

The current role of endovascular intervention in the management of diabetic peripheral arterial disease

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Poor arterial inflow continues to be a major contributing factor in the failure to heal diabetic foot wounds. Options for revascularization have significantly increased with the development of sophisticated endovascular techniques. However, the application of this technology is variable due to relatively little prospective, randomized data on newer techniques. Further, multiple specialties are capable of performing endovascular interventions and proper referral can be difficult. This article will review the basics of application of endovascular intervention in the diabetic patient with arterial disease and provide a broad understanding of the literature behind the decision-making on appropriate therapy.

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The last decade has witnessed an explosion in the number of endovascular interventions being performed for the treatment of peripheral arterial disease (PAD). Today, many advocate an endovascular-first approach to all PAD (1). While it is unquestionable that endovascular approaches have many benefits and advantages, they are also plagued by many limitations especially in terms of restenosis. This is particularly true in the diabetic patient.

The purpose of this article is to review some of the evidence in favor of endovascular interventions, describe some of the expected results from such interventions, and highlight the limitations, with the purpose of helping the clinician make an informed decision in terms of revascularization options pertaining to the diabetic foot.

Unique aspects and challenges for endovascular work in the diabetic patient

In contrast to traditional PAD on which most of the recommendations are based, diabetic-associated PAD presents several unique characteristics. The most evident is the presence of significant medial calcinosis. Large calcium burden is known to increase the risk of embolization with intervention, increase difficulty of crossing total occlusions, and increase the incidence of restenosis

in treated segments. In addition, severe medial calcinosis makes standard measures of severity of disease unreliable and complicates the follow-up of lesions. The ankle-brachial (ABI) and toe-brachial (TBI) indices may not be obtainable in many patients due to calcified digital vessels or missing digits from prior amputation. Doppler waveforms will often remain monophasic due to the non-compliant nature of the vessel. Pulse volume recording (PVR) will tend to underestimate the degree of disease and is not quantitative. Transcutaneous oxygen measurement will be unreliable in the presence of edema or infection. Duplex ultrasound has a difficult time insonating calcified vessels (2). The clinician is therefore frequently left to his or her clinical judgment and acumen, specifically evaluating the progress of a wound or lack thereof, following revascularization. Lack of progress of a wound should mandate re-evaluation.

However, one should be mindful of the fact that wound healing after endovascular intervention is frequently more prolonged than after open bypass surgery. Several studies have attempted to quantify wound healing after revascularization for critical limb ischemia (CLI). In general, wound healing, on average, after endovascular therapy requires 7 months, whereas it requires only 4 months after open-revascularization, although the overall rate of wound healing may be equal (3–5).

Advantageous aspects of endovascular interventions in the diabetic patient

There is no question that endovascular techniques have afforded us the ability to treat many patients who have no open surgical options. This may be the case because of poor target and run-off, which would not sustain a bypass, absence of adequate saphenous vein conduit, poor medical condition, or a failed prior open revascularization. Furthermore, endovascular techniques often give us the ability to treat a multitude of tibial vessels, as opposed to open bypass where usually just one vessel is targeted. Multiple revascularizations may provide better flow as well as angiosome-specific revascularization. Furthermore, endovascular interventions are relatively non-invasive and not associated with the potential wound morbidity of open bypasses. No extensive preoperative cardiac work up is necessary, and interventions can be easily repeated.

Open versus endovascular revascularization

To date, BASIL (Bypass versus Angioplasty in Severe Ischaemia of the Leg) remains the only prospective randomized trial comparing bypass surgery to percutaneous angioplasty for the treatment of PAD (6). The study comprised 452 patients and was conducted in the United Kingdom. Patients had to be declared candidates for both surgery and angioplasty. Primary amputations were thus excluded. Interventional techniques were relatively limited and consisted of primary balloon angioplasty of the superficial femoral artery (SFA) with stenting only for suboptimal angioplasty result. Only 42% of the study group was afflicted with diabetes; therefore, relatively few interventions were infrageniculate. In the angioplasty group, early failure rates were high and repeated interventions were more common. Early limb salvage rates were equivalent in both groups at the cost of repeated interventions. At 2 years, the data favored open bypass surgery.

Other reviews on this subject have produced similar findings. A Swiss prospective study evaluated 426 limbs with CLI, 46% of which were diabetic (7). The study was not randomized; 207 limbs were treated with angioplasty, 85 with surgery, and 108 were observed. The initial clinical success was better in non-diabetics versus diabetics, but more frequent re-interventions in diabetics made the results equivalent to the non-diabetic patients. The limb salvage rate was the same in endovascular and open surgery in the diabetic group. Romiti et al. (8) published a meta-analysis of 30 studies. At 3 years, primary patency was much better for bypass (72%) than angioplasty (49%) but limb salvage remained the same.

It is unclear as to whether the addition of newer technology, such as atherectomy, covered stenting, or drug elution, will change the balance in favor of endovascular therapy. In a more contemporary analysis

of vein bypass, amputation-free survival continues to be >80%, even in high-risk patients (9). Single institutional studies and device-companies-directed registries have demonstrated promise in the improvement of outcomes in endovascular intervention for newer techniques; however, they have not been validated in any randomized fashion (10–14).

Open surgery and endovascular interventions may also differ in terms of foot wound healing. A recent review analyzed 106 infrainguinal interventions for tissue loss (3). Wound healing within 4 months occurred in only 21% of cases. The total wound healing rate was 50% with a mean healing time of 7 months. Limb salvage was 83% at 2 years in patients with tissue loss. Repeat interventions were required in 38% of patients. Patients with a combination of diabetes and congestive heart failure did not fare as well as others in terms of wound healing. In general, for open bypasses, wound healing on average is achieved at 4 months (4).

Implications of Failed Endovascular Interventions

The literature is still unclear as to whether a failed endovascular intervention attempt on an extremity implies a lesser likelihood of limb salvage from a subsequent surgical bypass. Al-Nouri et al. (15) reported that 40% of their SFA stenting interventions failed after 1 year. Failures were more likely to occur with TransAtlantic InterSociety Consensus (TASC) C and D lesions (refers to radiographic anatomy of severity of occlusive disease on a scale of severity, where A is the least and D the most) for which surgery is generally recommended. Failed interventions had a negative impact on ultimate limb salvage. Whether this represents a sub-selection of difficult cases or whether this represents a consequence of the failed stenting is difficult to ascertain from a retrospective study. Similarly, Nolan et al. (16) demonstrated a higher graft occlusion and amputation rate in patients undergoing prior percutaneous intervention versus those taken directly to open bypass. However, this theory is not universal, and others have demonstrated no detrimental effect of an 'endovascular first' approach to CLI. Khan et al. (17) presented a retrospective review of 140 primary bypasses to 92 bypasses carried out after previous endovascular intervention. They found that patency rates and limb salvage rates were the same.

There is, however, little doubt that a failed endovascular intervention may alter the nature of the ultimate surgical intervention to be performed. For instance, if stents are extended across the popliteal artery, what may have been a femoral to popliteal bypass may now become a femoral to tibial bypass, with a higher failure risk and lower long-term patency. In a study by Joels et al. (18), 24 patients with early failures of SFA intervention were described. The distal bypass target site was altered in

nearly a third of the subjects. In addition to shifting the outflow to a more distal target, the most feared complication of endovascular therapy is distal embolization, which may render the limb unsalvageable.

In open surgery, an early failure of a bypass attempt often means a higher risk of limb loss as opposed to late failure. However, this is not demonstrated in early failed endovascular interventions (19). It seems that, barring intra-procedural embolizations or significant dissection, a failed endovascular intervention does not necessarily doom the extremity, provided the operator is aware of possible surgical options. A failed endovascular intervention may, however, be associated with a less desirable surgical outcome than otherwise thought.

A main tenet in treatment of diabetic wounds is an understanding of the different metabolic demands for wound healing versus normal metabolism. It has been postulated that endovascular therapy may increase limb salvage despite poorer patency long term as long as patency is maintained until the wound closes. However, this has not been evaluated in any prospective or systematic fashion in endovascular interventions. In open revascularization, late graft failure in operations performed for tissue loss results in recurrent wounds. Toursarkissian et al. (20) reported that in the diabetic patient, the implications of a failed femoral to distal bypass carry a 50% chance of limb loss.

Repeat endovascular interventions do not have the same patency rates as primary interventions. In a review of 70 cases from New England over 7 years, the 2-year primary patency was 33% and secondary patency was 63% for the repeat intervention (21). These numbers are lower than those for the initial interventions. The study included mostly claudication patients with SFA interventions. The earlier the first intervention fails, the less likely is the second intervention to remain patent. Early failure (within 6 months) of the primary intervention predicts poor success for any secondary intervention.

Results of tibial interventions

Tibial artery occlusive disease is the primary cause of limb loss in the diabetic patient with neuropathic and ischemic tissue loss. Tibial interventions are frequently required in diabetic patients and are usually performed for limb salvage. A review of the literature on this subject suggests a 50% recurrence rate at less than 1 year and roughly a 25% limb loss rate yearly. A review published in the *Annals of Vascular Surgery* in 2009 (22) examined 45 patients undergoing tibial intervention for CLI. A total of 90% of patients were diabetic and 45% were on dialysis. Nearly half required concomitant superficial femoral angioplasty. Symptoms recurred in 43% at 8 months. There was also a 25% major amputation rate in that time period. Another review of 176 cases was published in the *Journal of Vascular Surgery* in 2008 (23).

At 1 year, there was a 46% primary patency and 84% limb salvage rate. A total of 15% of patients required surgical bypass. Those unsuitable for bypass had a higher rate of restenosis and limb loss.

There is some data to suggest that atherectomy may be of benefit in the diabetic patients with PAD. In a comparison of diabetic versus non-diabetic patients, Sixt et al. (24) demonstrated equivalent outcomes with respect to major adverse events and improvement in ischemia measures in a comparison of 80 diabetic patients versus 92 non-diabetics. Empirically, debulking of the heavy plaque burden in the calcified vessels may lead to an improvement of overall endovascular therapy.

In our practice, balloon expandable drug eluting stents for focal tibial lesions have been performed with good results, but this has not been validated in any trial to date. None are available in long lengths for extensive chronic total occlusions (CTO). Drug eluting balloons appear to be of benefit over regular balloons in infrapopliteal lesions but are not available in the US (25).

Results of SFA interventions

The SFA is often diffusely narrowed and calcified in diabetic patients. It is therefore a frequent target of endovascular treatments. Many endovascular options are available, including angioplasty, atherectomy, and stenting. Plain balloon angioplasty leads to average primary patency rates of 61% at Year 1 and 51% at Year 3 based on the original TASC reports (26). From the FemPac Pilot and Thunder Trials (13, 27), a 50% restenosis rate at 6 months can be expected with simple angioplasty in the SFA. In both these trials, the lesion length averaged 7 cm, 20% were CTO and half the patients were diabetic. The prognostic factors that carry a negative prognosis include a limb salvage indication as opposed to claudication, a longer length of the lesion, an occlusion as opposed to a stenosis, fewer tibial runoff vessels, and the presence of diabetes.

More extensive disease, while still technically treatable, leads to less satisfactory results. A recent review from Pittsburgh of occluded SFA (TASC D lesions) treated by endovascular means showed 1-year primary and secondary patencies of 52 and 88%, respectively. The difference between primary and secondary patencies reflects the high restenosis rates and the need for repeat interventions to maintain patency (28).

CTO frequently require stenting for suboptimal angioplasty result. Self-expanding stents are normally used. The literature has conflicting studies regarding whether routine stenting is beneficial in SFA lesions. Covered stents are available from many manufacturers. They have not shown any particular benefit for routine use in the SFA and the consequences of their failures are more significant. However, a single institution study has demonstrated that the freedom from amputation is

equivalent between covered SFA stents and prosthetic popliteal bypass (14).

Summary and recommendations

Endovascular interventions for CLI in the diabetic patient can result in limb salvage but have a high likelihood of repeat interventions to maintain patency. Vein bypass continues to be the gold standard for treatment of CLI with predictable results. However, many of these patients are not candidates for an extensive revascularization due to lack of conduit (veins often harvested previously for coronary surgery or a prior leg bypass), extensive calcification precluding arterial clamping, poor functional status making them a prohibitive operative risk, and poor collateralization of the plantar circulation. Endovascular therapy can offer expeditious, often outpatient, care without the need for general anesthesia or significant metabolic impact on the patient. In addition, multiple outflow vessels can be targeted and therapy can be directed to the specific vascular bed feeding the wound.

However, as with any new technology, new problems have arisen with the explosion of endovascular intervention in the diabetic patient. Loss of suitable bypass targets with failed, or complicated, intervention can lead to limb amputation. In our experience, an understanding of the patient's functional status and conduit options pre-intervention would help to decide the intensity and the techniques to be employed during intervention. In conclusion, with diligent and focused surveillance, acceptable limb salvage and patency rates can be obtained with either modality.

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