Optimal management of infrainguinal arterial occlusive disease

Abstract: Peripheral arterial occlusive disease is becoming a major health problem in Western societies as the population continues to age. In addition to risk of limb loss, the complexity of the disease is magnified by its intimate association with medical comorbidity, especially cardiovascular and cerebrovascular disease. Risk factor modification and antiplatelet therapy are essential to improve long-term survival. Surgical intervention is indicated for intermittent claudication when a patient's quality of life remains unacceptable after a trial of conservative therapy. Open reconstruction and endovascular revascularization are cornerstone for limb salvage in patients with critical limb ischemia. Recent advances in catheter-based technology have made endovascular intervention the preferred treatment approach for infrainguinal disease in many cases. Nevertheless, lower extremity bypass remains an important treatment strategy, especially for reasonable risk patients with a suitable bypass conduit. In this review, we present a summary of current knowledge about peripheral arterial disease followed by a review of current, evidence-based medical and surgical therapy for infrainguinal arterial occlusive disease.

Keywords: peripheral vascular disease, peripheral arterial disease, critical limb ischemia, claudication, infrainguinal bypass, endovascular infrainguinal intervention

Introduction

Lower extremity arterial occlusive disease is one of the most challenging problems facing vascular specialists, not only because of the complexity of the disease in the legs, but also because of the associated medical comorbidity of patients afflicted with this disease. About 8.5 million people in the US are affected by peripheral arterial disease (PAD), including 4.3% of adults older than 40 and 14.5% of those older than 70.1–3 Up to 60% of patients with PAD have associated coronary artery disease (CAD) or cerebrovascular disease and are at risk of myocardial infarct (MI), stroke, and cardiovascular death.4

The most commonly used, objective definition of PAD is a resting ankle-brachial index (ABI) lower than 0.90.2,6 Patients with PAD may be asymptomatic, or they may present with intermittent claudication (IC) or chronic critical limb ischemia (CLI). The management of patients with PAD is complex and includes modification of risk factors, pharmacological therapy, supervised exercise therapy, and surgery. Conservative management with analgesia and primary amputation might be appropriate in some patients.2

Infrainguinal arterial occlusive disease has been extensively studied, and new tools and techniques for treating it are continually being developed. In this review, we present a summary of current knowledge about the epidemiology, natural history, and clinical
progression of lower extremity arterial disease followed by a concise, comprehensive synopsis of current, evidence-based medical and surgical therapy.

**Risk factors**

Age is the most important, nonmodifiable risk factor for PAD, with a prevalence of 0.9% in people under age 50 and 23.2% in people over the age of 80.\(^1\) Ethnicity and sex are also important factors, with the highest prevalence of PAD seen in African American men and women (prevalence 19.2%) and Hispanic women (prevalence 19.3%).\(^1,2\) The overall prevalence of PAD is greater in men than women.\(^2\)

Several important modifiable risk factors have also been identified.\(^2,7\) The association between smoking and PAD is well known, and the risk is proportional to the number of cigarettes smoked, with heavy smokers sustaining a four fold risk of developing IC compared to nonsmokers.\(^5,8\)

PAD is about twice as common in diabetic patients as it is in nondiabetics. Furthermore, for every 1% increase in hemoglobin-A\(_1c\), there is a 28% increased risk of developing PAD.\(^9\)

Hypertension is associated with all forms of cardiovascular disease but is not as strong a risk factor for PAD as smoking and diabetes.\(^2\) Among those who have asymptomatic PAD, hypertension increases the likelihood that they will develop symptoms. The increased risk is 2.5-fold in men and 3.9-fold in women.\(^9,10\)

Numerous elements of dyslipidemia have been examined and found to have an association with PAD and IC.\(^2,7\)

These include total cholesterol level greater than 270 mg/dL, elevated ratio of total cholesterol to high-density lipoprotein (HDL), low HDL levels, and hypertriglyceridemia.\(^2\) Smoking magnifies the contribution of dyslipidemia in PAD.\(^2\)

Patients with renal insufficiency, especially postmenopausal women with a history of CAD, are more likely to develop PAD than other patients with a history of CAD who have normal renal function.\(^2,11\)

Hyperhomocysteinemia is a known risk factor for CAD and PAD. Its prevalence among patients with vascular disease is significantly higher than the general population.\(^2,12\) This is especially true among young patients with PAD, 30% of whom have elevated homocysteine level.\(^2\)

Less intuitive but intriguing is the association of C-reactive protein (CRP) with PAD.\(^2,7,12\) Recent studies have shown that asymptomatic patients with an elevated CRP are more likely to develop symptomatic PAD over a 5-year period than age-matched controls in whom CRP is not elevated.\(^2\) Even among patients with a normal CRP level, those with a level in the top quartile of the normal range are more than twice as likely to develop PAD as those whose CRP level is in the bottom quartile of the normal range.\(^12\)

**Natural history**

Patients with asymptomatic PAD and those with IC have a significantly different course than patients with CLI. PAD that is asymptomatic often remains so indefinitely.\(^2\) Symptoms of IC may worsen over time, but progression to rest pain or tissue loss is unusual.\(^2\) Factors that increase the likelihood of progression are those listed above, especially smoking and diabetes.\(^2\) Lower ABI at the time of diagnosis also increases likelihood of progression. Interestingly and importantly, patients with asymptomatic PAD and those with IC share the same increased risk of MI, stroke, and death.\(^2,7\) This increased risk of fatal cardiovascular and cerebrovascular events is profound compared to the risk of progression to limb-threatening ischemia, with mortality rates as high as 42% and 65% at 5 and 10 years, respectively (compared to a 5-year amputation rate of <5%).\(^13\)

The natural history of CLI is dismal compared to asymptomatic PAD and IC, both in terms of limb survival and overall patient survival.\(^2\) Mortality for these patients is mostly due to cardiac and cerebrovascular events, and is greater than 25% at 1 year after diagnosis,\(^13,14\) greater than 30% at 2 years, nearly 50% at 5 years, and 70% at 10 years.\(^14\) The risk of limb loss is also higher in patients with CLI and is inversely related to ABI. Patients with CLI and an ABI >0.50 have a 15% amputation rate at 1 year, whereas those with CLI and an ABI <0.50 have a 34% amputation rate at 1 year.\(^15\)

**Classification of lower extremity arterial disease**

Lower extremity arterial disease has historically been classified into two broad, clinical categories: IC and CLI, based on the distinctly different presentations, natural history, associated morbidity and mortality, and response to treatment characteristic of each. A third category is the population of patients who have an ABI <0.90 but are asymptomatic. Within this population are some patients who are truly asymptomatic and others who initially deny symptoms but have significantly shorter walking distances on treadmill testing and report decreased daily activity compared to patients without PAD.

Claudication is fatigue, aching, or burning in a muscle group that is caused by transient ischemia, exacerbated by
exercise, and relieved by rest. Though often confused with diabetic neuropathy and neurogenic claudication, vascular claudication may be distinguished from these entities by both subjective and objective findings. The pain of diabetic neuropathy is often constant, bilateral, and distributed in a “sock and glove” pattern, while the pain of IC is prominent during exercise, unilateral or asymmetric, and localized to a muscle group. The pain of neurogenic claudication is generally positional rather than exertional, and is relieved by sitting or leaning forward while walking. While vascular claudication is typically localized to a muscle group, such as calf muscles or thigh muscles, the pain of neurogenic claudication is often more diffuse, extending from the buttock to the foot.

CLI is characterized by ischemic rest pain that is persistent, recurring, and dependent on opiate analgesia for at least 2 weeks. In order to help distinguish CLI from nonvascular causes of distal limb pain, an ABI of less than 0.40 is also required to establish the diagnosis.2,16 In patients with heavily calcified arteries, in whom measurement of ABI is inaccurate or impossible, an ankle pressure of less than 50 mmHg or a toe pressure of less than 30 mmHg can be used in lieu of ABI to establish the diagnosis.2 Alternatively, ischemic ulceration and/or gangrene of the forefoot or toes may be combined with an ABI less than 0.40, an ankle pressure less than 50 mmHg, or a toe pressure less than 30 mmHg to establish the diagnosis.2,16-18 Patients who meet this standard definition can be subdivided into critical and subcritical groups. Those with rest pain and an ankle pressure greater than 40 mmHg are considered subcritical and have a 27% chance of limb survival at 1 year. Those with rest pain and either an ankle pressure less than 40 mmHg or tissue loss are considered critical and have a 5% chance of limb survival at 1 year.2,16

The anatomic patterns of arterial occlusive disease can be classified as inflow occlusion, outflow occlusion, or a combination of both.2 The infrarenal aorta and iliac system comprise the inflow vessels to the lower extremity. The claudication caused by chronic occlusion of these vessels is usually proximal (ie, thigh or buttock). If extensive bilateral disease is present, male patients may also complain of erectile dysfunction. The arteries of the leg below the inguinal ligament including superficial femoral artery (SFA), deep femoral artery, popliteal artery, and tibial arteries are considered the outflow vessels.2

IC is usually caused by single level occlusive disease, and the most commonly affected vessel is the SFA at the level of Hunter’s canal. Extensive collateralization via the deep femoral artery usually limits the effects of isolated SFA occlusion to IC. Conversely, CLI is usually caused by occlusive disease at two or more levels, and they are typically sequential and diffuse.19 Significant numbers of patients with CLI have occlusions in the popliteal or tibial arteries, and most have associated disease involving inflow or femoral arteries.19 Patients with end stage renal disease, diabetes mellitus (DM), and advanced ischemia are more likely to have occlusion in the popliteal and tibial vessels.19

Medical therapy
Risk factor modification
Initial treatment of PAD is cardiovascular risk factor modification and antiplatelet therapy to reduce risk of associated cardiovascular and cerebrovascular complications and improve long-term survival.2,16 This includes smoking cessation, glycemic control in DM, blood pressure control, statin therapy, and antiplatelet therapy.

While some controversy exists regarding the effect of smoking cessation on regression of symptoms of claudication, the effect of smoking on progression of symptoms,20 increased risk of amputation, failure of surgical therapy, and increased risk of death from cardiac and cerebrovascular events is undisputed.20 All patients with PAD should, therefore, be advised to stop smoking. Face to face counseling, involvement in support groups, and pharmacological therapy in the form of nicotine replacement and bupropion are usually needed.

Diabetes has been shown to increase risk of PAD and cardiac disease, but the effectiveness of tight glycemic control with regard to halting the progression of PAD, relieving symptoms of claudication, or increasing amputation-free survival is unclear. Nevertheless, poorly controlled diabetes should be addressed and corrected. The current recommendation for control of diabetes in PAD is to achieve hemoglobin-Ac of <7%.2,7

Hypertension should be treated according to the recommendations of the Eighth Joint National Committee.21 Patients older than 65 who do not have DM or chronic kidney disease (CKD) should maintain a systolic blood pressure <150 mmHg and a diastolic blood pressure <90 mmHg. Patients between the ages of 18 and 65 who do not have DM or CKD and patients of any age who do have DM and/or CKD should maintain a systolic blood pressure <140 mmHg and a diastolic blood pressure <90 mmHg. The choice of drug depends on race and the presence of CKD.21

The notion that reduction of blood pressure in a patient who
is acclimated to a hypertensive state might worsen symptoms and decrease walking distance has been shown to be inaccurate.

Patients with PAD are considered to have clinical atherosclerotic cardiovascular disease and are, therefore, included in the first of four major statin benefit groups, according to the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for treatment of blood cholesterol. These patients benefit from high-intensity statin therapy (atorvastatin 40–80 mg/day or rosuvastatin 20 mg/day). The expected response to high-intensity statin therapy is a reduction in serum low-density lipoprotein cholesterol by ≥50%. If this response is not achieved with high-intensity statin therapy, even in the setting of diligent compliance with lifestyle modification, addition of a nonstatin agent may be considered.

Antiplatelet therapy does not improve symptoms or walking performance in IC; nevertheless, patients with atherosclerotic occlusive disease should be started on long-term antiplatelet therapy in order to reduce the risk of MI, ischemic stroke, and cardiovascular death. A meta-analysis from the Antithrombotic Trialists’ Collaboration showed that antiplatelet therapy may reduce the risk of adverse cardiovascular events in patients with PAD by up to 23%. The benefits are similar for subgroups of PAD patients with IC, those undergoing open bypass surgery, and those receiving endovascular intervention. Aspirin was the most widely studied antiplatelet drug and doses of 75–150 mg daily are as effective as higher daily doses.

The Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events trial has found clopidogrel to be more effective than aspirin at further reducing the risk of ischemic stroke, MI, and vascular death in patients with atherosclerotic vascular disease. The overall safety of clopidogrel is equivalent to medium dose aspirin. There is, however, no benefit in combination therapy of aspirin and clopidogrel in this patient population.

Nonsurgical management of intermittent claudication

Exercise therapy is effective and recommended as initial treatment for patients with IC. Supervised exercise therapy is significantly more effective than nonsupervised therapy. A meta-analysis of 21 studies of exercise therapy showed that walking distance to maximal claudication pain increased up to 122%. The program is most effective when the duration of each session is greater than 30 minutes, the frequency is more than three sessions per week, and the overall program length is more than 6 months. There are also some studies that show exercise therapy to be equivalent and at times superior to surgical or endovascular intervention for patients with IC.

Pentoxifylline and cilostazol are the two drugs that have been approved by the US Food and Drug Administration for treatment of claudication. The effectiveness of other agents including L-arginine, propionyl-L-carnitine, ginkgo biloba, oral vasodilator prostaglandins, vitamin E, and chelation is not well established for IC. Cilostazol, a phosphodiesterase III inhibitor, increases walking distance up to 50% and improves quality of life scores. A trial therapeutic course of cilostazol (100 mg orally twice a day for 3–6 months) should be considered for patients with lifestyle-limiting IC. The side effects of cilostazol include headache and diarrhea, and it should not be prescribed in patients with congestive heart failure due to increased risk of cardiovascular death.

Pentoxifylline, a methylxanthine derivative, is thought to improve oxygen delivery by a rheolytic effect and may also inhibit platelet aggregation. Early trials attributed a 12% improvement in walking distance to this drug. It may be considered as second-line alternative therapy, especially in patients who are intolerant to cilostazol.

Revascularization

Diagnosis of lower extremity arterial disease must begin with a thorough and comprehensive history, with special attention paid to signs and symptoms of undiagnosed cardiovascular and cerebrovascular disease. Both lower extremities and feet should be thoroughly examined for signs of ischemia. Signs of previous intervention related to vascular disease, such as surgically absent digits and incisions in the groin or legs, may also be noted. Careful assessment of cardiopulmonary reserve and surgical risk is paramount in developing appropriate treatment strategy for these patients. The diagnosis of PAD can be confirmed with ABI and noninvasive vascular testing. The distribution and pattern of disease are ascertained using duplex ultrasound, imaging studies such as computed tomographic angiography or magnetic resonance angiography, and catheter-based angiogram. Finally, duplex vein mapping of lower and upper extremities is performed to evaluate for the availability of autogenous conduit for bypass.

Surgical options for management of infrainguinal arterial occlusive disease are conceptually grouped into two major categories: open reconstruction/bypass and endovascular therapy. Multiple factors determine which approach is most beneficial for a given patient, and a comprehensive understanding of the patient’s needs and goals for therapy is, therefore, an essential companion to thorough knowledge of the expected...
risk and durability of the surgical options available. The goal of therapy in claudication is improvement in symptoms and quality of life.\textsuperscript{2} For CLI patients, the goal of therapy is pain control, wound healing, and preservation of a functional limb for ambulation.\textsuperscript{2,17}

The Transatlantic Inter-Society Consensus (TASC) Working Group classified PAD based on anatomical location (aorto-iliac, femoropopliteal, or infrapopliteal) and severity of the disease (type A, B, C, or D).\textsuperscript{2} Recommendations for an open or endovascular approach are based on the likelihood of therapeutic success. Endovascular therapy is generally preferred for type A/B lesions, whereas open revascularization is recommended for more severe type C/D lesions.\textsuperscript{2} For type B/C lesions, endovascular and open therapy are both acceptable depending on patient's surgical risk, individual practitioner's preference, and expected durability of the intervention.

Inflow disease involving aortic and iliac levels should always be addressed first with endovascular or open reconstruction prior to or during treatment of infrapopliteal occlusive disease. The most important determinant of success in open bypass is the quality of the conduit. For endovascular intervention, the most important determinants of success are the anatomical and morphological characteristic of the lesions.\textsuperscript{2,17} The quality of runoff vessels also correlates with the success of both open and endovascular interventions. For a patient with IC or rest pain, treatment of single level disease, such as an iliac (inflow) vessel or the SFA, might be sufficient for symptomatic relief. A patient with tissue loss (ie, ulcer or gangrene), however, requires in-line flow with either open or endovascular revascularization to establish pulsatile blood flow to the foot for successful wound healing and limb salvage.

Endovascular therapy

Endovascular treatment of PAD has become increasingly popular and successful as improvements in techniques and devices have resulted in better efficacy and longer patency. It has replaced open revascularization as the most commonly used modality in the treatment of lower extremity PAD.\textsuperscript{26} Likely reasons include the less invasive nature of these newer techniques and the belief that failed endovascular intervention will not negatively affect the outcome of subsequent open surgery. The “endovascular first” approach has, however, been challenged recently, with some studies demonstrating a disadvantageous change in the bypass target and an overall worse outcome following open bypass in patients who experienced failure of an initial endovascular intervention.\textsuperscript{29–32}

The complications of lower extremity endovascular intervention are categorized by location into puncture site, intervention site, distal vessel, and systemic complications.\textsuperscript{33} Up to 10\% of patients may experience complications from their intervention that result in open surgery, amputation, and/or death. The most common complications are at the puncture site (bleeding, pseudoaneurysm, arteriovenous fistula) and occur in up to 4\% of patients. Thrombosis and arterial rupture at the intervention site, embolization, and dissection in the distal vessel can also occur. Systemic complications, such as renal failure, MI, and stroke, are reported in <1\% of patients.\textsuperscript{33}

The efficacy of endovascular intervention is affected by both clinical and anatomical factors. Outcomes are worse for patients with DM, end stage renal disease, history of previous vascular intervention, and tissue loss at the time of intervention.\textsuperscript{2,34,35} Likewise, long segment occlusions and heavily calcified lesions predict worse outcomes following endovascular intervention. Success is better with short stenosis up to 10 cm in length.\textsuperscript{2} While long-term antiplatelet therapy with aspirin or clopidogrel is recommended after infrainguinal intervention unless contraindicated, there is no level I evidence for this practice, and the recommendation is likely extrapolated from data in coronary intervention studies.\textsuperscript{2}

To date, there is only one prospective, randomized, controlled trial comparing the outcomes of open versus endovascular interventions for patients with CLI.\textsuperscript{31} The Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial randomized 452 patients from 27 United Kingdom hospitals to bypass-first or balloon angioplasty-first strategy. The participants had severe limb ischemia secondary to infrainguinal disease and were suitable candidates for both approaches. The main outcomes, including overall survival and amputation-free survival, were similar between the two strategies at 2 years after randomization. Interestingly, a survival benefit was noted for patients who randomized to bypass-first in the subset of patients who survived beyond 2 years.\textsuperscript{31} Overall hospital cost and quality of life were similar for both groups.\textsuperscript{32} When the results of the BASIL trial were analyzed by treatment received, patients who received surgical bypass after failed percutaneous transluminal angioplasty (PTA) had significantly worse outcomes compared to patients who initially underwent bypass with an autogenous conduit. When bypass was done with a prosthetic conduit, patients who initially underwent angioplasty appeared to fare better.\textsuperscript{32}

There are a number of limitations and criticisms for this trial, including the power of the trial, the selection of study...
population, the lack of lesion standardization, the use of angioplasty as the sole technique in endovascular intervention, and the outcomes examined. Further clinical trials are required to determine optimal approach for patients with CLI.

**Infringuinal disease**

As previously mentioned, the TASC classification system for PAD is specific for each level of disease. With regard to infringuinal disease, a single stenosis ≤10 cm in length or a single occlusion ≤5 cm in length are considered type A lesions. A single stenosis between 10 and 15 cm in length (not involving the below-knee portion of the popliteal artery), a single occlusion between 5 and 15 cm in length (also not involving the below-knee portion of the popliteal artery), multiple stenoses or occlusions (each ≤5 cm in length), lesions in the absence of continuous tibial vessels, heavily calcified occlusions ≤5 cm in length, and single popliteal stenoses are all considered type B lesions. Multiple stenoses or occlusions totaling >15 cm, with or without heavy calcifications; lesions with recurrent stenosis; and lesions that still require treatment after two endovascular interventions, are all considered type C lesions. Chronic, total occlusions of the common femoral artery or SFA measuring >20 cm, with involvement of the popliteal artery; or chronic, total occlusion of the popliteal artery and proximal trifurcation vessels, are considered type D lesions.

PTA with selective stent placement is the most commonly used technique for femoral popliteal disease.2,7,36 Primary stent placement is generally not recommended in the common femoral or popliteal artery.2,7 Subintimal angioplasty or other adjunctive techniques, including atherectomy and reentry devices, can be utilized to help with initial recanalization of the occluded vessels. Other newer techniques such as self-expanding stents, stent grafts, cutting balloons, and drug-eluting balloons and stents are increasingly used to enhance the effectiveness of PTA, though data available for these promising new technologies are limited.2,7,37,38

Evidence for PTA with selective versus routine stent placement in infringuinal disease, especially in SFA and proximal popliteal arteries, is controversial. Some studies have shown better patency and lower restenosis rate with routine placement of a bare metal stent19,40 while others have reported no significant benefit over selective stent placement.41,42 The results of recent meta-analyses have supported the preferred strategy of primary PTA and selective stent placement for femoral popliteal disease.36,43

Some investigators have studied the use of stent grafts for treatment of long segment femoropopliteal occlusive disease, and reported similar long-term patency when compared to conventional femoral-popliteal bypass using synthetic conduit.44,46 The cost of stent grafts is significantly higher compared to conventional bare metal stents, and there are limited data to recommend their routine use in infringuinal disease.26 Drug-eluting stents and drug-coated balloons are designed to limit the process of intimal hyperplasia in hopes of avoiding in-stent restenosis. A number of trials have shown promising early results for their use in femoral popliteal disease.26,47 Nevertheless, data for this evolving technology are limited, and further studies are required to prove long-term, cost-effective benefit in lower extremity arterial disease.26

**Infraopliteal disease**

As with infringuinal PAD, the TASC classification divides infrapopliteal lesions into four classes:2,48 Type A lesions are single stenoses <1 cm long. Multiple focal stenoses <1 cm long or stenoses <1 cm involving the trifurcation are considered type B lesions. Stenoses 1 to 4 cm long, occlusions up to 2 cm long, or extensive stenoses involving the trifurcation are considered type C lesions. Occlusions >2 cm long or diffuse disease constitute type D lesions.

Endovascular intervention for infrapopliteal occlusive disease is usually reserved for limb salvage in the setting of CLI and is not recommended for IC.7 Infraopliteal PTA can be performed safely with reported initial technical success of 93%.48,49 An endovascular approach is acceptable for TASC A, B, and C lesions and has even been performed successfully in TASC C/D lesions, although technical failure was more common with TASC D lesions.48,49 As expected, secondary interventions are frequently required, but assisted patency and limb salvage rates are acceptable.48,49 Although outcomes are generally similar between the strategies of PTA alone and primary stent placement, routine placement of bare metal stents in infrapopliteal vessels is not recommended.2,7 Other techniques, including subintimal angioplasty, atherectomy, and drug-eluting balloons and stents have been used successfully in infrapopliteal occlusive disease, but data for these newer technologies are limited.2,7

**Open reconstruction**

Infrainguinal lower extremity bypass (LEB) using a good-quality vein is the gold standard for revascularization, especially for patients with CLI.31,50 Using the combined data from multiple randomized control trials,31,50,51 the Society of Vascular Surgery has summarized the expected outcomes of patients who underwent open revascularization for CLI.51
The overall reported perioperative mortality rate is 2.7%. The major adverse cardiovascular event rate, including death, MI, and stroke, is reported to be 6.2%. The early LEB graft occlusion rate is around 5%, and the expected amputation rate is 2%. At 1 year, the limb salvage rate is 88% and amputation-free survival is more than 75%.

Infrainguinal bypass is a major arterial reconstruction using a bypass conduit (whether autogenous or prosthetic) that originates at or below the inguinal ligament. Thus, inflow vessels may include the common, deep, or superficial femoral arteries, and can even include the popliteal or tibial arteries depending on pattern of the occlusive disease.\textsuperscript{2,52} Successful bypass depends on the bypass conduit, the quality of the inflow vessel, and the outflow target vessel. Endarterectomy might be required if the inflow is common femoral artery, proximal SFA, or deep femoral artery.\textsuperscript{2,52} In addition to optimal inflow selection and preparation, proper selection of a distal outflow site is essential for successful bypass. A general principle of all LEB is that the ideal outlet of the bypass conduit should be the most proximal artery that has at least one continuous runoff to the foot, as long as there is adequate length of suitable conduit.\textsuperscript{2,52} The outflow vessel most commonly used is a popliteal artery with tibial or peroneal runoff to the foot. Patients with CLI will usually require the use of a tibial or pedal artery as an outflow target due to the more extensive and diffuse nature of the occlusive disease.\textsuperscript{2,19,53}

The most important determinant of success of an LEB is the type and quality of conduit selected.\textsuperscript{2,17,52} Autogenous vein is superior to synthetic graft as conduit for LEB,\textsuperscript{2,53–55} and the great saphenous vein (GSV) is superior to other autologous alternatives.\textsuperscript{55,56} An essential step in preoperative planning is evaluation of the GSV with duplex mapping and identification of alternative vein conduits, if needed. An ideal vein conduit should be soft, compressible, at least 3 mm in diameter, and should not be calcified or sclerotic. If the ipsilateral GSV is unsuitable or unavailable, the contralateral GSV should be used. If no suitable GSV is available, a small saphenous vein or arm vein can be used for bypass with acceptable patency rates.\textsuperscript{2,57,58} The 5-year patency of femoral to above and below knee popliteal bypass with vein is reported to be 66%–76%, depending on the indication for revascularization.\textsuperscript{2,7} In patients with a suitable GSV, femoral-tibial bypass can be performed with excellent long-term patency (74%–80% 5-year patency).\textsuperscript{7}

If a vein conduit is truly unavailable, several synthetic options including heparin-bonded dacron graft, human umbilical vein, polytetrafluoroethylene (PTFE), and expanded PTFE covalently bonded with heparin can be used for LEB.\textsuperscript{59–65} A prosthetic conduit such as PTFE has acceptable outcomes in the above-knee position with reported 5-year patency up to 60%.\textsuperscript{2,66} It is, however, less satisfactory in vessels below the knee, and the reported 5-year patency is 31%–65%.\textsuperscript{2,67} Some surgeons have utilized adjunctive procedures including vein cuff patch and arteriovenous fistula in hopes of improving the patency of a prosthetic LEB that incorporates below-knee arteries.\textsuperscript{2,68–70} Others have utilized cryopreserved vein as a bypass conduit, especially in the absence of a suitable autogenous conduit when immediate revascularization is necessary following removal of infected graft.\textsuperscript{71,72}

Completion studies such as angiography, duplex ultrasound, and angiography are effective in detecting intraoperative technical problems and are used by many surgeons to ensure technical adequacy of their LEBs.\textsuperscript{52} Utilization of completion studies varies widely among vascular surgeons, with some routinely performing a completion study (in addition to continuous waveform Doppler) and others only selectively.\textsuperscript{73} Recent study by our group has shown that completion study did not significantly improve bypass patency at discharge or 1 year for both autogenous and prosthetic LEB, and the strategy of selective use of completion imaging intraoperatively is as effective as those who are using it routinely.\textsuperscript{74}

Routine clinical examination and duplex surveillance are important elements of postoperative care to ensure long-term graft patency.\textsuperscript{2,52} Multiple studies have shown the cost-effectiveness of routine surveillance after LEB.\textsuperscript{2,74,75} Duplex ultrasound should be performed in the immediate postoperative period and at regular intervals for at least 2 years after surgery.\textsuperscript{2} If a low graft velocity (<45 cm/s), a drop of >0.15 in ABI, a focal lesion associated with peak systolic velocity of >300 cm/s, or a velocity ratio >3.5 on duplex ultrasound is found,\textsuperscript{2,52} angiogram is indicated to identify possible de novo graft stenosis that should be addressed with endovascular angioplasty or open surgical revision.\textsuperscript{2}

In addition to the protective effect on cardiovascular and cerebral diseases, antiplatelet therapy, in the form of aspirin or clopidogrel, is beneficial for graft patency and is recommended after LEB.\textsuperscript{3} The beneficial effect of antiplatelet therapy seems to be greater in prosthetic LEB.\textsuperscript{2,76} Anticoagulation with warfarin therapy was shown to be significantly better for autogenous LEB in some studies but can be associated with a higher risk of bleeding.\textsuperscript{2,76,77} The decision for long-term anticoagulation after LEB should be made on an individual basis and might be indicated in
high-risk patients with poor arterial runoff, suboptimal vein conduit, and those who underwent redo operation.

**Primary amputation**

Primary amputation without revascularization might be appropriate in patients with overwhelming foot infection or unbearable symptoms in the setting of disease not amenable to reconstruction. It should also be considered in patients with significant comorbidities, especially when they are nonambulatory at baseline.

**Conclusion**

Management of patients with infrainguinal occlusive disease is challenging, and the complexity of the disease is magnified by its intimate association with medical comorbidity. Treatment of associated risk factors and long-term antiplatelet therapy are paramount in these high-risk populations. Intervention for patients with IC should be reserved for those with severe symptoms after failed conservative management. Early revascularization is indicated in appropriately selected patients for limb salvage in patients with CLI. Endovascular interventions have become the preferred initial approach for treatment of infrainguinal arterial occlusive disease. Open infrainguinal bypass remains the gold standard for revascularization in CLI, especially for patients at appropriate surgical risk and with suitable bypass conduit.

**Disclosure**

The authors report no conflicts of interest in this work.

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