasty. The everolimus-eluting resorbable scaffold (Esprit, Abbott) has a poly-L-Lactic acid (PLLA) structure and is coated with a 7-µm poly(D,L-lactide) (PDLLA) surface polymer, which controls the release of everolimus at a concentration of 100 µg/mm^2. Strut thickness is dependent on the scaffold diameter, ranging from 99 to 120 µm, and scaffold lengths for the trial were 18, 28, and 38 mm with 2.5, 3, 3.5, and 3.75-mm diameters.[10]

The primary efficacy endpoint (defined as freedom from above-ankle amputation of the target limb, occlusion of the target vessel, clinically driven TLR, and binary restenosis of the target lesion at 1 year) was observed in 135 of 173 patients treated with the scaffold and 48 of 88 patients treated with angioplasty (Kaplan-Meier estimate, 74% vs 44%; absolute difference, 30 percentage points; 95% CI, 15-46; one-sided P < .001 for superiority). The primary safety endpoint, defined as freedom from major adverse limb events at 6 months and perioperative death, was reported in 165 of 170 patients in the scaffold group and 90 of 90 patients in the angioplasty group (absolute difference, −3 percentage points; 95% CI, −6 to 0; one-sided P < .001 for noninferiority). Serious adverse events related to the index procedure occurred in 2% of scaffold-treated patients and 3% of angioplasty-treated patients.[9]

MOTIV BTK Pilot Study

Updated 24-month data were reported at CIRSE 2023 by the investigators of the MOTIV BTK trial (NCT03987061) exploring the Motiv sirolimus-eluting BRS (Reva Medical).[11] The Motiv sirolimus-eluting BRS consists of a proprietary Tyrocore polymer and has a strut thickness ranging from 95 to 115 µm. In this prospective, single-arm, multicenter study of 58 patients (60 limbs), 76 Motiv scaffolds were placed (mean lesion length, 29.46 mm) in both primary de novo and restenotic lesions (n = 37) as well as in areas of flow-limiting dissection or restenosis after PTA of a longer lesion (n = 23). At 24 months, clinically driven TLR was 2% and the limb salvage rate was 95%.

RESOLV 1 Trial

The RESOLV I first-in-human trial (NCT04912323) is evaluating the Magnitude drug-eluting resorbable scaffold (R3 Vascular), a PLLA resorbable scaffold coated with PDLLA with a 98-µm strut thickness on a balloon-expandable platform, which resorbs in a benign, controlled manner over approximately 18 months. Preliminary 6-month results were presented at VIVA 2023.[12] Freedom from binary restenosis (by angiography) or absence of flow (by duplex ultrasound when angiography was not available) was observed in 100% of Rutherford class 3 and 4 patients and 90% of Rutherford class 5 patients.

EFEMORAL I Trial

The EFEMORAL I first-in-human, prospective, single-arm, open-label, multicenter clinical study (NCT04584632) is evaluating the Efemoral Vascular Scaffold System (EVSS) with FlexStep technology (Efemoral Medical) in the femoropopliteal arteries. The study is being conducted in New Zealand and Australia. EVSS received FDA Breakthrough Device designation for treatment of de novo or restenotic infrapopliteal artery lesions in patients with CLTI in February 2024.

CONCLUSION

Given the desire to avoid permanent stents in the infrainguinal arterial segments and the encouraging results from different new technologies evaluated for above and below the knee, BRSs will play an important and relevant role in the near future in the endovascular field. The main issues of failure with earlier-generation BRSs seem to have been overcome, and the newer technologies have an adequate radial outward force and an adequate time frame of resorption to overcome the issue of activated inflammatory response. ■

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