Randomized Trials and Registries of Superficial Femoral Artery Stenting

The current data and future directions of SFA stenting technology.

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Endovascular treatment of superficial femoral artery (SFA) disease is increasingly common. Over the past decade, a number of new stent technologies have been developed that may offer new options for treatment and improved outcomes. This article reviews the current evidence for SFA stenting, with a focus on randomized trials and registries of nitinol self-expanding stents, drug-eluting stents, and covered stent grafts. We also highlight the limitations of the currently available data and future directions in SFA stent technology.

RANDOMIZED STUDIES OF NITINOL SELF-EXPANDING STENTS

The Vienna-ABSOLUTE trial was the first randomized study that showed a benefit of SFA stenting compared to provisional angioplasty.[1] The investigators used self-expanding nitinol stents (Dynalink or Absolute, Abbott Vascular, Santa Clara, CA). This trial enrolled patients with severe, lifestyle-limiting claudication, and approximately one-third of patients had chronic total occlusions of the SFA. At 12 months, assessment with duplex ultrasonography showed significantly lower rates of restenosis among patients who were randomized to stenting (37% vs 63%; $P = .01$). Angiography at 6 months postprocedure also confirmed lower restenosis rates with stenting, as determined both by intention-to-treat and on-treatment analyses. These results were sustained at 2-year follow-up.[2] The ASTRON trial of intermediate SFA lesions reported similar results in a multicenter study among lesions that were, on average, slightly shorter (mean, 98 vs 71 mm).[3]

Contemporaneous to the Vienna-ABSOLUTE study, the FAST trial randomized patients with shorter SFA lesions (mean length, 45 mm) to angioplasty or stenting with the Luminexx 3 stent (Bard Peripheral Vascular, Inc., Tempe, AZ).[4] The majority of patients in the trial had lifestyle-limiting claudication. Restenosis rates at 1 year were only 32% in the stenting group versus 39% in the angioplasty group. These comparisons were not statistically significant in both intention-to-treat and on-treatment analyses. This study was initially designed to detect a 20% difference in restenosis rates between the two treatment modalities; it was therefore underpowered for the unexpectedly low rates of restenosis with balloon angioplasty. These results have led to the recommendation that short SFA lesions can effectively be treated using a provisional balloon angioplasty approach with bailout stenting.

The RESILIENT trial randomized patients with claudication and SFA stenosis < 150 mm in length to balloon angioplasty or stenting with the self-expanding LifeStent (Edwards Lifesciences, Irvine, CA, acquired by Bard Peripheral Vascular, Inc).[5] Patients were randomized 2:1 to stenting. In the trial design, bailout stenting in the

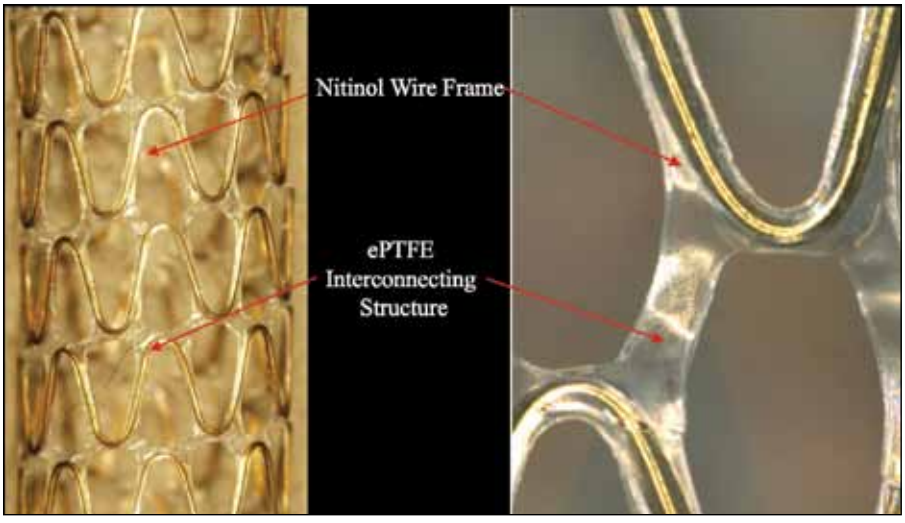

Figure 1. The Tigris stent has a nitinol wire frame and an ePTFE interconnecting structure. This stent design maximizes flexibility while minimizing stent elongation.

angioplasty group was treated as a target lesion revascularization (TLR). With this analysis, stenting was superior to angioplasty, with a primary patency rate of 81.3% for stenting versus 36.7% for angioplasty at 12 months. In an as-treated analysis in which provisional stenting was not counted as a treatment failure, stent placement remained associated with a 12-month primary patency rate of 80.4% versus 61.5% for balloon angioplasty (P = .03). Importantly, the stent fracture rate at 12 months was only 3.1% when assessed by dedicated x-ray. Although follow-up ultrasound was not mandated after 1 year, the 3-year follow-up of TLR confirmed the long-term benefit of primary stenting, with a freedom from TLR of 75% for stenting and 42% for balloon angioplasty.[6]

The Tigris stent (Gore & Associates, Flagstaff, AZ) is a next-generation stent with a nitinol wire frame and interconnecting expanded polytetrafluoroethylene (ePTFE) linking regions, thereby allowing greater flexibility but less elongation during deployment (Figure 1). The lumen of the stent is also lined with a covalently bonded, reduced-molecular-weight heparin that may lessen the risk of thrombus formation. The recently initiated TIGRIS trial will be the first randomized study to directly compare two nitinol stent platforms in the SFA. In this study, patients with claudication and SFA disease will be randomized in a 2:1 design to placement of either Tigris or LifeStent.

REGISTRIES OF NITINOL SELF-EXPANDING STENTS

Recent registries of second-generation nitinol stents with greater flexibility have also produced promising results in moderate-to-long SFA lesions. The EverFlex stent (ev3 Inc./Covidien, Plymouth, MN) is a nitinol stent with spiral-cell connections that may allow greater flexibility and reduce the incidence of stent fractures. Initial studies with this stent platform in the DURABILITY I study of 151 subjects with claudication showed freedom from restenosis of 91.3% and 71.2% at 6 and 12 months, respectively.[7] The recently presented DURABILITY II study found comparable rates of patency at 12 months, with a stent fracture rate of only 0.4%.[8]

The Complete SE stent (Medtronic, Inc., Minneapolis, MN) has an offset crown design that may minimize crown interaction while flexing, with associated kink resistance and flexibility. The recently presented 12-month results with this stent in intermediate-length SFA lesions also showed favorable primary patency rates of 73% and a TLR rate of only 9.4%.[9]

Although most studies of nitinol self-expanding stents have focused on short-to-medium–length stenosis, the majority of lesions in clinical practice are often considerably longer. The Supera stent (Idev Technologies, Webster, TX) is a self-expanding nitinol stent with six pairs of interwoven nitinol wires in a closed-cell configuration (Figure 2). These design features may contribute to increased radial strength and stronger crush resistance when compared to other nitinol stents. In a recently published registry of 107 patients with complex SFA disease, freedom from restenosis by duplex ultrasonography was 85% at 12 months and 76% at 24 months.10 Among the 91 patients with follow-up x-rays, there were no stent fractures. These data suggest that newer nitinol stent designs may be associated with significantly lower rates of stent fracture, with associated lower rates of restenosis and stent failure. The SUPERB registry is further studying the use of this stent in the US.

DRUG-ELUTING STENTS

Early studies of drug-eluting stents in the SFA failed to show any clinical benefit of sirolimus-eluting or everolimus-eluting platforms compared to bare-nitinol stents.[11,12] Enthusiasm for drug-eluting stents in the SFA has resurged with the use of a second-generation stent platform linked to a polymer-free, paclitaxel-eluting system. The Zilver PTX paclitaxel-eluting stent (Cook Medical, Bloomington, IN) was recently studied in a prospective, randomized

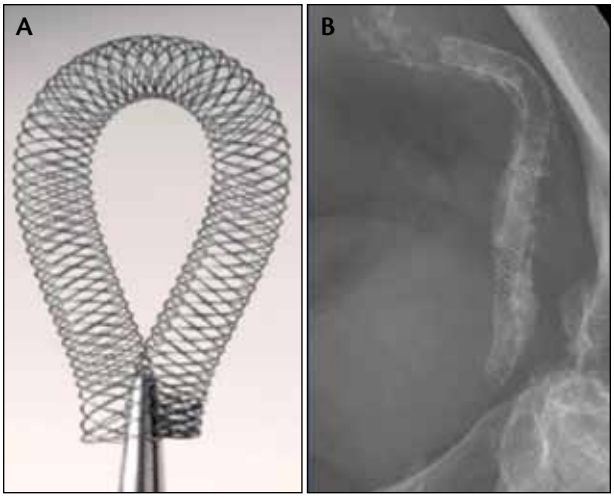

Figure 2. The Supera stent is composed of six pairs of interwoven nitinol wires in a closed-cell design. The stent is extremely flexible, yet resists deformation (A). A study of Supera stents in the distal femoral and popliteal arteries found no evidence of stent fracture at 1 year, despite deployment at sites of significant flexion (B).

trial of 474 patients with claudication.[13] Because balloon angioplasty often fails acutely, the study had a second randomization step in the case of failed angioplasty, in which patients were again randomized to a drug-eluting or bare-metal stent. Primary patency was superior at 12 months for patients randomized to the drug-eluting stent in both the initial treatment and second randomization group. The prevalence of stent fracture rates at 12 months was only 0.4%. Recently presented 3-year TLR rates continued to favor the drug-eluting stent arm over the percutaneous transluminal angioplasty plus bare-metal stent arm (83% vs 70.2%, respectively).[14] These encouraging results suggest that drug-eluting stents may have new applications in SFA disease, and the Zilver PTX is currently under review by the FDA; in October 2011, an FDA advisory panel recommended approval.

COVERED STENTS

Covered stents represent an alternative approach to endovascular treatment of SFA lesions. This approach is analogous to a surgical bypass, in that the entire region of disease is excluded with a graft. The Viabahn covered stent graft (Gore & Associates) consists of a nitinol stent frame lined internally with ePTFE. The device has evolved over time, with the addition of a heparin bioactive surface and, more recently, a contoured proximal edge. Results with the Viabahn stent graft have been studied in comparison to traditional surgical bypass, in relation to nitinol self-expanding stents, and in very long femoropopliteal lesions.

An early study of patients with SFA stenosis and symptomatic claudication randomized patients to Viabahn stent grafting or surgical bypass.[15] Patency rates were similar between the two groups out to 4-year follow-up. The VIBRANT trial is a multicenter, randomized trial comparing Viabahn stent grafting to uncovered nitinol stent placement in SFA lesions longer than 80 mm. This study used an older version of the Viabahn stent with a heparin-coated surface but without a contoured edge. Interim analysis of the 1-year results showed comparable outcomes between the two approaches, and final analysis of the 3-year outcomes is currently underway.[16]

The VIPER registry studied the use of newer-generation Viabahn stent grafts with a contoured edge in long femoropopliteal lesions (mean length, 19 cm). At 1 year, primary patency was 74%, and assisted patency was 87%. A secondary analysis of device oversizing found that primary patency increased to 87% if the device was oversized < 20%.[17] Overall patency rates were similar for lesions longer than 200 mm, suggesting that Viabahn graft patency may not be as dependent on lesion length. The VIASTAR trial is a European-based randomized study of Viabahn versus bare-nitinol stent placement. Preliminary 12-month results from this study suggest restenosis rates of 27% with Viabahn stent grafting compared to 59% for bare-nitinol stents.[18]

LIMITATIONS AND FUTURE DIRECTIONS

Significant progress has been made since the first studies of stenting versus balloon angioplasty for SFA disease. Newer-generation stents have increased flexibility and yielded very low fracture rates, and novel designs may continue to address the anatomic variables specific to the SFA. Recent results with the Zilver PTX paclitaxel-eluting stent may also provide a new approach to the arsenal of SFA disease treatment.

Although these results are encouraging, significant room for improvement remains in the treatment of SFA disease, and data are lacking in important clinical categories. The majority of published studies are limited to patients with claudication and short SFA lesions. In clinical practice, a significant proportion of patients with SFA disease may have critical limb ischemia and longer SFA lesions. Despite the improvements in stent design, overall restenosis rates remain unacceptably high, and the currently available treatments for femoropopliteal in-stent restenosis have significant limitations.[19] New studies comparing the relative efficacy of stenting, drug-eluting balloons, and other approaches will be necessary to determine the best treatment approaches in this challenging patient population. ■

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