Improving Outcomes in Lower Extremity Arterial Diseases With New Intervention Technologies

Written by Emma Hitt Nichols, PhD

Lower extremity arterial diseases can cause substantial morbidity. Recent improvements in interventional technologies have resulted in improved outcomes. Michael J. Rinaldi, MD, Sanger Heart and Vascular Institute, Charlotte, North Carolina, USA, discussed medical therapy for claudication. Lower extremity claudication can be caused by not only atherosclerosis but also venous claudication, cystic adventitial disease, popliteal entrapment syndrome, iliac fibromuscular dysplasia, and iliac artery fibrosis. In most cases, surgery or stenting is indicated. However, medical therapy can improve survival, although it may not alter the symptoms of claudication. Class I recommendations for medical therapy include smoking cessation, statin therapy, antiplatelet therapy, management of hypertension, and control of diabetes. In addition, an exercise program can improve symptoms of claudication. Dr. Rinaldi stated that 4 to 6 weeks of a walking program is long enough to elicit improvements in patients who will benefit from an exercise program. The addition of cilostazol to a walking exercise program can also increase walking distances and improve quality of life, although side effects of the drug may limit its use.

J. Michael Bacharach, MD, MPH, North Central Heart Institute, Sioux Falls, South Dakota, USA, examined the role of anatomy in determining when to intervene in patients with peripheral artery disease (PAD). In general, intervention is most likely indicated when medical therapy does not resolve lifestyle-limiting claudication and if the patient experiences rest pain, nonhealing ulcers, or gangrene. In determining the best intervention, the patient's PAD should be differentiated as aortoiliac disease or infrainguinal disease. For aortoiliac disease, endovascular therapy or surgical revascularization may be indicated, whereas infrainguinal disease may require provisional stenting, surgical revascularization, or referral to a pharmacotherapy clinical trial. Depending on the underlying disease etiology, endovascular procedures have varying success rates, with the highest for infrainguinal disease, femoropopliteal disease, and aortoiliac occlusive disease; however, in many cases, long-term durability may be questionable, and restenosis or reocclusion can occur. Dr. Bacharach expressed his interest in new technologies that may improve outcomes in stenting of PAD.

Ehrin J. Armstrong, MD, MSc, VA Eastern Colorado Healthcare System, Denver, Colorado, USA, discussed the association of the stent type used in iliac intervention and outcomes. Balloon-expandable stents are best used for disease with bifurcations, calcified lesions, or disease located in the common iliac, whereas a self-expanding stent should be used for tortuous vessels, long lesions, or disease located in the distal external iliac. The MELODIE trial [Stockx L et al. *J Endovasc Ther* 2010], MOBILITY OE trial [NCT01396525], and ACTIVE trial [Molnar RG et al. *J Endovasc Ther* 2013] showed that balloon-expandable iliac stents provide excellent outcomes in patients with straightforward lesions, with primary patency rates ranging from 89.1% to 99.2% for up to 12 months of follow-up (Table 1). Similarly, self-expanding stents demonstrated primary patency rates of ≥90% in the CRISP-US trial [Ponec D et al. *J Vasc Interv Radiol* 2004], Zilver trial [Krol KL et al. *J Vasc Interv Radiol* 2008], and MOBILITY AP trial [NCT00844532].

Gary M. Ansel, MD, Ohio Health/Riverside Methodist Hospital, Columbus, Ohio, USA, discussed treating the femoral and popliteal arteries. Initial stent technologies for femoral or popliteal artery diseases had patencies ranging from 28% to 53% [Rocha-Singh KJ et al. *Catheter Cardiovasc Interv* 2007]; however, new technologies have improved these rates. For example, the use of bare-metal stents (BMSs) increased the primary patency rate in noncomplex lesions from 38% with percutaneous transluminal angioplasty (PTA) to 80% with PTA plus LifeStent ($p < .0001$)

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Table 1. Outcomes of Varying Stent Types by Trial

Stent Type	Primary Patency Rate (%)	Restenosis Rate (%)	Follow-up (months)
Balloon expandable			
MELODIE	92.1, 87.8	n/a	6, 24
MOBILITY OE	90	9	9
ACTIVE	99.2 (1 year)	n/a	9
Self-expandable			
CRISP-US	94.7,[a] 91.1[b]	3.5[a],2.7[b]	12
Zilver	92.9	n/a	9
MOBILITY AP	n/a	8.4	9

[a]SMART. [b]Wallstent.

[Laird JR et al. *Circ Cardiovasc Interv* 2010]. The STROLL trial [NCT00739102] had a primary patency rate of 74.9% with a BMS at 2 years [Jaff MR et al. *Endovasc Ther* 2014]. The DURABILITY II trial showed that at 3 years, the loss of primary patency was 60% [Matsumura JS et al. *J Vasc Surg* 2013]. However, in complex superficial femoral artery (SFA) disease, primary-assisted patency rates were 88% at 3 years, compared with a rate of 69.8% for a polytetrafluoroethylene-lined stent [Geraghty PJ et al. *J Vasc Surg* 2013]. In addition, the use of a nonheparin-bonded stent graft did not significantly increase 1-, 2-, or 4-year patency rates compared with a BMS [McQuade K et al. *J Vasc Surg* 2010; Kedora J et al. *J Vasc Surg* 2007]. However, in terms of freedom from loss of primary patency, a heparin-coated contoured-edge stent graft had a rate of 74% at 12 months in the VIPER registry [Saxon RR et al. *J Vasc Interv Radiol* 2013]. The VIPER registry also indicated that sizing of the stent was important; the rate of freedom from loss of patency was 88% in stents that were ≤ 20% oversized, compared with 70% that were > 20% oversized ($p < .05$). Furthermore, a randomized controlled trial showed that the Viabahn heparin-coated contoured-edge stent resulted in significant improvements in freedom from loss of patency compared with a BMS ($p < .01$) [ISRCTN48164244]. Drug-eluting stents (DESs) have also shown an improvement in primary patency over PTA at 12 months ($p < .01$), as well as BMSs at 24 months ($p = .05$) [Dake MD et al. *J Am Coll Cardiol* 2013].

Lawrence A. Garcia, MD, Tufts University School of Medicine, Boston, Massachusetts, USA, discussed lower extremity revascularization and specifically the role of debulking therapies in the current endovascular landscape. Although endovascular therapy has become the primary approach for the treatment of lower extremity diseases, debulking therapies have had a resurgence for a myriad of reasons. Dr. Garcia reviewed the data from laser, directional, and rotational devices. Directional atherectomy is an alternative that is safe and effective. The DEFINITIVE LE trial [NCT0083246] showed that directional atherectomy achieved primary patency rates of up to 78% in patients with lesion lengths up to 20 cm and an overall primary patency rate of 76% in calcified lesions at 12 months across multiple anatomic beds. Specifically, for the SFA, the patency rates in the ≤10-cm lesions were 83%. Periprocedural complications included distal embolization (3.8%), flow-limiting dissection (2.3%), and perforation (5.3%). However, for calcific lesions, aggressive rotational or directional devices are indicated. Rotational atherectomy for infrapopliteal revascularization showed improvement by the Rutherford-Becker scale in 78% of patients with critical limb ischemia (CLI) at 6 months [Safian RD et al. *Catheter Cardiovasc Interv* 2009]. The data set for rotational devices is growing with the future of LIBERTY 360 on the horizon, which will shed some light on orbital atherectomy and its use for both the claudicant and CLI patient. The potential for any debulking therapy to be used in conjunction with drug-coated balloon technology seems attractive though, to date, still untested. The DEFINITIVE AR study has a completed enrollment for this purpose and will be presented in 2015.

Table 2. 2-Year Outcomes of Drug-Coating Balloon Therapy in Critical Limb Ischemia, % (n)

	DEB	PTA	p Value
Death (any cause)	18.5 (12)	16.5 (11)	.8
Major amputation	1.4 (1)	2.8 (2)	1
TLR	17.5 (14/80)	41 (32/78)	< .001
Lesions with > 1 TLR	2 (2)	11 (9)	.03
MAE	36 (24)	52 (37)	.05
New restenosis 12 to 24 months	n = 4	n = 6	
Cumulative restenosis	30 (24/80)	78 (61/78)	< .001
Secondary patency	92 (61/66)	64 (39/61)	< .001
Complete wound healing	93 (53/57)	86 (48/56)	.1

DEB=drug-eluting balloon; MAE=major adverse events; PTA=percutaneous transluminal angioplasty; TLR=target lesion revascularization.

A presentation from Carlos Mena, MD, Yale University School of Medicine, New Haven, Connecticut, USA, discussed the treatment of CLI. The DEBATE-BTK trial randomly assigned patients with CLI and diabetes to undergo stenting with a drug-coated balloon (DCB) or standard PTA [Liistro F et al. *Circulation* 2013]. At 1 year, treatment with DCB significantly improved binary restenosis, target lesion revascularization (TLR), and complete ulcer healing, compared with PTA ($p \leq .01$); advantages were generally maintained at 2 years (Liistro F, LINC 2014;Table 2).

However, researchers of the IN.PACT DEEP trial found that drug-eluting balloon treatment had no effect on clinically driven TLR at 12 months but was noninferior to PTA for 6-month death, major amputation, or clinically driven TLR ($p = .021$) [Zeller T et al. *LINC* 2014]. DES therapy in 3 trials improved TLR rates compared with BMSs or PTA [Bosiers M et al. *J Cardiovasc Surg (Torino)* 2011; Rastan A et al. *Eur Heart J* 2011; Scheinert D et al. *JACC Cardiovasc Interv* 2012]. In addition, the primary patency rates were significantly improved, from ~56% with BMSs or PTA to ~82% with DESs. The YUKON-BTK trial [NCT00664963] showed that treatment with DESs resulted in significantly greater event-free survival compared with BMSs at 24 months ($p = .02$), as well as significantly fewer major or minor amputations ($p = .04$).

Dmitriy N. Feldman, MD, Weill Cornell Medical College, New York, New York, USA, described management of patients following peripheral intervention. Potential complications after intervention include bleeding, pseudoaneurysm, and arteriovenous fistula formation, as well as thrombosis, infection, and neuropathy. To reduce postprocedural complications or their effects, clinicians should ensure that they are readily available after the procedure, consider routine access site angiography, pay close attention to the final angiography using multiple orthogonal views, and be prepared to handle complications in terms of availability of equipment and staff education. After hospital discharge, follow-up after revascularization should include a long-term surveillance program with Doppler ultrasound at baseline and every 12 months after the first year to evaluate for patency [Mohler ER et al. *J Am Coll Cardiol* 2012]. A meta-analysis of 22 trials with ≥3500 patients revealed no benefit for any single or combination therapy to prevent reocclusion; however, cilostazol treatment did result in a lower rate of reocclusion compared with ticlopidine ($p = .01$) and low-molecular-weight heparin plus aspirin decreased occlusion and restenosis in patients with CLI ($p = .0003$) [Robertson L et al. *Cochrane Database Syst Rev* 2012].

Treatment of lower extremity arterial diseases has improved with newer technologies, including the use of BMSs and DESs. Although reocclusion remains a challenge, new technologies and techniques have increased success rates and improved reocclusion rates.