



H.F. El-Sayed, M.D.

ENDOVASCULAR TECHNIQUES IN LIMB SALVAGE: STENTS

Hosam F. El-Sayed, M.D.

Methodist DeBakey Heart & Vascular Center, The Methodist Hospital, Houston, Texas

Abstract

In patients with critical limb ischemia, the first-line approach for limb salvage has shifted over the past decade from bypass surgery to endovascular intervention. Stenting for the treatment of lower-extremity arterial occlusive disease is an important tool and continues to evolve, with new stent designs and technologies that have been developed to provide superior patency rates and limb salvage. In this article, we discuss the role of peripheral stenting in the treatment of patients with critical limb ischemia, including a review of the relevant current literature and the future directions of such interventions.

Introduction

Critical limb ischemia (CLI), manifested by ischemic rest pain or tissue loss in the form of nonhealing wounds or gangrene, constitutes a major clinical problem that results in significant healthcare and economic burdens to the community. Currently, infrainguinal bypass surgery and percutaneous endovascular interventions are the two approaches available to restore blood flow to the foot. During the past decade, however, the primary approach to limb salvage has transitioned from bypass surgery to endovascular intervention.¹ This article discusses the role of peripheral stenting in the treatment of CLI and reviews the relevant current literature and future direction of such interventions.

Principles of Stenting

The term “stent” is derived from Charles Stent (1807-1885), an English dentist who applied the term to a dental apparatus used for making molds.² The concept of vascular stents was first described in 1912 by Alexis Carrel. However, it was not until 1964 that Charles Dotter revisited the concept, describing the need to leave an endoluminal splint after angioplasty to prevent early failure due to recoil and dissection.³ The age of metallic stent therapy for cardiovascular disease officially began in the United States in 1993, when the US Food and Drug Administration approved the Gianturco-Roubin stent for coronary interventions.⁴ More recent clinical practice has been characterized by an expanded variety of available stents and additional indications for stent deployment.

Percutaneous endovascular intervention for CLI is intended to improve perfusion of the affected limb by restoring flow in the vessels occluded by atherosclerotic disease. This goal is achieved by first crossing the affected lesion, then maintaining wire access in the true lumen of the vessel distally, and lastly treating the occlusion through any one or combination of three available endovascular interventions: balloon angioplasty, stenting, and/or atherectomy. The principle of balloon angioplasty and its different modalities is to disrupt the plaque, thus creating a controlled dissection and restoring the vessel lumen. However, the use of balloon angioplasty alone cannot address the problem of elastic recoil of the lesion. Furthermore, balloon angioplasty can result in uncontrolled dissections, which create flow-limiting intimal flaps

in the treated vessels that can, in turn, lead to technical failure or early loss of patency. In these situations, the use of stents becomes a reasonable method to repair the flow-limiting dissection or avoid the elastic recoil (Figure 1). The other problem inherent in all endovascular interventions is the relatively low patency rates compared to those for standard open surgical bypass. Multiple studies have demonstrated that the one-year restenosis rate after balloon angioplasty alone is 40-60%.⁵ The patency rate also is lower when dealing with longer lesions, with 1-year rates of restenosis exceeding the 70% range for lesions longer than 100 mm.⁶ A promise of stents is that they can improve patency rates when used as part of endovascular therapy (Figure 2).

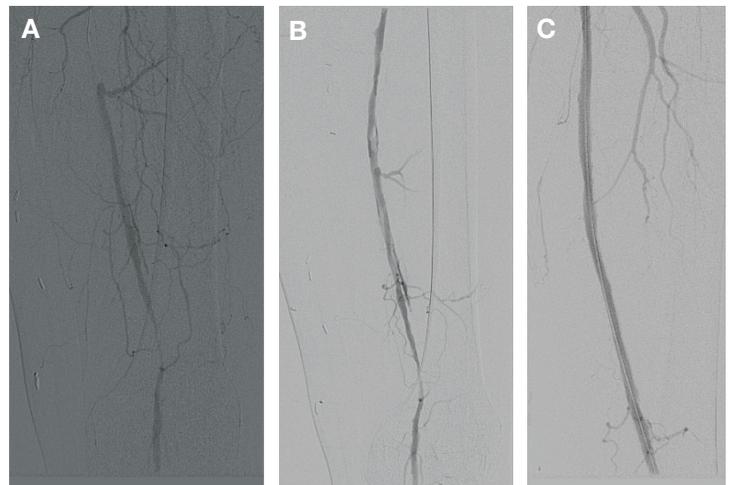


Figure 1. Stent use for flow-limiting dissection after balloon angioplasty. (A) Superficial femoral artery disease; (B) unacceptable result following balloon angioplasty with flow-limiting dissection; (C) stenting using 6 mm nitinol stent with excellent hemodynamic result.

The Biologic Response to Stents

The biologic response to vascular stenting starts immediately after the stent has been deployed. Upon deployment, the electropositively charged stent struts attract the negatively charged circulating proteins and platelets. This creates a thin layer of

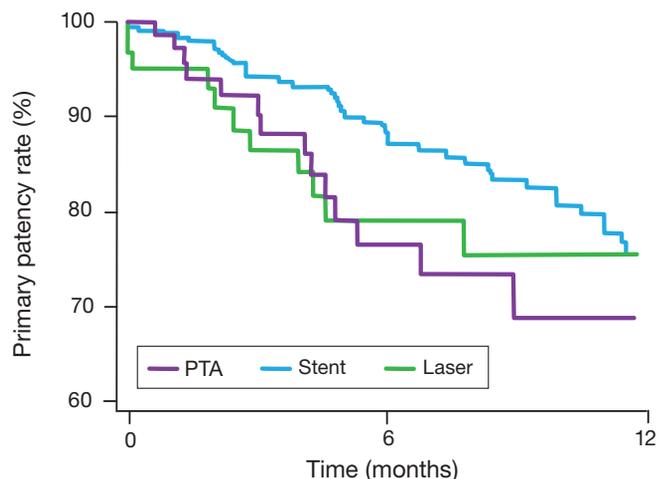


Figure 2. Primary patency of percutaneous interventions using percutaneous transluminal angioplasty (PTA), PTA with stenting (Stent), and laser-based intervention strategies (Laser). Redrawn after Bosiers et al.¹³

randomly oriented fibrinogen strands and platelets that neutralize the stent surface.^{7,8} Endothelial cells from the surrounding intima then start migrating over the thin protein layer on the stent struts in an attempt to facilitate full endothelialization of the stent and thus minimize thrombosis.⁹ Meanwhile, due to the effects of the activated platelets, inflammatory cells are recruited to platelet-rich thrombi. This is followed by migration and proliferation of smooth muscle cells in response to cytokines, mitogens, and growth factors. The clinical outcome associated with this process is in-stent restenosis.

Multiple techniques have been developed to help prevent or slow the process of in-stent restenosis. One approach is pharmacologic manipulation of platelet function with antiplatelet medications, including double antiplatelet coverage. Other approaches have included changes in the stent design (including cell design), material choice, and radial force characteristics, and the development of covered stents to prevent ingrowth of the neointima through the stent cells. Another promising modification is the drug-eluting stent that delivers antiproliferative agents into the arterial wall to prevent hyperproliferation during the healing process. All of these techniques have been used with varying degrees of success in conjunction with lower-extremity stenting.

Stent Use in the Lower Extremities

For many years, arterial stents have been used in an attempt to improve the outcome of endovascular interventions for the lower extremities.¹⁰ The initial reports evaluated the use of balloon-expandable stents compared with angioplasty alone.¹¹ Those reports found that there is no difference in 1- and 2-year angiographically determined patency rates between these groups. Since then, use of nitinol stents has expanded with somewhat conflicting results, although there is evidence of the beneficial effect of these stents, especially in long lesions.^{6,12} Furthermore, many new nitinol designs have become available in the past few years. In fact, multiple randomized trials have illustrated the potential benefits of stenting in the lower extremity, especially in the femoropopliteal segment, compared to angioplasty alone. There also have been isolated reports of stent use in the infrapopliteal segment, especially with the development of the drug-eluting stent technology; however, the experience of stent use in that segment is still limited.¹³

More recently, covered stents (stent grafts), namely the VIABAHN[®] stent (W.L. Gore & Associates, Inc., Flagstaff, AR), have been used successfully in the superficial femoral artery to address in-stent restenosis due to the accumulation of cells and ground substance (neo-intima) through the stent interstices.¹⁴ The use of covered stents, however, does not address the risk of edge stenosis that appears on both ends of the stent, the so-called candy wrapper stenosis.¹⁵ Also, these stents have the potential to cover important collaterals in the treated segment compared to bare metal stents, which tend to preserve such collaterals. This difference in collateral preservation may be an important factor in the degree of ischemia the limb suffers in cases of stent occlusion.

Since its success in the coronary circulation, the technology of drug-eluting stents has been developing rapidly over the past few years.^{16,17} The application of a drug coating on a stent surface inhibits the inflammatory response and smooth muscle cell proliferation in the vessel wall and delays the process of intimal hyperplasia. The use of these drug coatings for the treatment of femoropopliteal lesions has been tested in multiple studies, with promising results.¹⁸

As the permanence of an artificial stent implant is thought to be the potential trigger for late restenosis, stenting technology has moved towards the development of temporary implants composed of biocompatible materials that mechanically support the vessel during the high-risk period for recoil and then completely degrade in the long term.¹⁹ Most of the available work on this technology has been performed in the coronary circulation; however, recent reports on the use of this new technology in the lower extremity below the knee have emerged.¹⁹⁻²¹ So far, the available evidence suggests that although the technology has been proven safe for use in that vascular bed, restenosis rates are significantly higher than those for bare metal stents and drug-eluting stents.^{19,22,23}

Current Literature Review

The use of stents for lower-extremity revascularization is usually limited to the femoropopliteal segment. While use in the infrapopliteal segment is developing, the available literature describing this revascularization approach is limited.

Stent Use for the Femoropopliteal Segment

The stents that are used within the femoropopliteal segment currently include nitinol self-expanding bare metal stents, VIABAHN covered stents, and the newly introduced drug-eluting stents. Multiple published studies have examined the use of each of these stent options in that segment.

The nitinol bare metal stent is the most commonly used and extensively studied device in the femoropopliteal segment. The ABSOLUTE trial was the first randomized trial to compare balloon angioplasty and nitinol stenting of the superficial femoral artery (SFA).⁶ The trial randomly assigned 104 patients to primary stenting or balloon angioplasty alone with secondary stenting for suboptimal results. At 6 months, the rate of restenosis was 24% in the stent group and 43% in the angioplasty group, a statistically significant difference ($P = .05$). At 12 months, the difference was more significant, with a restenosis rate of 37% in the stented group and 63% in the angioplasty group ($P = .01$). The investigators concluded that primary implantation of self-expanding nitinol stents for the treatment of SFA lesions was associated with superior anatomical and clinical intermediate-term results compared to the recommended approach of balloon angioplasty with optional secondary stenting (Figure 3).⁶

Similar to the ABSOLUTE trial, the RESILIENT trial was a multicenter randomized trial that compared nitinol bare metal

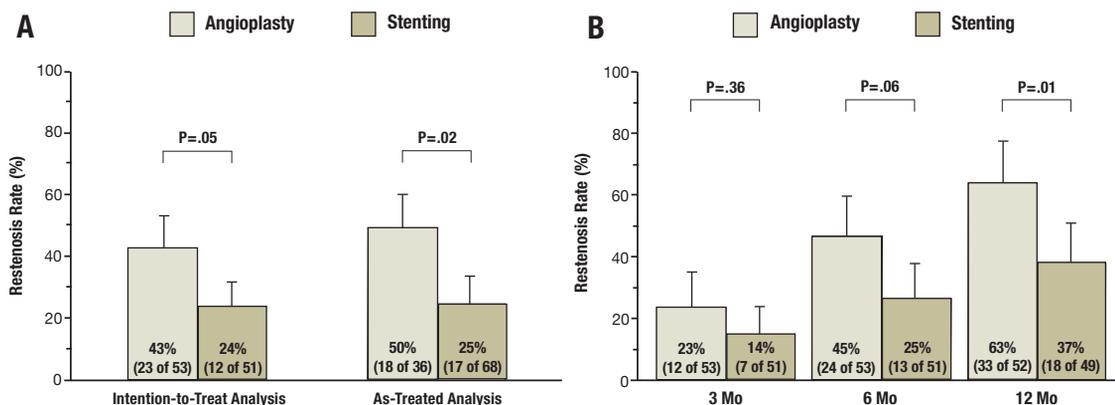


Figure 3. (A) Rates of restenosis on angiography and (B) duplex ultrasound. Redrawn after Schillinger et al.⁶

stents with balloon angioplasty for moderate-length lesions (mean of 62 mm) in the SFA and popliteal artery.²⁴ In the study, 206 patients from 24 centers in the United States and Europe were randomized to primary nitinol stenting versus balloon angioplasty alone, with bailout stenting for suboptimal results that occurred in 40% of patients in the angioplasty group. At 12 months, freedom from target lesion revascularization was 87% for the stent group compared with 45% for the angioplasty group ($P < .0001$).

The DURABILITY I study was a nonrandomized prospective multicenter study evaluating the long-term efficacy and integrity of nitinol stent implantation in longer SFA lesions with a mean length of 96 mm.²⁵ A total of 151 patients from 12 centers in Europe were treated using the nitinol PROTÉGÉ® EverFlex™ Self-Expanding Stent (ev3 Inc., Plymouth, Minnesota). The rates for freedom from >50% restenosis at 6 and 12 months were 91% and 72%, respectively, which is significantly higher than the literature restenosis rates with angioplasty alone.

One frequently noted problem associated with nitinol stent use in the femoropopliteal segment is that of stent fracture. Stent fractures have been recognized with all available nitinol stents in varying percentages. Stent type is a major factor associated with the risk of stent fracture, ranging from 2% in some stents to 50% in others; this indicates that stent design may substantially influence the likelihood of fractures.²⁶ The length of the stented segment also has been identified as a key determinant of material fatigue and subsequent fracture due to its presence in the hostile femoropopliteal segment environment, with extensive mechanical stresses involved (Figure 4).²⁶⁻²⁸ The relationship between stent

fracture and restenosis rates has been inconsistent. Some studies reported that the presence of stent fractures influenced restenosis rates at a statistically significant level, while other studies did not identify a relationship between the two.^{24, 26}

Use of covered stents in the femoropopliteal segment also has been studied. The VIABAHN covered stent graft has been compared to both prosthetic bypass and bare metal nitinol stents and evaluated for the treatment of very long lesions in the femoropopliteal segment. In a randomized prospective study, McQuade et al. compared the use of the VIABAHN covered stent to prosthetic femoralpopliteal bypass in the treatment of SFA occlusive disease.²⁹ One hundred limbs in 86 patients were randomized into one of two treatment groups: percutaneous treatment with angioplasty and placement of one or more stent grafts, versus a surgical group with a femoral to above-knee popliteal artery bypass using synthetic conduit. Patients were followed for 48 months. The primary and secondary patency rates at 12, 24, 36, and 48 months were not statistically different between the two groups. The authors noted that use of this technique might offer an alternative to treatment of the SFA segment when prosthetic bypass is being considered or when autologous conduit is unavailable.

The VIBRANT trial is a multicenter randomized trial comparing VIABAHN stent grafting to uncovered nitinol stent placement in the SFA for lesions longer than 80 mm. 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.³⁰ The VIASTAR trial is a European-based study similar to the VIBRANT in the United States. Preliminary 1-year results suggest a restenosis rate of 27% using the VIABAHN stent compared to 59% for bare nitinol stents.³¹

The VIPER registry studied the use of the newer generation of VIABAHN covered stents for the treatment of SFA lesions with a mean length of 19 cm. The 1-year primary and assisted patency was 74% and 87%, respectively. Additionally, the patency rates were similar for lesions longer than 20 cm, suggesting that the VIABAHN covered stent patency may not be as dependent on lesion length.³²

Since drug-eluting stents with active stent coatings have proven beneficial in the treatment of coronary artery disease, the applicability of these drug coatings to the treatment of femoropopliteal lesions has also been tested.¹⁸ The SIROCCO (sirolimus-coated cordis self-expandable stent) study was the first randomized trial to publish results on the use of drug-eluting stents for treatment of these lesions. The trial failed to prove superiority

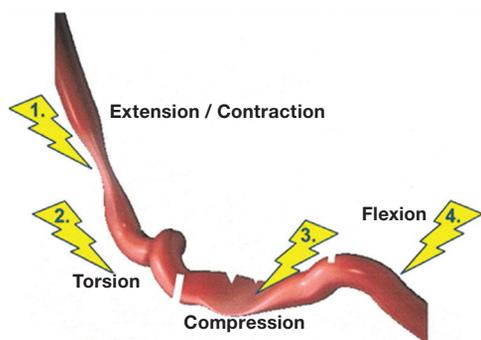


Figure 4. Forces affecting the superficial femoral artery creating a hostile environment to stents placed in the femoropopliteal segment. Reprinted from Machan²⁸ with permission from Elsevier

of the drug-eluting stent over bare metal stents in the SFA.^{33,34} However, the 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[®] Drug-Eluting Stent (Cook Medical, Inc., Bloomington, Indiana) study is composed of two components. The first is a randomized multicenter trial in the United States, Germany, and Japan with two levels of randomization. The first level randomized patients with SFA lesions up to 14 cm in length to Zilver PTX stenting or balloon angioplasty alone. The second level of randomization addressed those patients with failed primary balloon angioplasty; this group was randomized to receiving either Zilver PTX or Zilver bare metal stents. The second component of the study is a registry of 794 patients treated using Zilver PTX for lesions of the SFA up to 28 cm in length.¹⁸ Collectively, there were 1034 total patients treated with the Zilver PTX stent. One-year results for both the single-arm study and the randomized study were published in 2011.^{35,36} In the randomized trial, primary patency in the Zilver PTX group was significantly higher than the primary angioplasty group (83% versus 32%; $P < .001$). In the secondary randomized group, the Zilver PTX-treated patients showed significantly superior primary patency compared to the bare metal stent group (89% versus 73%; $P = .01$). Two-year results for primary patency in the Zilver PTX and bare metal stent groups are shown in Figure 5. The recent 3-year target lesion revascularization rates continue to favor the drug-eluting stent arm over the angioplasty plus bare-metal stent arm (83% versus 70%, respectively).³⁷ These encouraging results suggest that drug-eluting stents may have new applications in SFA disease. In October 2011, an FDA advisory panel recommended approval for their use in treating femoropopliteal lesions.

Stent Use for the Infragenicular Segment

The role of stenting in infragenicular vessels is still debated, with only a few small studies available despite introduction over 15 years ago.³⁸ A collaborative systematic review and meta-analysis of clinical studies focusing on below-the-knee stenting in patients with CLI has been published on 640 patients.³⁹ These were studies reporting percutaneous transluminal angioplasty (PTA) with stent implantation in the tibial arteries in at least 5 patients and at least 1 month follow-up. Of these patients, 232 were treated with

balloon-expandable bare metal stents, 116 with self-expanding bare metal stents, and 272 with drug-eluting stents. In addition, 20 patients were treated using absorbable metal stents.

Pooled analysis revealed that 12-month primary patency was 79%, secondary patency was 92%, and the limb salvage rate was 96%. Head-to-head comparison showed that balloon-expandable bare metal stents reported results similar to those of self-expanding bare metal stents. Conversely, studies showed that sirolimus drug-eluting stents had better outcomes in terms of primary patency compared to both bare metal and paclitaxel drug-eluting stents. At the end of the analysis, the authors recommended that percutaneous infragenicular stent implantation after failed or unsuccessful angioplasty is associated with favorable results in patients with CLI.³⁹

Summary

Stents have become an important tool in the treatment of lower-extremity arterial occlusive disease. This endovascular approach continues to evolve as new stent designs and technologies have been developed to provide superior patency rates and limb salvage. More studies are needed to determine the best candidates for stent use and to define the optimum role of stenting in the treatment of lower-extremity critical limb ischemia.

Conflict of Interest Disclosure: The author has completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

Funding/Support: The author has no funding disclosures.

Keywords: critical limb ischemia, endovascular intervention, femoropopliteal lesions, lower extremity, stenting, superficial femoral artery

References

- Venkatachalam S, Shishehbor MH, Gray BH. Basic data related to endovascular management of peripheral arterial disease in critical limb ischemia. *Ann Vasc Surg.* 2012 Oct;26(7):1039-51.
- Cumpston N. Stent—who started it? *Cathet Cardiovasc Diagn.* 1997 May;41(1):93.
- Dotter CT, Judkins MP. Transluminal treatment of arteriosclerotic obstruction. Description of a new technic and a preliminary report of its application. *Circulation.* 1964 Nov;30:654-70.
- Levy E. Vascular Stents. In: Baum S, Pentecost MJ, editors. *Abrams' Angiography Interventional Radiology.* Second ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006. p. 205-19.
- Johnston KW. Femoral and popliteal arteries: reanalysis of results of balloon angioplasty. *Radiology.* 1992 Jun;183(3):767-71.
- Schillinger M, Sabeti S, Loewe C, Dick P, Amighi J, Mlekusch W, et al. Balloon angioplasty versus implantation of nitinol stents in the superficial femoral artery. *N Engl J Med.* 2006 May 4;354(18):1879-88.
- Palmaz JC. Intravascular stents: tissue-stent interactions and design considerations. *AJR Am J Roentgenol.* 1993 Mar;160(3):613-8.
- Ratner BD, Johnston AB, Lenk TJ. Biomaterial surfaces. *J Biomed Mater Res.* 1987 Apr;21(A1 Suppl):59-89.
- Barth KH, Virmani R, Strecker EP, Savin MA, Lindisch D, Matsumoto AH, et al. Flexible tantalum stents implanted in aortas and iliac arteries: effects in normal canines. *Radiology.* 1990 Apr;175(1):91-6.
- DeRubertis BG. Balloon angioplasty and stenting for femoral-popliteal occlusive disease. In: Moore WS, Ahn SS, editors. *Endovascular Surgery.* Fourth ed. Philadelphia, PA: Elsevier Saunders; 2011. p. 301-7.

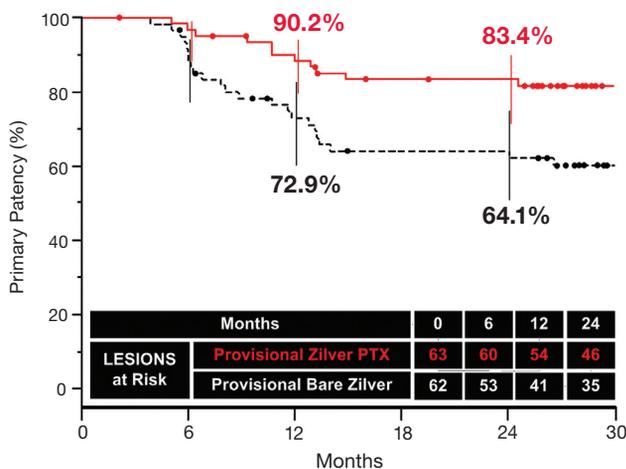


Figure 5. Primary patency following Zilver[®] PTX[®] (paclitaxel-coated Zilver stent) compared to Zilver[®] BMS (bare metal stent), 2-year results.³⁷ Reprinted with permission from Cook Medical, Inc.

11. Cejna M, Thurnher S, Illiasch H, Horvath W, Waldenberger P, Hornik K, et al. PTA versus Palmaz stent placement in femoropopliteal artery obstructions: a multicenter prospective randomized study. *J Vasc Interv Radiol*. 2001 Jan;12(1):23-31.
12. Krankenberg H, Schluter M, Steinkamp HJ, Burgelin K, Scheinert D, Schulte KL, et al. Nitinol stent implantation versus percutaneous transluminal angioplasty in superficial femoral artery lesions up to 10 cm in length: the femoral artery stenting trial (FAST). *Circulation*. 2007 Jul 17;116(3):285-92.
13. Bosiers M, Hart JP, Deloose K, Verbist J, Peeters P. Endovascular therapy as the primary approach for limb salvage in patients with critical limb ischemia: experience with 443 infrapopliteal procedures. *Vascular*. 2006 Mar-Apr;14(2):63-9.
14. Schneider JR, Verta MJ, Alonzo MJ, Hahn D, Patel NH, Kim S. Results with Viabahn-assisted subintimal recanalization for TASC C and TASC D superficial femoral artery occlusive disease. *Vasc Endovascular Surg*. 2011 Jul;45(5):391-7.
15. Geraghty PJ. Covered stenting of the superficial femoral artery using the Viabahn stent-graft. *Perspect Vasc Surg Endovasc Ther*. 2006 Mar;18(1):39-43.
16. Mauri L, Orav EJ, Candia SC, Cutlip DE, Kuntz RE. Robustness of late lumen loss in discriminating drug-eluting stents across variable observational and randomized trials. *Circulation*. 2005 Nov 1;112(18):2833-9.
17. Roiron C, Sanchez P, Bouzamondo A, Lechat P, Montalescot G. Drug eluting stents: an updated meta-analysis of randomised controlled trials. *Heart*. 2006 May;92(5):641-9.
18. Bosiers M, Deloose K, Keirse K, Verbist J, Peeters P. Are drug-eluting stents the future of SFA treatment? *J Cardiovasc Surg (Torino)*. 2010 Feb;51(1):115-9.
19. Bosiers M, Peeters P, D'Archambeau O, Hendriks J, Pilger E, Duber C, et al. AMS INSIGHT—absorbable metal stent implantation for treatment of below-the-knee critical limb ischemia: 6-month analysis. *Cardiovasc Intervent Radiol*. 2009 May;32(3):424-35.
20. Peeters P, Bosiers M, Verbist J, Deloose K, Heublein B. Preliminary results after application of absorbable metal stents in patients with critical limb ischemia. *J Endovasc Ther*. 2005 Feb;12(1):1-5.
21. Bosiers M, Deloose K, Verbist J, Peeters P. Will absorbable metal stent technology change our practice? *J Cardiovasc Surg (Torino)*. 2006 Aug;47(4):393-7.
22. Siablis D, Kraniotis P, Karnabatidis D, Kagadis GC, Katsanos K, Tsolakis J. Sirolimus-eluting versus bare stents for bailout after suboptimal infrapopliteal angioplasty for critical limb ischemia: 6-month angiographic results from a nonrandomized prospective single-center study. *J Endovasc Ther*. 2005 Dec;12(6):685-95.
23. Rand T, Basile A, Cejna M, Fleischmann D, Funovics M, Gschwendtner M, et al. PTA versus carbofilm-coated stents in infrapopliteal arteries: pilot study. *Cardiovasc Intervent Radiol*. 2006 Jan-Feb;29(1):29-38.
24. Laird JR, Katzen BT, Scheinert D, Lammer J, Carpenter J, Buchbinder M, et al. Nitinol stent implantation versus balloon angioplasty for lesions in the superficial femoral artery and proximal popliteal artery: twelve-month results from the RESILIENT randomized trial. *Circ Cardiovasc Interv*. 2010 Jun 1;3(3):267-76.
25. Bosiers M, Torsello G, Gissler HM, Ruef J, Muller-Hulsbeck S, Jahnke T, et al. Nitinol stent implantation in long superficial femoral artery lesions: 12-month results of the DURABILITY I study. *J Endovasc Ther*. 2009 Jun;16(3):261-9.
26. Scheinert D, Scheinert S, Sax J, Piorkowski C, Braunlich S, Ulrich M, et al. Prevalence and clinical impact of stent fractures after femoropopliteal stenting. *J Am Coll Cardiol*. 2005 Jan 18;45(2):312-5.
27. Sabeti S, Mlekusch W, Amighi J, Minar E, Schillinger M. Primary patency of long-segment self-expanding nitinol stents in the femoropopliteal arteries. *J Endovasc Ther*. 2005 Feb;12(1):6-12.
28. Machan L. Drug eluting stents in the infrainguinal circulation. *Tech Vasc Interv Radiol*. 2004 Mar;7(1):28-32.
29. McQuade K, Gable D, Pearl G, Theune B, Black S. Four-year randomized prospective comparison of percutaneous ePTFE/nitinol self-expanding stent graft versus prosthetic femoral-popliteal bypass in the treatment of superficial femoral artery occlusive disease. *J Vasc Surg*. 2010 Sep;52(3):584-90; discussion 90-1, 91 e1-91 e7.
30. Ansel G. 3-year VIBRANT results. Paper presented at: *Vascular Interventional Advances*; 2011 Oct 18; Las Vegas, Nevada.
31. Lammer J. Randomized trials of bare metal stents vs covered stents in the SFA. Paper presented at: *International Symposium on Endovascular Therapy*; 2012 Jan 18; Miami, Florida.
32. Saxon RR. Heparin bonded stent-grafts in the SFA: VIPER one-year results. Paper presented at: *International Symposium on Endovascular Therapy*; 2012 Jan 18; Miami, Florida.
33. Duda SH, Bosiers M, Lammer J, Scheinert D, Zeller T, Tielbeek A, et al. Sirolimus-eluting versus bare nitinol stent for obstructive superficial femoral artery disease: the SIROCCO II trial. *J Vasc Interv Radiol*. 2005 Mar;16(3):331-8.
34. Duda SH, Bosiers M, Lammer J, Scheinert D, Zeller T, Oliva V, et al. Drug-eluting and bare nitinol stents for the treatment of atherosclerotic lesions in the superficial femoral artery: long-term results from the SIROCCO trial. *J Endovasc Ther*. 2006 Dec;13(6):701-10.
35. Dake MD, Ansel GM, Jaff MR, Ohki T, Saxon RR, Smouse HB, et al. Paclitaxel-eluting stents show superiority to balloon angioplasty and bare metal stents in femoropopliteal disease: twelve-month Zilver PTX randomized study results. *Circ Cardiovasc Interv*. 2011 Oct 1;4(5):495-504.
36. Dake MD, Scheinert D, Tepe G, Tessarek J, Fanelli F, Bosiers M, et al. Nitinol stents with polymer-free paclitaxel coating for lesions in the superficial femoral and popliteal arteries above the knee: twelve-month safety and effectiveness results from the Zilver PTX single-arm clinical study. *J Endovasc Ther*. 2011 Oct;18(5):613-23.
37. Ansel G. Zilver PTX randomized controlled trial of paclitaxel-eluting stents for femoropopliteal disease. Paper presented at: *The 21st Annual Meeting of the Japanese Association of Cardiovascular Intervention and Therapeutics*; 2012 Jul 12-14; Niigata, Japan.
38. Dorros G, Hall P, Prince C. Successful limb salvage after recanalization of an occluded infrapopliteal artery utilizing a balloon expandable (Palmaz-Schatz) stent. *Cathet Cardiovasc Diagn*. 1993 Jan;28(1):83-8.
39. Biondi-Zoccai GG, Sangiorgi G, Lotrionte M, Feiring A, Commeau P, Fusaro M, et al. Infragenicular stent implantation for below-the-knee atherosclerotic disease: clinical evidence from an international collaborative meta-analysis on 640 patients. *J Endovasc Ther*. 2009 Jun;16(3):251-60.