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ENDOVASCULAR TECHNIQUES IN LIMB SALVAGE: INFRAPOPLITEAL ANGIOPLASTY

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Abstract

Critical limb ischemia (CLI) results from inadequate blood flow to supply and sustain the metabolic needs of resting muscle and tissue. Infragenicular atherosclerosis is the most common cause of CLI, and it is more likely to develop when multilevel or diffuse arterial disease coincides with compromised run-off to the foot. Reports of good technical and clinical outcomes have advanced the endovascular treatment options, which have gained a growing acceptance as the primary therapeutic strategy for CLI, especially in patients with significant risk factors for open surgical bypass. In fact, endovascular recanalization of below-the-knee arteries has proven to be feasible and safe, reduce the need for amputation, and improve wound healing. The distribution of various vascular territories or angiosomes in the foot has been recognized, and it appears advantageous to revascularize the artery supplying the territory directly associated with tissue loss. In addition, the targeted application and local delivery of drugs using drug-coated balloons (DCB) during angioplasty has the potential to improve patency rates compared to balloon angioplasty alone.

Introduction

Critical limb ischemia is the result of inadequate blood flow to supply and sustain the metabolic needs of resting muscle and tissue. Objectively, CLI is defined by an ankle brachial index (ABI) <0.50 that is associated with rest pain. Patients with CLI present with symptoms related to peripheral ischemia, such as lack of a pulse or Doppler signals in the affected limb, motor or sensory dysfunction, skin temperature or color changes, rest pain, ulceration, and even gangrene. While risk factor modification is essential, native atherosclerotic disease can continue even in patients who have undergone risk factor modification.

In general, most patients with CLI and tissue involvement progress to amputation, thus highlighting the importance of prompt therapy and revascularization. Expeditious and appropriate evaluation can lead to an increase in revascularization rates and even a 50% reduction in amputation rates.[1,2] However, delayed treatment and referral of patients to a vascular surgeon can hinder limb preservation efforts and lead to amputation.[2] When amputation is performed, patients remain at risk for stump complications and conversion to a higher level amputation. Even when amputation cannot be avoided, infrapopliteal percutaneous angioplasty may allow a lesser amputation in patients who would otherwise need a major one.[3] Cost-utility analyses use health information to evaluate treatments that have an impact on survival and clinical outcomes. Amputation is associated with lower utility scores and quality of life.[4]

Unfortunately, patients with infrapopliteal disease are among those with the highest likelihood of coronary artery disease, and the mortality for patients presenting with CLI is approximately 50-70% at 5 years.[5, 6] As such, patients with CLI are inherently at increased risk of developing complications related to open surgical interventions and would likely find a less invasive approach appealing. Many interventionists and surgeons are now assessing the role of infrapopliteal artery bypass surgery as a first-line therapy for CLI and even considering distal bypass revascularization procedures a "tainted" gold standard.[7] In addition, patients with significant medical comorbidities whose veins are not an adequate conduit for open revascularization may find percutaneous intervention to be a less morbid and more realistic therapeutic alternative. Endovascular means for restoring flow to the infrapopliteal vessels has gained acceptance and preference over the past decade and can be used as a first-line treatment option for patients with CLI (Figure 1).

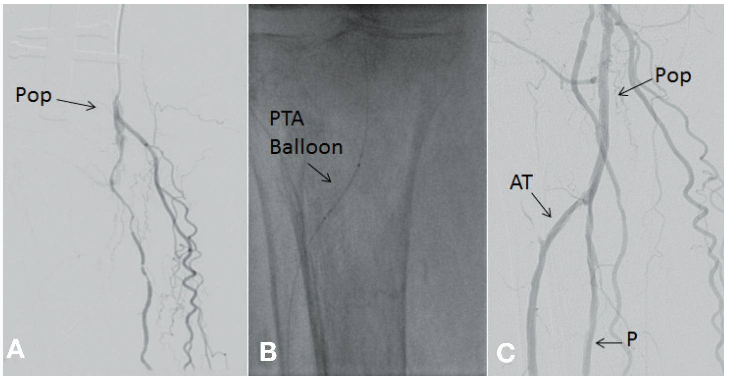

Figure 1. A diabetic patient experiencing right foot rest pain with an ankle brachial index <0.40. Magnified views showing (A) an occluded distal popliteal artery (Pop). Occluded proximal anterior tibial (AT) and peroneal (P) arteries with distal reconstitution (not shown) via collaterals. An occluded posterior tibial artery without distal reconstitution. (B) Successful crossing of the lesion and initiation of the PTA. A deflated balloon is noted crossing the distal Pop and proximal AT segment. (C) Completion arteriogram showing recanalization of the Pop, AT, and P arteries.

Outcomes of Percutaneous Balloon Angioplasty

The Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial showed that overall survival and amputation-free survival were no different at 2 years after randomization to angioplasty-first or bypass-first revascularization.[8] In the following 2 years, those patients who received autologous veins benefited the most, and patients who had received prosthetic bypass grafts fared more poorly.[8] At the end of follow-up, it was noted that bypass surgery carried a higher morbidity and that 56% of the patients overall had died as a result of their underlying medical comorbidities.[9] It appears that the major determinants for survival are within these first 2 years and that a less invasive and morbid procedure such as percutaneous balloon angioplasty (PTA) is reasonable in these patients.

The past decade has brought forth a paradigm shift in the management of CLI that favors endovascular therapy. Angioplasty and bypass surgery have achieved a similar approximate 80% limb salvage rate at 3 years, and some have suggested these modalities to be complementary.[10] Conte and colleagues have suggested objective performance goals to evaluate catheter-based treatment for CLI. Bypass with autologous vein was considered the established standard with a 1-year amputation-free survival of 76.5%, against which catheter-based treatments can be evaluated.[11]

Odink and associates retrospectively studied 90 consecutive patients with 57 infrapopliteal stenoses and 104 occlusions over a 5.5-year period. They sought to determine the effectiveness of infrapopliteal PTA in treating CLI. Based on intention to treat, 89% of patients were successfully revascularized. The limb salvage rate at 3 years for those patients with previously untreated lesions was 87%. In addition, the limb salvage rate for 61 patients who had total vessel dilatation was 89%. The 30-day mortality was 7%, and there were no amputations after the first year. The authors concluded that PTA of infrapopliteal arteries appears to be an effective treatment for patients with CLI and could be augmented by total vessel dilatation.[12] As such, these results compare favorably with the previously published performance goals.[11]

Kudo and associates evaluated the effectiveness of PTA of the tibial arteries for treating CLI in 52 limbs.[13] The primary, assisted primary, and secondary patency; continued clinical improvement; and limb salvage rates at 3 years were 23.5%, 41.8%, 46.1%, 51.1%, and 77.3%, respectively. Hypertension, multiple segment lesions, and TransAtlantic InterSociety Consensus (TASC) classification type D were significant independent risk factors for worse outcomes. The authors conclude that PTA is a feasible, safe, and effective procedure for the treatment of CLI. They attributed their limb salvage rate to their high assisted primary and secondary patency rates and suggest that angioplasty can be the primary choice for treating CLI due to infrainguinal arterial occlusive disease.[13] Bosiers and colleagues used endovascular therapy as the primary approach for limb salvage in 443 infrapopliteal procedures. The 1-year primary patency and limb salvage rates for PTA alone were 68.6% and 96.7%, respectively. They postulate that endovascular intervention will become the primary treatment modality for below-the-knee lesions in patients with CLI, with 1-year primary patency and limb salvage rates that compare favorably with open surgical bypass.[14]

Implication of Diabetes in Infrapopliteal Disease

Metabolic syndrome (MetSyn) is associated with early onset of atherosclerosis, increased thrombotic events, and increased complications after cardiovascular intervention. In general, MetSyn can be defined as the presence of ≥3 of the following criteria: blood pressure ≥130 mm Hg/≥85 mm Hg; triglycerides ≥150 mg/dL; high-density lipoprotein ≤50 mg/dL for women and ≤40 mg/dL for men; fasting blood glucose ≥110 mg/dL; or body mass index ≥30 kg/m.[15] MetSyn is found in approximately 50% of patients with peripheral vascular disease. Its presence has been associated with decreased clinical efficacy following intervention, decreased freedom from recurrent symptoms, and decreased freedom from major amputation at 5 years. In addition, early failure within the first 6 months was more common in patients with MetSyn.

As a component of MetSyn, diabetes mellitus increases the risk of lower extremity peripheral arterial disease (PAD) by 2- to 4-fold and is present in 12–20% of individuals with lower extremity PAD.[16-20] In the Framingham Heart Study, diabetes increased the risk of intermittent claudication by 3.5- and 8.6-fold in men and women, respectively.[21] The risk of developing lower extremity PAD is proportional to the severity and duration of diabetes.[22,23] The risk of developing CLI is also greater in diabetics than nondiabetics.[24, 25] Diabetic patients with lower extremity PAD are 7- to 15-fold more likely to undergo a major amputation than nondiabetics with lower extremity PAD.[25-27]

Lida and colleagues reported treatment outcomes after endovascular therapy on 465 limbs with CLI and isolated below-the-knee lesions. They identified diabetes as one of the factors associated with major amputation.[28] Zhan and associates compared early and initial hemodynamic outcomes of endovascular therapy and open revascularization in 85 consecutive patients with diabetes and CLI who underwent 109 interventions collectively. There was a similar significant initial hemodynamic improvement between the two interventions.[29] This suggests that the inferior intermediate or long-term results seen in diabetic patients is not necessarily due to the initial hemodynamic response but more likely due to the effects of diabetes on plaque characteristics and cardiovascular health and the durability of the intervention in such patients. In a study by Ryu and colleagues comparing clinical outcomes between diabetic and nondiabetic patients with CLI who underwent infrapopliteal angioplasty, diabetic patients had an unfavorable primary patency at 2 years compared to nondiabetic patients.[30] However, there was no significant difference between the two groups in terms of limb salvage and survival. The authors noted that the main obstacles to recanalization or long-term patency include long, multiple, and calcified stenosis or small-diameter vessels that have a tendency towards restenosis.[30]

Impact of TASC Classification on Performance of PTA

Primary patency is influenced by the extent of disease.[31] The TASC classification for infrapopliteal lesions offers standardized criteria to define lesion characteristics. A single stenosis <1 cm long is classified as TASC A. TASC B includes multiple focal stenosis <1 cm long or 1-2 stenoses <1 cm involving the trifurcation. TASC C lesion characteristics include a stenosis 1-4 cm long, occlusion 1-2 cm long, or extensive stenosis involving the trifurcation. An occlusion >2 cm long or diffusely diseased arteries are considered TASC D lesions.[32]

When infrapopliteal PTA was stratified by TASC lesion, a higher restenosis, reintervention, or amputation rate was identified with worse TASC classification, even when the initial technical failures were excluded. Giles and associates suggest that infrapopliteal angioplasty is a reasonable primary treatment for CLI patients with TASC A, B, and C lesions and that PTA may be attempted as an alternative to primary amputation in all TASC lesion patients. The authors showed that a limb salvage rate of

84% at 3 years can be obtained with careful follow-up and, as others have also suggested, reintervention when necessary.[31, 33] A report by Sigala and colleagues also corroborated the poor performance of TASC D lesions, which lost primary patency significantly earlier than other TASC classes.[34] They further observed that TASC C lesions also exhibited a lower primary patency than TASC A and B lesions. In addition, patients with TASC C and D lesions underwent major amputation significantly earlier. Patients with TASC A and B lesions had a similar improved duration of primary patency and lived longer than those in class C or D. This is a further reflection of the overall severity of PAD that is imbedded within the TASC classification. Surprisingly, diabetes did not affect primary patency in this study but was associated with a need for major amputation.[34]

Angiosome-Based Approach in Tissue Loss

Dilatation of a proximal lesion is not sufficient to salvage a critically ischemic limb when the distal artery is severely diseased. For clinical success, straight-line blood flow must be restored to the pedal arteries by PTA in one or more tibial arteries.[35] Restoring blood flow in this population is challenging due to the combination of distinct peripheral arterial pathology and the increased blood flow necessary to heal tissue loss. A factor that affects clinical outcome is the number of patent arteries after PTA. A retrospective analysis of 1268 patients with CLI who underwent infrapopliteal PTA reported that the 1-year limb salvage rates for 0, 1, 2, and 3 patent infrapopliteal arteries were 56.4%, 73.1%, 80.4%, and 83.0%, respectively.[36] The greater the number of patent vessels after PTA correlates with a higher likelihood of functional limb salvage. Thus, restoring patency of one or both tibial arteries is generally preferred.

In addition to the number of vessels treated, there seems to be an advantage to revascularizing the arterial territory directly associated with the area of tissue loss on the foot. The distribution of the various vascular territories in the foot—called angiosomes—has been recognized since 1987, when Taylor and Palmer defined an angiosome as a three-dimensional anatomic unit of tissue fed by a source artery.[36] Subsequently, Attinger and associates defined six angiosomes in the foot originating from the three main arteries and their branches to the foot and ankle (Table 1).[37]

In the angiosome concept, the foot lesion location is related to a specific angiosome and the revascularization of this specific region becomes the target vessel or wound-related artery. Adjacent angiosomes are bordered by choke vessels, which link neighboring angiosomes to one another and demarcate the border of each angiosome. The choke vessels are important connections that allow a given angiosome to provide blood flow to an adjacent angiosome if the latter's source artery is diseased.

Recently published retrospective data evaluating endovascular treatment of CLI patients have found significantly improved results when using the direct angiosome revascularization approach.[38, 39] Attinger and colleagues reported a 9% healing failure rate when ulcers were treated directly by their angiosome in contrast to a 38% lack of success in wounds that were revascularized indirectly.[40] In a larger series of 203 consecutive limbs with ischemic ulcerations undergoing endovascular reconstructions, Iida and colleagues observed an 83% limb preservation rate in the angiosome-related group versus 69% in the nonspecific group.[39] On the other hand, Blanes and associates did not observe any statistical differences among 32 Rutherford category 5 and 6 patients when comparing the angiosome-targeted versus nontargeted percutaneous revascularizations.[41]

Angiosomes of the foot and ankle

Main artery	Arterial branches	Angiosomes
Posterior tibial	Calcaneal	Medial Heel
	Medial Plantar	Instep
	Lateral Plantar	Laterial mid-foot and fore-foot
Anterior tibial	Dorsalis Pedis	Dorsum of foot
Peroneal	Anterior perforating	Lateral upper ankle
	Calcaneal	Lateral plantar heel

Table 1. Angiosomes of the foot and ankle detailing its main artery supply and branches.

Application of Drug-Coated Balloon Angioplasty

Conventional PTA using modern low-profile systems is associated with high technical success rates. Initial data from recent trials suggest that local drug delivery to target lesions during angioplasty can achieve improved patency over PTA alone. The local delivery of drugs to reduce neointimal and smooth muscle cell proliferation has gained momentum in recent years. The concept of drug-coated balloon (DCB) PTA is based on the combination of PTA and a sufficient, uniform, local drug delivery into the vessel wall to achieve an efficient and long-term antiproliferative effect.[42] A recent study investigated the efficacy of DCB PTA in the treatment of infrapopliteal lesions using a paclitaxel-eluting balloon. In the study, 109 limbs (82.6 %) were treated for CLI with a mean lesion length of 176 ± 88 mm. The restenosis rate (>50%) at 1 year was 27.4%, with a limb salvage rate of 95.6 % for patients with CLI.[43] Results of the DEBELLUM randomized clinical trial confirmed the ability of paclitaxel-eluting balloons to reduce restenosis and lead to better clinical outcome than conventional balloons at 6 months after treatment of below-the-knee arterial disease in patients with CLI.[44] Further recommendations for the use of DCB PTA therapy should emerge as clinical trials and studies are conducted. For now, it is evident that the targeted local delivery of drugs using DCB can enhance the therapeutic window achieved with PTA.

Conclusions

Improved technical and clinical results have helped endovascular treatment options gain a growing acceptance as the primary therapeutic strategy in CLI, especially in subjects with significant risk factors for surgical bypass. In fact, with its proven safety and feasibility, improved would healing, and ability to avoid amputations in many cases, endovascular recanalization is becoming an established treatment option for limb salvage. Even though long-term limb salvage rates are substantially greater than patency rates, experience has shown that if wound healing is the primary objective of treatment in some patients with CLI, it may be sufficient to achieve only temporary patency until healing has taken place and the blood flow required for tissue survival is reduced. An adequate classification of patients by comorbidities and extent of disease may assist with patient selection and influence outcomes. In addition, the application of DCB PTA has the potential to improve patency rates compared to PTA alone.

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