Are DRS Ready for Prime Time in the Infrapopliteal Circulation?

A review of current-generation below-the-knee drug-eluting resorbable scaffolds, focusing on their appropriate use and where they are headed next.

By Abigail L. Kleine and Ramon L. Varcoe, MBBS, MS, FRACS, PhD, MMed(ClinEpi)

Peripheral artery disease (PAD) affects an estimated 6% of the global adult population and remains a major contributor to disability, primarily due to ischemia of the lower extremities.[1] In its most severe manifestation, chronic limb-threatening ischemia (CLTI), patients may present with rest pain, nonhealing ulcers, or tissue loss, all of which profoundly diminish quality of life.[2] PAD is frequently associated with systemic comorbidities, including diabetes mellitus, hypertension, dyslipidemia, and atherosclerotic cardiovascular or cerebrovascular disease, thereby placing affected individuals at substantially increased risk for major adverse cardiovascular events such as myocardial infarction and stroke.[3]

Atherosclerotic disease involving below-the-knee (BTK) arteries presents a distinct set of anatomic and technical challenges. The small caliber of these vessels, coupled with diffuse calcific burden and a high incidence of chronic total occlusions, significantly constrains the long-term efficacy of percutaneous transluminal angioplasty (PTA), which currently represents the standard revascularization modality for CLTI.[4] Although PTA remains the mainstay of endovascular therapy aimed at limb preservation, its utility is frequently limited by high rates of restenosis and the need for repeat interventions.[5]

Emerging technologies, such as drug-eluting resorbable scaffolds (DRS), have shown promise in overcoming some of the inherent limitations associated with PTA and permanent metallic stent placement.[6,7] This article aims to examine the evolving therapeutic landscape of BTK interventions in CLTI, critically assess the limitations of conventional modalities, and evaluate the potential of DRS technologies to enhance long-term clinical outcomes.

TRADITIONAL ENDOVASCULAR TREATMENT STRATEGIES

The endovascular management of infrapopliteal PAD leading to CLTI has undergone substantial evolution. Initially, PTA served as the mainstay of therapy, providing immediate luminal gain through mechanical dilation. However, in the absence of a scaffolding structure, PTA is prone to vessel recoil, dissection, and subsequent restenosis.[5]

The introduction of bare-metal stents improved procedural outcomes by offering structural support, yet long-term efficacy was undermined by intimal hyperplasia due to chronic mechanical irritation, resulting in persistent rates of restenosis and reintervention.[8] Despite these limitations, PTA remains a cornerstone in BTK revascularization due to its minimally invasive nature, repeatability, and ability to promptly restore perfusion. Nevertheless, PTA is less effective in the presence of arterial calcification, elastic recoil, or dissection, especially within the crural arteries, contributing to reduced patency and high restenosis rates.

Atherectomy has emerged as an adjunctive strategy for complex or heavily calcified BTK lesions, facilitating plaque debulking and enhancing balloon angioplasty outcomes. Although it may decrease the need for stenting by improving vessel compliance and distal flow, it carries notable risks, including perforation, distal embolization, and dissection, and it often necessitates further intervention due to incomplete mitigation of restenosis.[9]

DRUG-ELUTING RESORBABLE SCAFFOLDS

DRS are engineered to biodegrade within 12 to 36 months, aiming to mitigate the long-term compli-

cations associated with permanent implants such as bare-metal and drug-eluting stents. These complications include chronic vessel irritation, stent fracture, and imaging artifact. In contrast, the temporary nature of DRS preserves vascular integrity and facilitates future surgical or endovascular interventions, making them particularly suitable for patients with progressive disease or complex anatomy. Improved vessel patency with DRS has been associated with increased patient satisfaction and a reduced need for repeat procedures.

DRS typically consist of a synthetic biodegradable polymeric scaffold, most commonly poly-L-lactic acid (PLLA), which provides transient mechanical support while serving as a platform for localized drug delivery. PLLA degrades primarily through nonenzymatic hydrolysis of its ester bonds in the physiological environment, generating L-lactic acid, a naturally occurring metabolic intermediate. This byproduct is safely metabolized via the Krebs cycle or excreted renally, ensuring biocompatibility and minimizing inflammatory responses during degradation.[10]

Pharmacologically, DRS are coated with antiproliferative agents, such as sirolimus or its analogues, embedded within a polymer matrix. These agents inhibit neointimal hyperplasia by targeting the mammalian target of rapamycin signaling pathway, arresting vascular smooth muscle cell proliferation and migration.[11] This controlled antiproliferative effect is central to maintaining vessel patency and reducing the incidence of restenosis during scaffold resorption.[12]

CLINICAL EVIDENCE FOR DRS IN INFRAPOPLITEAL ARTERIES

The clinical utility of DRS in BTK interventions is increasingly supported by both early evidence and real-world outcomes. Compared to PTA, DRS have been associated with significantly fewer reinterventions, translating into improved patient quality of life and reduced health care resource utilization.[7]

A prospective single-arm study assessed the 5-year (2013-2018) results of an everolimus-eluting scaffold treatment for CLTI.[6] Included in the trial were 48 patients (55 limbs): 72.7% with CLTI and 27.3% with severe claudication. There was 45.8% mortality (22 patients) during a mean follow-up period of 35.2 ± 20.4 months, and there was no late or very late scaffold thrombosis. Clinical improvement was demonstrated in 90.9%, with a 100% limb salvage rate. Binary restenosis was detected in 15.5% (11/71) of scaffolds. At 60 months, rates of primary patency and freedom from clinically driven target lesion revascularization (CD-TLR) rates were 72.3% and 90.7% respectively.[6]

The LIFE-BTK trial (NCT04227899) further validated these findings, comparing the Esprit BTK everolimus-eluting scaffold (Abbott) to PTA in patients with CLTI.[7] At 1 year, the scaffold group achieved significantly higher composite efficacy (74% vs 44%; $P < .0001$) and fewer reinterventions, with no adverse effect on wound healing. At 2 years, the scaffold continued to show superior combined primary patency and limb salvage (61.5% vs 32.8%), while maintaining a comparable safety profile.[13] Cost-effectiveness analyses further supported economic value due to fewer repeat procedures.[14] Three-year data are anticipated in late 2025.

Several next-generation DRS platforms have since emerged. The MOTIV BTK study (NCT03987061) evaluated the Motiv sirolimus-eluting scaffold (Reva Medical) in 58 patients with BTK lesions ≤ 100 mm.[15] At 12 months, technical success was 99%, with 88% primary patency, 98.3% freedom from CD-TLR, and 97% limb salvage. At 3 years, results remained durable with 80% primary patency, 93% freedom from CD-TLR, and 95% limb salvage. Observed mortality (14%) was unrelated to the device.[16] A large multicenter, randomized trial evaluating this device is currently nearing enrollment completion (NCT05406622).

The RESOLV I first-in-human study (NCT04912323) investigated the Magnitude bioresorbable scaffold (R3 Vascular) in 30 patients with Rutherford class 3 to 5 BTK lesions.[17] At 6 months, angiographic primary patency was 100% for Rutherford class 3 and 4 lesions and 90% for Rutherford class 5 lesions. Lumen stenosis improved from a baseline mean of 78% to 20% to 29%, with 100% limb salvage and no major adverse events or perioperative deaths related to the device. These promising early findings support ongoing evaluation in the ELITE-BTK trial (NCT06071429), which recently commenced enrollment.

INSIGHTS INTO THE USE OF DRS

DRS offer several inherent advantages over PTA. Recent clinical data demonstrate superior patency and reduced need for reintervention compared to PTA.[7] Unlike metallic stents, DRS provide temporary scaffolding to address recoil and dissection without inducing chronic endothelial irritation. Once resorbed, they leave the vessel free of permanent implants, preserving options for future surgical or endovascular procedures and potentially restoring vasomotor function through vascular regeneration. In clinical practice, DRS should be the preferred endovascular strategy when long-term durability is a priority.

However, DRS have limitations. Lesions near the ankle joint are susceptible to mechanical stress and scaffold

deformation due to flexion and kinking. The performance of DRS in heavily calcified vessels remains uncertain. In cases where predilatation balloons cannot be fully expanded, DRS implantation may further compromise luminal integrity and should be avoided. Similarly, deploying DRS in a spot-stenting manner after long-segment angioplasty is not recommended, as outcomes are likely to mirror those of angioplasty alone rather than the high patency observed in trials such as LIFE-BTK, which mandated total lesion coverage. Bifurcation lesions also pose technical challenges, particularly regarding side-branch access and scaffold placement. We currently avoid these in our practice due to concerns around positioning accuracy and device deformation.

Barriers to broader adoption include the limited scaffold length, necessitating multiple implants for long chronic total occlusions and thus increasing procedural complexity and cost. Presently, treating lesions longer than 15 to 20 cm is impractical for most. Future advancements should focus on longer scaffold designs, improved flexibility, and cost reduction. Additional enhancements, such as radiopaque markers, thinner struts, self-expanding properties, and tapered geometries, would further optimize DRS performance in the long, diffuse, infrapopliteal lesions commonly encountered in clinical practice.

CONCLUSION

The advent of DRS marks a significant advancement in the endovascular management of BTK PAD, particularly in patients with CLTI. Clinical trials and real-world data consistently demonstrate that DRS offer superior vessel patency, reduced reintervention rates, and a favorable safety profile compared to conventional angioplasty. These devices provide temporary mechanical support, mitigate restenosis, and preserve future treatment options, positioning DRS as a compelling treatment modality for selected patients.

DRS are certainly ready for prime time, and they are here to stay. However, limitations exist, including challenges in treating certain lesion complexities, current device length constraints, and cost considerations. Continued technologic refinement and long-term data from ongoing trials will be critical in defining the broader role of DRS in clinical practice. ■

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Abigail L. Kleine
The Vascular Institute, POW
Sydney, Australia
Disclosures: None.

Ramon L. Varcoe, MBBS, MS, FRACS, PhD, MMed(ClinEpi)
The Vascular Institute, POW
Prince of Wales Hospital
University of New South Wales
Sydney, Australia
r.varcoe@unsw.edu.au
Disclosures: Consultant to Medtronic, Abbott, Philips, W.L. Gore, BD, Boston Scientific, R3 Medical, Vesteck, Nectero, InterVene, Surmodics, Endospan, Cook Medical, Concept Medical, and Inari Medical; declares equity in Provisio Medical and Vesteck.