Current assessment of endovascular therapy for infrainguinal arterial occlusive disease in patients with diabetes

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Endovascular therapy (EVT) has increasingly become the initial clinical option for treatment of lower extremity peripheral arterial disease (PAD), not only for patients with claudication, but also for those with critical limb ischemia. Despite this major clinical practice paradigm shift, the outcomes of EVT for PAD are difficult to evaluate and compare with established surgical benchmarks because of the lack of prospective, randomized trials, incomplete characterization of indications for intervention, mixing of arterial segments and extent of disease treated, the multiplicity of EVT techniques used, the exclusion of early treatment failures, crossover to open bypass during follow-up, and the frequent lack of intermediate and long-term patency and limb salvage rates in life-table format. These data limitations are especially problematic when one tries to assess the outcome of EVT in patients with diabetes. The purpose of the present report is to succinctly review and objectively analyze available data regarding the results of EVT in patients with diabetes. (J Vasc Surg 2010;52:92S-95S.)

Diabetes and cigarette smoking are the most important risk factors for developing peripheral arterial disease (PAD).[1] The coronary literature[2-4] clearly demonstrates a significantly increased mortality rate and need for repeat interventions in patients with diabetes who undergo angioplasty compared to surgical bypass. The increased mortality rate and increased rate of secondary interventions imply that patients with diabetes have higher restenosis rates after endovascular interventions. In contrast, there are no prospective randomized studies comparing infrainguinal endovascular therapy (EVT) with surgical bypass in patients with diabetes. Patients with diabetes more commonly present with involvement of the deep femoral and tibial arteries compared with patients who are not diabetic; however, patients with diabetes present with heterogeneous patterns and may have arterial occlusive disease in any vascular territory. EVT is less effective in smaller arteries such as tibial arteries, compared to the femoropopliteal arteries[5,6] regardless of the presence of diabetes.

Factors that influence the outcome of EVT. Because PAD has multiple risk factors and the severity of disease encompasses a vast range, large cohorts of patients with PAD will include a myriad of presentations. This complicates the analysis of outcomes for claudication and critical limb ischemia (CLI) treatment, especially in patients with diabetes. Even the definition of CLI is not optimal. Consider that in the placebo arm of the Circulase trial,[7] patients with CLI who did not undergo revascularization had a limb salvage rate of 87% at 6 months. This was similar to the amputation-free survival rates seen in both the open surgery and EVT arms of the BASIL trial.[8] The heterogeneity of the patients combined with the lack of a more specific working definition for CLI makes defining outcomes challenging. Factors that have been shown to negatively impact EVT outcomes include: the indication[9,10] for the procedure, lesion length,[5] Trans Atlantic Inter-Societal Consensus (TASC) classification,[11] runoff score,[12-15] occlusion vs stenosis,[5] renal failure,[13] and excessive or heavy calcification[16,17] (Table). Evaluating the impact of diabetes on EVT remains difficult because patients with diabetes more commonly have multiple adverse risk factors.

The influence of diabetes on outcomes of EVT and open surgical bypass. Technical success rates for infrainguinal endovascular interventions are worse in the tibial arteries[18-21] compared to the femoropopliteal arteries.[13,22] Similarly, heavy lesion calcification portends technical failure.[16,17] Because patients with diabetes are more susceptible to developing more heavily calcified atherosclerotic arteries and tibial artery occlusive disease, it is intuitive that patients with diabetes would have lower technical success rates compared with patients without diabetes. In a retrospective review of infrainguinal endovascular interventions primarily in the femoropopliteal segment, Lazaris et al[23] found a decreased technical success rate in patients with diabetes, 81% compared to 93% (P = .05) in patients without diabetes. More dramatically, they found a significantly increased rate of complications in patients with diabetes, 16.7% vs 3.9% (P = .03).

The available infrainguinal revascularization data are primarily nonrandomized and retrospective. Nonetheless,

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Table. Factors affecting primary patency after endovascular therapy: comparative results of published series

Series	*Number treated*	*Average lesion length*	*Primary patency*	*Technical failures included*	*Factors affecting patency (RR)*
Multilevel interventions					
DeRubertis 2007[26] (79% fem-pop, 21% tibial) (86% primary, 14% reinterventions)	1000	NR	60% 1 y 50% 2 y 48% 2.5 y	0%	CLI (2.5) Diabetes (1.7) Hypercholesterolemia (1.7) CAD (1.4) TASC D (1.3)
Femoropopliteal interventions					
Cheng 2003[10] (stent only)	73	16 cm	56% 1 y 35% 2 y 22% 4 y 22% 4 y	0%	Indication Lesion >10 cm
Johnston 1992[12] (PTA only)	254	<10 cm	70% 1 y 57% 2 y 50% 3 y 43% 5 y	4%	Runoff
Clark 2001[13] (PTA only)	219	4 cm	87% 1 y 80% 2 y 69% 3 y 55% 5 y	5%	Runoff (8.5) Diabetes (5.5) Renal failure (4.0)
Jamsen 2003[14] (PTA only)	218	5.2 cm	46% 1 y 25% 5 y	16.5%	Runoff
Ihnat 2008[15] (stent only)	109	15.7 cm	63% 1 y 52% 2 y 52% 3 y	0%	Runoff (2.6) TASC D (5.5)
Lugmayr 2002[30] (stent only)	54	3-4 cm	87% 1 y 85% 2 y 76% 3 y	0%	Diabetes
Sabeti 2005[31] (stent only)	65	16 cm (all greater than 5 cm)	54% 1 y	0%	Diabetes (3.8)
Dearing 2009[32] (primary stenting)	161	12.9 cm	70% 1 y 55% 2 y 39% 3 y	4.4%	TASC D (6.2) TASC C (3.8) Hypercholesterolemia (2.1)
Tibial interventions					
Vraux 2000[18]	40	NR	56% 1 y	22%	>10-cm occlusion
Vraux 2006[19]	50	NR	46% 1 y	18%	>10-cm occlusion Extension into popliteal artery
Giles 2008[21]	176	NR	53% 1 y 51% 2 y	7%	TASC D (2.8) No target (2.2)

CAD, Coronary artery disease; *CLI,* critical limb ischemia; *fem-pop,* femoropopliteal; *NR,* not reported; *PTA,* percutaneous angioplasty; *RR,* relative risk; *TASC,* TransAtlantic InterSocietal Classification.

large series of infrainguinal surgical bypasses generally demonstrate no difference in the technical success or patency rates of patients with diabetes compared to patients without diabetes.[24,25] In contrast, DeRubertis et al[26] evaluated 1000 consecutive percutaneous interventions in the femoropopliteal and tibial arteries and found a diminished primary patency rate in patients with diabetes (hazard ratio [HR], 1.7). In fact, diabetes was one of the most important risk factors affecting primary patency, second only to the indication for the procedure (HR, 2.5). In a prospective, nonrandomized study, Dick et al[27] compared both surgical and endovascular interventions for iliac, femoropopliteal, and tibial artery occlusive disease and found poorer sustained clinical benefit in patients with diabetes. Sustained clinical benefit was defined as improvement in Rutherford et al's[28] category, amputation-free survival, and freedom from target extremity revascularization; however, the difference was primarily due to target extremity revascularization. Both secondary sustained clinical benefit and limb salvage were equivalent to patients without diabetes. The authors concluded that multiple revascularizations might be required in patients with diabetes to achieve similar limb salvage rates.

EVT for PAD of the femoropopliteal arteries. These reports are comprised of heterogeneous groups of patients with both multilevel and single-level arterial occlusive disease involving different arterial territories. However, some clinical investigators have focused on the results of EVT in a single arterial territory. In a registry of 219 limbs that underwent femoropopliteal angioplasty, Clark et al[13] found diabetes to be significantly associated with reduced primary patency (relative risk [RR], 5.5; this was a stronger association than renal failure (RR, 4.0), but weaker than poor tibial runoff (RR, 8.5). Another retrospective study[29] compared subintimal angioplasty with placement of covered stents in long-segment superficial femoral artery occlusions, and found diabetes to be strongly associated with decreased primary patency (HR, 7.2). Investigators[30,31] evaluated patients who underwent femoropopliteal stenting and found diabetes significantly decreased patency rates, whereas others[15,32] have not. Baril et al[33] evaluated predominantly claudicants with TASC II B and C femoropopliteal lesions, and did not find an association between diabetes and restenosis. Bakken et al[34] separately evaluated patients with claudication and critical limb ischemia who underwent EVT of superficial femoral artery occlusive disease. In the claudication group, insulin-dependent diabetics maintained primary patency rates similar to patients without diabetes, but decreased assisted patency rates and increased restenosis rates at 3 years. Conversely, in patients with CLI, diabetes did not affect patency or restenosis rates, although it did negatively impact limb salvage rates.

EVT for PAD of the tibial arteries. In the tibial arteries, Giles et al[21] evaluated 176 patients, 72% of whom had diabetes and underwent infrapopliteal artery angioplasty, and found only TASC D lesions and poor runoff predicted restenosis, reintervention, decreased patency, and reduced limb salvage rates. Sadek et al[35] treated 89 limbs with tibial artery EVT, and found improved secondary patency in patients who underwent endovascular interventions for multilevel disease compared to isolated tibial artery disease. Interestingly, the limb salvage rates were equivalent. Similarly, Gray et al[36] reviewed their database of patients treated for tibial artery occlusive disease. They found that one-third of patients had isolated tibial artery disease; the remainder had multilevel occlusive disease. Patients with isolated tibial artery disease had worse outcomes with respect to overall survival, amputation-free survival, limb salvage, maintenance of ambulatory status, independent living, and secondary patency. Interestingly, isolated tibial disease was not an independent predictor for the worse outcomes, but instead, the presence of tissue loss and end-stage renal disease (ESRD) correlated most strongly with poor outcomes. These authors suggested that isolated tibial artery disease is a surrogate marker for more severe tissue loss. None of these studies found an association between diabetes and reduced EVT patency rates.

Limb salvage, morbidity, and mortality. The surgical bypass literature[24,37] generally suggests that limb salvage rates are not significantly worse in patients with diabetes compared to those without. Conversely, Bakken et al[34] found decreased limb salvage rates in patients with insulin-dependent diabetes mellitus treated with EVT for femoropopliteal artery occlusive disease, despite similar patency rates. This finding remained statistically significant after patients with ESRD were excluded. Similarly, Conrad et al[38] evaluated EVT of the femoropopliteal arteries in 110 patients with critical limb ischemia (15% with ESRD) and found diabetes significantly increased the risk of amputation (HR, 11.5). Conversely, Dick et al[27] found no difference in limb salvage rates of patients with diabetes, and attributed their results to close surveillance and an aggressive policy of multiple, secondary interventions.

Because endovascular therapy is minimally invasive, unless a major bleeding complication occurs, mortality is usually more a reflection of the patient's underlying comorbidities rather than the stress of the procedure itself. Jamsen et al[14] also found an increased mortality rate for patients with diabetes (odds ratio, 2.0) in 304 patients who underwent infrainguinal revascularization with an endovascular attempt first approach; only 10.5% underwent surgical bypass. The BASIL trial[8] did not detect a significant decrease in survival rates for patients with diabetes, although less than one-third of patients in this trial of EVT vs bypass for severe limb ischemia had diabetes. Instead, the investigators found a decrease in survival for patients living more than 2 years who underwent EVT first.

In summary, patients with diabetes mellitus undergoing infrainguinal EVT are a heterogeneous group, and further investigation is required to more completely understand the impact of diabetes on outcomes. Patients undergoing EVT with diabetes most likely have higher rates of technical failure and subsequent amputation. Also, patients with diabetes probably have higher rates of restenosis after EVT in the femoropopliteal arteries; data are less clear for tibial EVT. The impact of diabetes on patency and restenosis rates in the femoropopliteal arteries is probably less important than TASC classification and tibial artery runoff. Among patients with diabetes and CLI, those presenting with isolated tibial artery occlusive disease are more likely to have more advanced tissue loss, ESRD, and a worse prognosis.

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