COMPLETE SE and Other SFA Trials

A look at the ongoing trials of self-expanding stents in the superficial femoral artery.

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Endovascular treatment of peripheral artery disease (PAD) involving the superficial femoral artery (SFA) has evolved with increasing physician experience and improving technologies. Balloon angioplasty alone has excellent initial technical success rates of more than 95%, with a low risk of complications.[1] However, restenosis and clinical failure can be high, with restenosis rates in treated segments ranging from 40% to 60%.[1-3] With long-segment disease, calcification, total occlusions, and poor runoff, results after balloon angioplasty are suboptimal. Stenting has been promulgated as a treatment option, but stents placed in the SFA are subject to complex and varied mechanical stresses, and stent fractures can occur. Concerns about stent fracture and restenosis in the SFA have made the use of self-expanding stents in the SFA controversial. Despite these difficulties, there has been considerable advancement in the development of stents for the SFA.

Schillinger et al performed a randomized controlled trial comparing the use of self-expanding stents versus balloon angioplasty in 104 patients with severe claudication or critical limb ischemia with disease of the SFA.[4] In this study, these investigators from Austria used nitinol self-expanding Dynalink or Absolute stents from Abbott Vascular (Santa Clara, CA). The investigators showed by duplex ultrasound that stenting was associated with significantly lower rates of restenosis at 12 months (37% vs 63%, $P = .01$). This was associated with significantly improved walking distance as well. On the other hand, the FAST trial compared the use of the Luminexx nitinol self-expanding stent (Bard Peripheral Vascular, Tempe, AZ) to balloon angioplasty for shorter SFA lesions and did not demonstrate any reduction in restenosis with stenting (31.7% vs 38.6%, $P = .38$).[5] As such, there remains considerable debate regarding the long-term benefit of routine use of stents in the SFA.

Currently in the United States, the Food and Drug Administration has approved only three self-expanding stents for use in the SFA. These are the IntraCoil (ev3 Inc., Plymouth, MN), the Viabahn (W. L. Gore & Associates, Flagstaff, AZ), and the LifeStent (Bard Peripheral Vascular). Of these, only the Viabahn and the LifeStent are commercially available.

Figure 1. The Complete SE stent and delivery system.

Trials to evaluate the use of newer self-expanding stents in the SFA are currently underway in the United States; some of these trials are already completed with preliminary results. These include the Zilver PTX trial (Zilver PTX peripheral drug-eluting self-expanding stent vs Zilver bare-metal stent, Cook Medical, Bloomington, IN)[6] and the RESILIENT trial (LifeStent, Bard Peripheral Vascular).[7] Other stent trials are ongoing, and they are expected to further improve our understanding of the optimal endovascular treatment of SFA disease. At the same time, the outcomes of these studies will provide the basis for the regulatory approval of the respective stents. These studies include the COMPLETE SE (Medtronic Inc., Minneapolis, MN), STROLL, (SMART stent, Cordis Corporation, Bridgewater, NJ), DURABILITY II (Protégé EverFlex stent, ev3 Inc.), and SUPERB (Supera stent, IDev Technologies, Inc., Houston, TX) trials.

For the current US SFA stents trials, the study population includes patients with moderate-to-severe claudication and rest pain (Rutherford category 2–4). The study designs are prospective, nonrandomized, single-arm registries designed to determine efficacy (primary patency)

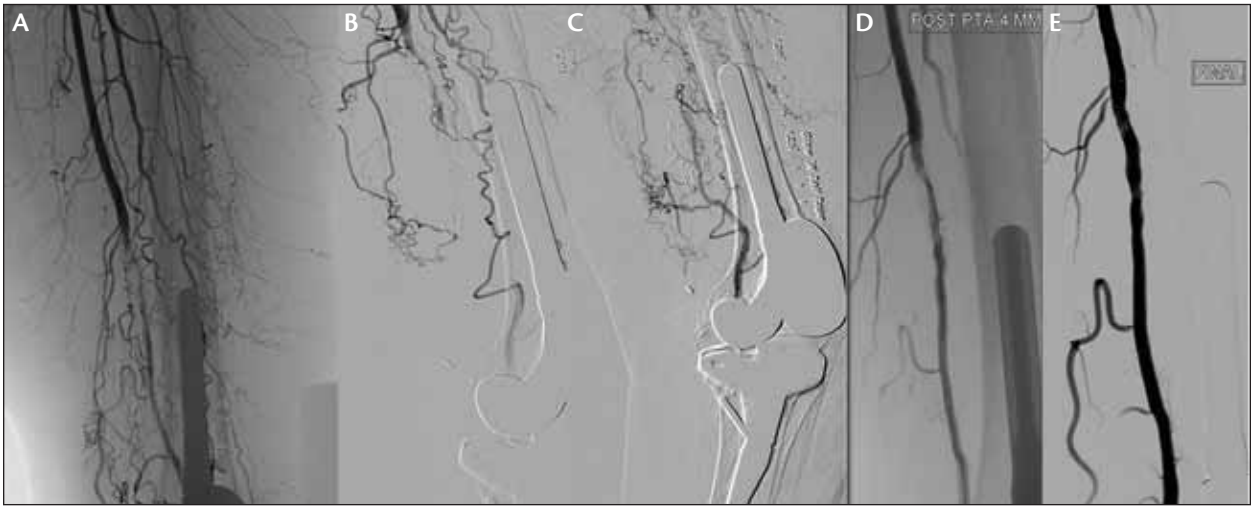

Figure 2. Preprocedure angiogram with occlusion in the SFA (A). Delayed filling of the SFA from collaterals distal to the occlusion (B, C). Angiographic results after balloon dilatation (D). Final angiographic results after implantation of the Complete SE stent (E).

and safety (major adverse events [MAEs]). Many of the inclusion/exclusion criteria and protocol features are similar among studies. In most of these studies, lesion length is usually limited to no more than 140 mm in order to allow for use of a single 150-mm stent. In this brief review, we will highlight the COMPLETE SE SFA trial as a typical study of self-expanding stents in the SFA and comment on the other ongoing trials in the United States.

COMPLETE SE SFA STUDY

The use of the Medtronic Complete self-expanding (SE) stent (Figure 1) in the SFA is currently under investigation in the COMPLETE SE SFA study. This is a prospective, multicenter, single-arm study, the aim of which is to evaluate the safety and efficacy of the Complete SE SFA stent system in the treatment of de novo and/or restenotic lesions or occlusions in the SFA and/or proximal popliteal artery in subjects with symptomatic PAD. The study is currently enrolling patients, and enrollment is expected to be complete by June 2010.

Design

The study will include up to 30 sites in the United States and Europe, with an estimated target enrollment of 196 patients. Patients may be included if they have symptomatic PAD (Rutherford class 2–4) with a lesion ≥ 50%, a target vessel reference diameter ≥ 4 mm and ≤ 7 mm, a total lesion length ≥ 40 mm and ≤ 140 mm, and adequate distal runoff to the foot (at least 1 patent runoff vessel). Lesions must be located above the knee and be amenable to percutaneous angioplasty and stenting. The COMPLETE SE SFA study will have core laboratory evaluation. Angiograms will be evaluated by an independent angiographic core lab (Brigham and Women's Angiographic Core Lab, Boston, MA), and duplex ultrasound and x-rays will be evaluated by another independent core lab (VasCore at Massachusetts General Hospital, Boston, MA).

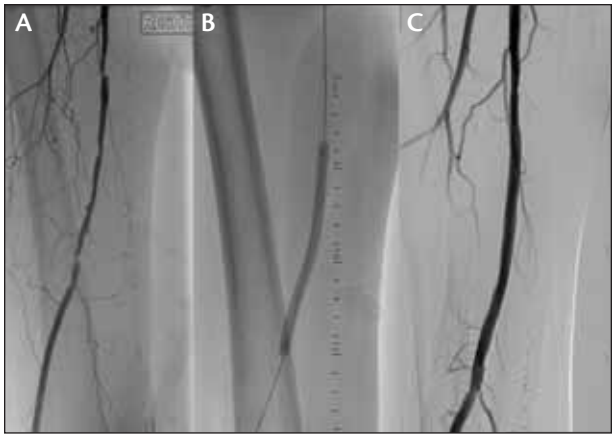

Figure 3. Preprocedure angiogram with severe stenosis in the SFA (A). Implanted Complete SE stent with postdilation with a balloon (B). Final result (C).

Primary Endpoints

Analysis of the data will be based on intention-to-treat. The primary efficacy endpoint is defined as the primary patency rate at 12 months. Primary patency, in turn, is defined as uninterrupted patency with no procedures performed on or at the margins of the treated segment, with no restenosis ≥ 50% as documented by peak systolic veloc-

SECONDARY ENDPOINTS

1. MAE rate at 30 days and 6, 24, and 36 months
2. Acute success
3. Change in quality of life, defined as
   a. Improvement in Rutherford class by ≥ 1 category at 12 months from preprocedure; or
   b. Increase in ABI or toe-brachial index ≥ 0.15 at 12 months from preprocedure; or
   c. Decline in Rutherford class by ≥ 1 category at 30 days when compared to preprocedure
4. Assisted primary patency at 12 months, defined as vessel patency resulting from any procedure performed in the treated segment before thrombosis that might prevent eventual failure
5. Secondary patency at 12 months, defined as vessel patency resulting from any procedure that restores patency after thrombosis
6. Stent integrity at 12, 24, and 36 months

ity ratio ≥ 2 as assessed by duplex ultrasound. The primary safety endpoint is defined as the MAE rate at 12 months. MAEs are defined as device and/or procedure-related death (or any death occurring after the procedure through day 30), target limb loss, and clinically driven target lesion or target vessel revascularization. See *Secondary Endpoints* sidebar for a list of the secondary endpoints.

Study subjects must meet study inclusion and exclusion criteria, of which the key ones are listed in the *Inclusion/Exclusion Criteria* sidebar.

OTHER TRIALS

SUPERB

The SUPERB trial (Comparison of the Supera Peripheral System to a Performance Goal Derived from Balloon Angioplasty Clinical Trials in the SFA) is a prospective, single-arm trial of 258 subjects at up to 40 sites in the United States. It is a nonrandomized, open-label, safety and efficacy study that is currently enrolling. The main objective of this study is to demonstrate the safety and effectiveness of the IDev Supera nitinol stent system in treating subjects with obstructive SFA disease. The primary endpoint will be the primary patency of the SFA evaluated at 12 months. This outcome will be compared to a performance goal based on clinical trials of percutaneous transluminal angioplasty alone.

DURABILITY II

DURABILITY II is a multicenter, nonrandomized, open-label, safety and efficacy study that examines the use of

INCLUSION/EXCLUSION CRITERIA

Inclusion Criteria

1. The subject has an occlusion or de novo and/or restenotic (nonstented) SFA/proximal popliteal artery lesion ≥ 50%
2. The target lesion is located at least 1 cm distal to the takeoff of the profunda femoris artery and at least 3 cm proximal to the distal cortical margin of the intercondylar femoral epiphysis
3. The target vessel reference diameter is ≥ 4 mm and ≤ 7 mm
4. The total lesion length is ≥ 40 mm and ≤ 140 mm
5. If two lesions will be treated, the combined lesion length must be ≤ 140 mm, the lesions must be in the same limb, and the treatment must not require more than 160 mm combined total stent length
6. The subject is symptomatic with Rutherford classification 2 through 4
7. The subject has an ABI ≤ 0.9, or if ABI is not feasible due to medical condition (eg, noncompressible vessels), a toe-brachial index ≤ 0.8
8. The subject has adequate distal runoff to the ankle in the target limb (defined as having at least one patent calf vessel < 50% stenosed)
9. The subject must be a suitable candidate for emergent femoropopliteal bypass surgery

Exclusion Criteria

1. The subject has any condition that precludes safe access with percutaneous transluminal angioplasty devices, such as excessive peripheral artery disease, acute thrombus in the target lesion/vessel, or a target lesion/vessel that is excessively tortuous or calcified
2. The subject has a nontarget lesion that requires intervention during the index procedure or within 30 days before or after the index procedure
3. Previous treatment to the target lesion within the 3 months before enrollment
4. Any history of femoral-popliteal bypass surgery in the target vessel
5. The target lesion was previously stented
6. The target lesion is located within an aneurysm or associated with an aneurysm in the vessel segment either proximal or distal to the target lesion
7. The target lesion requires treatment other than standard percutaneous transluminal angioplasty before stent placement (eg, cutting balloons and laser atherectomy)

the Protégé Everflex nitinol stent in the endovascular treatment of symptomatic SFA or proximal popliteal artery disease. The study design is similar to the COMPLETE SE trial and is currently recruiting. However, an additional exclusion criterion is the presence of symptomatic contralateral disease. The primary efficacy outcome is primary patency at 1 year. The primary safety outcome is MAE at 30 days. For more on this trial, see page 58.

STROLL

The STROLL trial is a multicenter, nonrandomized, single-arm, prospective trial evaluating the safety and effectiveness of the SMART nitinol stent in approximately 250 patients with obstructive SFA disease. The primary efficacy outcome is primary patency at 12 months, defined as no significant reduction of flow detectable by duplex ultrasound through the index lesion. The primary safety outcome is 30-day freedom from all causes of death, index limb amputation, and target lesion revascularization. It is currently enrolling subjects. For more on STROLL, see page 63.

VIPER

The Viabahn endoprosthesis is a self-expanding covered stent and is already approved by the Food and Drug Administration for use. The VIPER trial is a nonrandomized, open-label, single-group, postmarketing study of the updated Gore Viabahn endoprosthesis. The most recent iteration of the device comes heparin-bonded and has a new proximal modification with a lower-profile streamlined delivery system. The primary outcome is primary patency at 12 months, defined as no evidence of restenosis or occlusion within the originally treated lesion based on color-coded duplex sonography. See page 66 for a closer look at the VIPER trial.

COMPLETE SE CASE STUDIES

Case 1

A 63-year-old woman with diabetes and hyperlipidemia presented with severe claudication of her left leg. Noninvasive studies showed an ankle-brachial index (ABI) of 0.53, and computed tomographic angiography showed occlusion in her left SFA, which was confirmed on angiography. This was successfully treated with balloon angioplasty and stenting as part of the COMPLETE SE study (Figure 2).

Case 2

A 54-year-old man with hypertension, hyperlipidemia, diabetes mellitus, and tobacco use presented with right lower extremity lifestyle-limiting claudication. His physical examination showed a strong femoral pulse but absent right popliteal, dorsalis pedis, and posterior tibial pulses. The resting right ABI was 0.9, and with exercise, this decreased to 0.3. Computed tomographic angiography showed focal severe stenosis of the right mid SFA. He then underwent diagnostic angiography, which showed severe stenosis of the right SFA. This was successfully treated with balloon angioplasty and stenting with a Complete SE stent as shown in Figure 3.

CONCLUSION

There are conflicting data regarding the benefits of femoropopliteal stenting. Despite the large amount of SFA stenting that has been performed in recent years, there are currently three stents that are FDA approved for use in the SFA. Of these, only the LifeStent and the Viabahn are commercially available. Studies such as the COMPLETE SE, SUPERB, Durability II, and STROLL trials are currently in progress to examine the use of other self-expanding stent platforms for use in the SFA for patients with intermittent claudication and rest pain. These trials will provide additional data on the safety and efficacy of these stents in the SFA and will form the basis for regulatory approval for additional devices. ■

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