Principles of Revascularization: Clinical Indications and Patient Selection

The surgical management of patients with peripheral arterial disease (PAD) is derived from the wider context of the epidemiology and natural history of the disease, and the influence of coexisting medical conditions such as coronary artery disease, diabetes mellitus, and renal disease. The spectrum of clinical presentation of PAD is broad and can be classified into 3 categories: asymptomatic disease, intermittent claudication (IC) and limb-threatening ischemia (critical limb ischemia [CLI]). With rare exception (e.g., to create an iliac conduit for a thoracic aortic endograft), reconstruction for occlusive disease is never indicated in asymptomatic patients. The clinical decision process for revascularization in IC and CLI is distinct and merits elaboration. Although the anatomic pattern of occlusive disease is a major factor in the revascularization strategy, it
Nonstandard Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>ABI</td>
<td>ankle-brachial indices</td>
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<td>AIOD</td>
<td>aortoiliac occlusive disease</td>
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<tr>
<td>BASIL</td>
<td>Bypass versus Angioplasty in Severe Ischaemia of the Leg</td>
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<td>CFA</td>
<td>common femoral artery</td>
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<td>CLI</td>
<td>critical limb ischemia</td>
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<td>GSV</td>
<td>great saphenous vein</td>
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<td>IC</td>
<td>intermittent claudication</td>
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<td>PAD</td>
<td>peripheral arterial disease</td>
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<tr>
<td>PTFE</td>
<td>polytetrafluoroethylene</td>
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<td>TASC</td>
<td>Trans-Atlantic Inter-Society Consensus</td>
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should be stressed that the physiological state of the patient and the status of the limb primarily determines the appropriateness and urgency of intervention for PAD.

Intermittent Claudication

Although the cellular and biochemical changes in the limb with claudication are complex, symptoms of IC occur only during physical activity, when the metabolic demands of the muscles are not met by the capacity of the circulatory system. Many patients with PAD remain asymptomatic because their activity level does not exceed this threshold. In particular, patients with coexistent heart failure, severe pulmonary disease, or advanced musculoskeletal disease such as arthritis may never manifest symptoms despite having hemodynamics just above the inception of rest pain. Conversely, competitive cyclists may have symptoms of thigh claudication during exercise as a result of external iliac artery end-of-fibrosis, despite having a normal pulse examination and normal anatomic imaging at rest. The classic symptoms of claudication are calf muscle aching, fatigue, or cramping, although it can also involve the buttocks, thigh or hip. The hallmark features are symptoms that are reproducibly elicited with physical activity and are alleviated during rest with abatement during a period of 10 to 15 minutes. A detailed history and a careful physical examination can help differentiate PAD from other causes of lower extremity pain such as spinal stenosis (pseudoclaudication), radiculopathy, arthritis, symptomatic Bakers cysts, benign nocturnal cramps, or other less common diagnoses.

The principal disability in IC is limited exercise performance and walking ability. This translates into a subjective reduction in physical functioning and quality of life. Outside of special populations, the natural history of claudication is often stable during subsequent years. In a classic study from England, of the 1476 patients followed up for ≤10 years, only 11% of claudicants had a clinical deterioration during the observation period. These findings have been reiterated in numerous other reports. Hemodynamic assessment by ankle-brachial indices (ABI) suggests that some populations have a gradual deterioration over time, particularly those at the lowest strata of ankle pressures. Nevertheless, a decline in ABI does not necessarily translate into clinical deterioration, which may be a result of molecular and biochemical adaptation, gradual collateral network formation, a change in the patient’s perception of their disability or the patient altering their gait or activity level to alleviate symptoms. In the absence of diabetes mellitus, <2% of claudicants experience major amputation during a 5-year period. Patient education, risk factor reduction (especially smoking cessation), medical management, and exercise therapy are the primary initial treatment strategies in IC and are reviewed elsewhere in this Compendium.

Revascularization, either percutaneous or surgical, may be appropriate for selected patients with IC who are significantly disabled, impaired in their occupation or activities of daily life, and who have not improved with conservative management. Evidence suggests that successful revascularization in claudicants leads to improved quality of life and functional performance; however, there is little in the way of comparative effectiveness studies in this arena. More clinical trials are needed to develop evidence-based guidelines for the treatment of IC across all subgroups using patient-oriented outcome measures. Until then, the approach for revascularization in IC is individualized—taking into account risks, anticipated benefit, and clinical durability. Ideal patients are those who have a significant disability from IC, have optimized medical management including a trial of exercise, and have revascularization options with a favorable risk:benefit ratio. Given the non–limb-threatening nature of the problem, invasiveness of the procedure, anatomic durability, and freedom from repeat interventions are important considerations in the equation. Patients with bilateral symptoms may not realize functional gain without a successful outcome in both limbs, another factor that must be carefully weighed before deciding to intervene.

Critical Limb Ischemia

CLI is a clinical syndrome of chronic, advanced limb ischemia manifested as rest pain, nonhealing ulcers, and gangrene (necrosis). It is typically associated with markedly impaired perfusion as measured by noninvasive hemodynamic studies (ankle pressure <50 mm Hg or toe pressure <30 mm Hg). In contrast to IC, the fate of both the patient and the limb with CLI is starkly dissimilar. High-quality data from several prospective studies shows annual 10% to 20% mortality for this patient population. The Circulate trial, a randomized placebo-controlled pharmacotherapy trial for CLI patients without revascularization options, demonstrated an all-cause mortality of 10% within the first year in both placebo and treatment arms. The Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial randomized patients with advanced ischemia to either percutaneous or open surgical revascularization. At 2 years, all-cause mortality was 25% independent of treatment type.

The fate of the limb with CLI is also disadvantaged. Natural history data are muddled as most patients receive some form of therapy. Survey data show ranges of primary amputation ≤40% in some centers, whereas other centers offer revascularization in 90% of cases. Data from prospective trials in CLI suggest that the rate of major adverse limb events, defined as any above ankle amputation or major revascularization, approaches 20% in the first year after an intervention.
are no proven options to preserve the limb and relieve ischemic symptoms at this stage of disease other than effective revascularization. Unremitting pain, nonhealing wounds, loss of ambulatory function, and recurrent infections accompany untreated CLI. Therefore, all patients with CLI who have a reasonable life expectancy and functional status should be evaluated for revascularization.

The principle trade-off between endoluminal and open surgical revascularization is the reduced periprocedural morbidity for endovascular interventions versus enhanced hemodynamic gain and long-term durability of bypass surgery. Most of the benefit of reduced short-term morbidity with endovascular interventions comes from avoiding the complications of surgical wounds and the associated recovery, but major adverse cardiovascular events and periprocedural mortality are broadly similar between the 2.16 Evidence-based treatment algorithms in CLI are a moving target, especially as new generations of endovascular technologies are being developed for clinical applications, such as drug-eluting balloons and stents.17,18 An additional limitation of comparative data in this field is the lack of an adequate staging system for the limb to appropriately stratify outcomes. The Society for Vascular Surgery has proposed a Threatened Limb Classification System (wound, ischemia, and foot infection) to fill this void, taking into consideration characteristics of tissue loss, severity of infection, and the extent of ischemia.19 This scheme should allow for more rigorous comparison of outcomes and optimization of treatment protocols.

The only prospective comparative effectiveness data in CLI come from the BASIL trial, now over a decade old.16 In this randomized trial of open versus endovascular interventions for advanced limb ischemia, early results were broadly similar. However, those patients who received a bypass procedure first and survived at least 2 years had lower mortality and greater amputation-free survival in comparison with those treated first with endovascular interventions.11 In addition, patients who required a surgical bypass after a failed endovascular intervention fared worse than those who underwent a bypass first. Current guidelines suggest that patients who are of appropriate surgical and anesthetic risk and who are projected to survive at least 2 years should preferentially receive a vein bypass graft for advanced limb ischemia.20 Higher risk patients with shorter life expectancy, lower functional status, those with favorable occlusive anatomy for percutaneous revascularization, or those who lack adequate autologous conduit should be considered for endovascular treatment.21 A new generation of comparative effectiveness studies to readress this important question is underway, including 2 large multicenter randomized trials in the US (Best Endovascular vs. Best Surgical Therapy in Patients With Critical Limb Ischemia [BEST-CLI]) and UK (BASIL-2).22

**Imaging**

Patients with symptomatic PAD who are deemed suitable candidates for revascularization should undergo imaging to define the anatomic pattern of occlusive disease. High-quality vascular imaging studies are paramount for developing an operative strategy. Catheter-based digital subtraction angiography is generally required for evaluating infrageniculate arterial anatomy before distal bypass surgery. It is of particular importance in CLI, where reliable imaging of the tibial and pedal arteries is mandatory for evaluating the runoff vessels into the foot. Duplex ultrasound also plays an important role in defining the pattern of infrainguinal disease and suitability for endovascular treatment, but is not often used as a stand-alone technique for surgical planning.

In contrast, for aortoiliac disease, surgeons often proceed directly to open surgical revascularization based on computed tomography and MR angiogram imaging alone. Computed tomography angiogram, in particular, informs the operator about the location and distribution of calcified lesions, important in the planning of open aortic surgery. However, diagnostic catheter-based angiography may still be preferred in some cases, such as in the presence of prior stenting or those with spine hardware artifact, which can render computed tomography or MR less accurate.

**Revascularization Strategy**

The emergence of endovascular techniques has changed the landscape of vascular therapy in PAD, but has not fundamentally altered the selection of candidates most likely to benefit from revascularization. As summarized in previous sections, the indication for treatment is predicated on the severity of clinical presentation, with broadly dissimilar initial management strategies (primarily medical versus primarily revascularization) depending on whether the symptoms are claudication or CLI.

Once it is determined that revascularization is an appropriate treatment option, determination of the optimal strategy is highly individualized. Choosing between open versus endovascular approaches takes into consideration a wide variety of factors, including but not limited to the pattern of occlusive disease, anesthetic risk, severity of comorbid conditions, durability of the intervention, extent of tissue loss, previous failed interventions, or other specific anatomic considerations. In contemporary practice, vascular surgeons and interventionalists should be broadly trained with deep understanding of both approaches to provide flexible solutions for the wide range of disease and patient-specific factors encountered and to minimize the downstream consequences of failure on subsequent interventions.

The principle advantages of endovascular interventions are reduced periprocedural morbidity and shorter hospital stays, whereas the frequent drawback is less hemodynamic gain and inferior long-term durability compared with bypass surgery. Aortoiliac disease is particularly well suited for endovascular interventions given the excellent durability in larger caliber vessels and the attendant risks of open aortic reconstruction. However, as noted in the section on aortoiliac revascularization, some situations call for open revascularization, such as a concomitant aortic aneurysm, prior failed interventions, or a significant burden of disease (ie, aortic occlusion). For femoropopliteal disease, technical success for initial treatment can almost always be accomplished with endovascular techniques; however, consideration should be given to the known specific factors that limit durability (lesion length, diameter of vessel, etc). The choice of revascularization is even more complicated in tibiofibular disease, as most patients with CLI have significant comorbidities that translate into shorter life...
expectancy, and endoluminal interventions in tibioperoneal vessels have poor long-term durability (eg, <40% primary patency at 1 year).23

Fundamental Concepts in Surgical Revascularization

Endarterectomy

Endarterectomy is the direct removal of obstructive plaque from an arterial segment and it is best applied for focal lesions in large caliber vessels, particularly at bifurcations (eg, carotid, aortoiliac, common femoral arteries; Figure 1). Initially described by dos Santos,25 then popularized by Wylie in the 1950s, it takes advantage of a cleavage plane between the plaque and the underlying deep media. The advantages of endarterectomy are its autogenous nature without need for conduit. Limitations of endarterectomy relate to adequate securing of the end points, thrombogenicity of the resulting surface in low flow environments, and the subsequent healing response of the artery (intimal hyperplasia), which may lead to recurrent stenosis.

The success of angioplasty and stenting in the aortoiliac segment, particularly for focal disease, has largely led to abandonment of endarterectomy in this location. However, femoral endarterectomy remains a common and important procedure in PAD, allowing for durable reconstruction of the common femoral artery (CFA) and the profunda femoris artery, the key source of collateral circulation to the lower leg. It may be performed in an isolated fashion or as part of a hybrid or open bypass revascularization. Femoral endarterectomy is performed most commonly via longitudinal arteriotomy, with removal of the plaque followed by patch closure (prosthetic or biological materials) allowing for a degree of scarring to occur without subsequent lumen compromise (Figure 1).

Bypass

Surgical bypass is a versatile and flexible tool allowing for revascularization across a broad range of disease patterns, from the aorta down to the foot. The principal elements of technical success are unobstructed inflow, good-quality conduit, and adequate outflow. The inflow source should be free of any hemodynamically significant disease, and outflow should be sufficient to resolve the clinical ischemic syndrome and maintain sufficient flow rates through the conduit. The large caliber arteries and the high-flow environment of aortoiliac reconstructions favor prosthetic grafts for reconstruction. Both Dacron and PTFE have excellent long-term results. Modern fabrication practices with either collagen or gelatin-impregnated Dacron or PTFE have resulted in synthetic materials that have minimal blood loss through the graft, excellent long-term structural integrity, and ability to incorporate into native tissues. A randomized multicenter trial of aortoiliac reconstructions comparing PTFE to knitted Dacron showed no difference in 5-year patency by graft type.26 In general, all commercially available prosthetic grafts perform well in this location. The limitations of prosthetic conduits in these environments relate to the potential for infection (an infrequent, although highly morbid complication), anastomotic pseudoaneurysms, and thrombosis (Tables 1 and 2).

In contrast, small caliber conduits typically required for infrainguinal bypass (≤6 mm) face a more demanding hemodynamic environment for patency. The ideal bypass conduit is an arterial autograft, with its antithrombotic endothelial surface, fidelity to the physiological and mechanical properties of native arterial wall, resistance to infection, and resistance to inflammatory changes that result in stenosis or occlusion. Unfortunately, unlike coronary disease, arterial autografts are not a viable solution for PAD. Superficial extremity veins of appropriate caliber may be readily harvested in relevant lengths and offer a nonthrombogenic, autogenous solution. Venous conduits were first used for surgical reconstructions in the 1940s, initially by Dos Santos as a patch for enterectomy, and later by Kunlin27 for peripheral bypass. In today’s practice, great saphenous vein (GSV) is the dominant conduit for small and medium vessel bypass. Despite significant advances in material sciences, small caliber synthetic conduits have significant limitations, particularly at the graft–vessel interface.

For infrainguinal reconstructions, autologous vein is well established as the optimal conduit. The quality of the vein is the single greatest determinant of long-term outcomes of lower extremity bypass. A single high-quality segment of GSV has been shown in prospective trials to be superior to all other conduits in primary and assisted patency.28 Unfortunately,
limited long-term interface. Recent improvements in prosthetic graft technology, notably heparin-bonding surface technology, may improve patency by altering the compliance at the graft–vessel interface.34,35 When forced to use prosthetic grafts for infrageniculate by-pass, tunneling a graft through a grossly infected field in the absence of available autogenous conduit, as they are more infection resistant than prosthetic materials.

Hybrid Approaches
As endovascular interventions evolve, vascular surgeons are increasingly using hybrid approaches, a combination of catheter-based and open techniques to achieve limb revascularization with less invasiveness. Common examples include open common femoral endarterectomy with concomitant angioplasty and stenting of aortoiliac disease, iliac stenting combined with femoral–femoral or femoral–distal bypass, and superficial femoral artery angioplasty combined with popliteal to pedal bypass. Contemporary vascular surgeons and interventionalists must be broadly trained and competent with both open and endovascular techniques to provide creative and flexible solutions for the range of disease encountered.

Specific Strategies and Expected Outcomes
Strategies for surgical revascularization of PAD are based on the clinical presentation and the anatomic pattern of occlusive disease. Classically, 3 anatomic levels of disease are described: aortoiliac (inflow), femoropopliteal, and tibiopedal (outflow). The CFA is the center point of the limb and is considered a special case of inflow disease. In general, inflow optimization always precedes outflow reconstruction. Claudicants may present with multiple levels of disease, but typically treatment is focused on the most proximal involved segment first, and progresses distally only if required. In some patients with CLI and tissue loss, simultaneous multilevel reconstruction is immediately required to achieve pulsatile flow to the foot for limb salvage.

CFA Disease
Unobstructed inflow to the CFA and outflow via the profunda femoris is the single most important determinant of adequate circulation to the lower extremity. Because the first common femoral endarterectomy performed by Portuguese surgeon Dos Santos in 1948, a variety of techniques have been described, including the closed, semiclosed, evasion, and the most common, the patch angioplasty (Figure 1).25 Because of ease of surgical exposure of the CFA and the ability to perform the procedure under regional anesthesia, even patients with advanced comorbid conditions and isolated disease are candidates for this procedure. Nevertheless, isolated CFA disease is uncommon. Given the importance of the common femoral and profunda femoris arteries, femoral endarterectomy is usually an adjunct procedure during other inflow or outflow revascularizations. However, in patients with rest pain or minor tissue loss in the setting of common femoral disease and a superficial femoral artery (SFA) occlusion, treating the common femoral and profunda femoris alone may often be an adequate solution.

The surgical management of common femoral disease has been challenged by aggressive application of percutaneous techniques. Flexion and extension of the CFA, both during ambulation or when transferring from the seated to the supine position, creates significant motion at the iliofemoral junction. Even flexible self-expanding stents fare poorly in this location

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<th>Table 1. Expected 5-Year Patency Rates for Direct and Extra-Anatomic Surgical Revascularization for Aortoiliac Occlusive Disease</th>
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<td>Intervention</td>
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<td>Aortofemoral bypass</td>
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| ≤40% of patients needing revascularization will not have ade-
| quate ipsilateral GSV available.29 In this scenario, contralat-
| eral GSV, lesser saphenous, and arm veins are the next best 
| options, either as single segments or spliced grafts. Because 
| of the central importance of venous conduit to success of 
| the operation, it is recommended that routine preoperative 
| evaluation includes ultrasound vein mapping. 

Although it is expected that the majority of lower extremity revascularizations can be performed with autogenous vein, there are circumstances where prosthetic grafts may be necessary. Prospective trials have shown a short-term equivalency between prosthetic and vein grafts for femoral to above knee popliteal bypass, with favorable runoff.30,31 However, the preponderance of evidence suggests that even for above knee bypass, autogenous vein outperforms prosthetic grafts at ≥2 years.32 When good-quality vein is not available, a prosthetic is a suitable alternative for bypass to the popliteal level. Some authors have also reported acceptable patency for prosthetic grafts to more distal targets.33 Other putative advantages of prosthetic are shorter operative times and less surgical dissection. However, a major limitation, in addition to reduced patency, is the life-long risk of prosthetic infection, which can be a life- and limb-threatening complication.

Unlike vein grafts, the level of the distal anastomosis has a significant effect on the durability of prosthetic bypasses. Whereas the 5-year patency of prosthetic grafts to the above knee popliteal artery is on the order of 40% to 50%, at the tibioperoneal level, the 5-year patency falls to 15% to 30%.33 When forced to use prosthetic grafts for infrageniculate bypass, surgical modifications of the distal anastomosis, such as with the Miller cuff, Taylor patch, or St. Mary’s boot, may improve patency by altering the compliance at the graft–vessel interface.34 Recent improvements in prosthetic graft technology, notably heparin-bonding surface technology, may improve on the comparatively lower patency rates reported above.

Cryopreserved venous homografts have limited long-term patency as well, with outcomes akin to prosthetic grafts.36,37

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<th>Table 2. Expected 5-Year Patency Rates for Various Infragenicular Revascularization Procedures</th>
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<tr>
<td>Intervention</td>
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<tr>
<td>Femoral endarterectomy</td>
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<td>Femoral-popliteal bypass with vein</td>
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<td>Femoral-tibial bypass with vein</td>
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<td>Femoral-popliteal bypass with prosthetic</td>
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<td>Femoral-tibial bypass with prosthetic</td>
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<td>Pedal bypass with vein</td>
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They are primarily used when treating graft infections or tun-

elining a graft through a grossly infected field in the absence of available autogenous conduit, as they are more infection resistant than prosthetic materials.
Technical success of femoral endarterectomy is the rule, with outcomes of >90%. Late failures are typically the result of progression of occlusive disease. The program can produce functional outcomes equivalent to reconstructing a pressure gradient across hemodynamically significant lesions.

Occlusive disease of the common iliac or internal iliac arteries (AIOD) in patients presents with lower extremity IC symptoms such as rest pain, nonhealing wounds, or gangrenous changes of the aortoiliac segment from pseudoclaudication syndrome. Although rest pain, nonhealing wounds, or gangrenous changes are rare with isolated AIOD and typically require multilevel atherosclerotic changes including involvement of the infringuinal circulation.

Many patients with IC present with palpable femoral pulses. Hemodynamically significant AIOD can be identified during the initial evaluation with noninvasive vascular laboratory studies. Doppler waveform analysis may reveal a delayed upstroke and reduced amplitude at the common femoral level. Although resting ABI can be diagnostic, hemodynamic testing with exercise ABIs is particularly useful in discriminated mild atherosclerotic changes of the aortoiliac segment from pseudoclaudication syndromes, such as spinal stenosis or radiculopathies, which often coexist in this patient population. Treadmill walking or 2-minute heel raises reduce the distal peripheral vascular resistance, creating a pressure gradient across hemodynamically significant stenosis while reproducing symptoms of IC.

There is mounting evidence that a supervised exercise program can produce functional outcomes equivalent to revascularization procedures for select patients with IC. The principle advantage of direct surgical revascularization is the durability of the intervention (Table 1). Ten-year patency rates of 85% for both aortofemoral bypass and aortoiliac endarterectomy are unmatched by endovascular interventions. For patients with unilateral disease, the 5-year patency rates for unilateral iliofemoral bypass exceed 90% in most series. Nevertheless, certain patient populations warrant special consideration. Female patients have consistently lower patency rates, in part because of smaller vasculature. Patients with multilevel disease also have worse long-term outcomes. Several reports also highlight that young patients with premature PAD (age <50 years) have markedly higher failure rates. This may be a reflection of poorly controlled risk factors, particularly tobacco abuse, as well as an aggressive vascular disease phenotype. The same holds true for endovascular
Aortobifemoral Bypass

The typical aortobifemoral bypass grafts a bifurcated prosthetic graft from the infrarenal abdominal aorta to each CFA (Figure 2). Developing the operative strategy requires careful consideration of the patient’s arterial anatomy and prior surgical history. Imaging studies are critical for determining the level of aortic and iliac artery control, the presence of coexistent renal or visceral arterial disease, the presence of concomitant aortoiliac aneurysms, and the status of the outflow vessels. Central to developing the operative strategy is careful management of the pelvic circulation (Figure 2). Inadvertent exclusion of pelvis flow can result in ischemic colitis, bilateral buttock claudication, and rarely spinal ischemia.

The proximal aortic anastomosis may be created in an end-to-end or end-to-side fashion, although the former is usually preferred (Figure 2). The aorta immediately distal to the renal arteries is more likely to be disease free and less likely to progress over time. In addition, the hemodynamics favor nonturbulent flow with the end-to-end anastomosis and the end-to-side anastomosis requires a longer segment of disease-free aorta, which is less frequently encountered with current patient selection algorithms. With the end-to-end anastomosis, pelvic perfusion is maintained via retrograde flow from the external iliac arteries and proximal lumbar and mesenteric collaterals.

The abdominal aorta is usually exposed via a transperitoneal approach through a midline incision. Transverse exposures offer generous access to the aorta, especially to the visceral segment; however, the incision requires division of the inferior epigastric arteries, which are major collateral pathways in AIOD. In the event of graft thrombosis, preservation of collateral networks will allow the patient to revert back to the original circulation rather than progressing to acute limb ischemia. Retroperitoneal approaches may be desirable in patients with significant prior intra-abdominal surgical histories, such as those with stomas; however, it can be challenging to develop the tunnel for the right limb of the bypass graft via a left retroperitoneal exposure.

Figure 2. Aortofemoral bypass grafting. Direct revascularization of the aortoiliac segment (A) can be performed in an end-to-end (B) or end-to-side (C) fashion. The orientation that maximizes pelvic circulation is chosen, with flow either prograde via the common iliac arteries (C) or retrograde via the external iliac arteries (B). Reprinted from Slovut and Lipsitz48 with permission of the publisher.

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suspicion for occult graft infections should be present when treating all pseudoaneurysms. Nonvirulent bacteria such as *Staphylococcus epidermis* can present with pseudoaneurysm formation long after the index procedure. Although late graft infections are rare, occurring in <2% of aortofemoral bypass grafts, they pose a challenging clinical problem. Other signs of graft infection include femoral draining sinus tracts, induration, or cellulitis. Graft infections emanating from an enteric fistula to the prosthetic graft may present with only decreased appetite and failure to thrive. Less subtle symptoms include abdominal tenderness, recurring gastrointestinal bleeds, ileus, or sepsis.

**Iliofemoral Bypass**

An iliofemoral bypass graft is typically applied for unilateral distal iliac disease, grafting a prosthetic graft from the common iliac artery to the CFA. Progression of atherosclerosis in the nonaffected limb is possible, but concerns over future obstructive disease should not preclude consideration of a unilateral iliofemoral bypass. By basing the graft distally without mobilizing the infrarenal aorta extensively, the option to return for direct revascularization of the contralateral side remains viable. Conversely, for high-risk patients, those that have had extensive prior abdominal surgeries or those with failure of a prior graft limb, a crossover femoral–femoral bypass graft is a useful approach. Unilateral axillary-femoral grafts are rarely indicated in elective scenarios, as the long-term results are inferior to direct revascularization or axillary-bifemoral bypasses.

**Other Direct Revascularization Options**

Before the wide spread adoption of prosthetic surgical bypass for AIOD, endarterectomy was the standard of care, with excellent technical success rates and durability. Advantages of the technique include avoidance of complications related to implanting prosthetic material, such as infection or pseudoaneurysm and potentially improved inflow into the hypogastric arteries. Although the technique has been largely surpassed by AFPG, the occasional patients with embolic complications of focal lesions in a large caliber vessel, who are otherwise not well served with percutaneous techniques, are good candidates for this type of intervention.

Finally, there are rare patients who are candidates for direct surgical revascularization but otherwise have an inaccessible abdominal aorta. This may be a result of failed previous aortic bypass, abdominal radiation, or significant atherosclerotic disease above the renal arteries. The thoracic aorta can be used as a source of inflow in these cases via a lateral thoracotomy or thoracoretroperitoneal approach. The durability of this procedure rivals that of aortofemoral grafting.

**Extra-Anatomic Bypass**

In patients with extensive comorbid conditions, such as uncorrectable coronary artery disease, poor ventricular function, advanced pulmonary disease, renal failure, or hostile abdominal anatomy, the increased risks of open surgery may make direct revascularization prohibitive, even in the setting of TASC D lesions. Aggressive endovascular techniques, which can achieve high levels of technical success by experienced providers, may be appropriate despite the absence of long-term outcome data. Conversely, extra-anatomic bypasses are an alternative approach in such patients, particularly when the indication for intervention is limb-threatening ischemia. These techniques, such as the femorofemoral bypass or the axillobifemoral bypass, limit the morbidity associated with major vascular surgery but come at the price of limited durability. Accordingly, these techniques are reserved for patients with CLI and are not generally performed for symptoms of IC.

**Femorofemoral Bypass**

The archetypal femorofemoral bypass grafts a prosthetic conduit from 1 CFA to the other (Figure 3). The principle advantage of the procedure is that it can be performed under local or regional anesthesia, avoiding the potential complications of direct surgical reconstruction of the aorta in patients at higher surgical risk. The procedure is well suited for patients with unilateral AIOD or those who have contralateral side that is free from hemodynamically significant stenosis. Classic examples include patients with a previous iliofemoral bypass or aortobifemoral bypass with a single thrombosed limb. The donor artery should be free of any hemodynamically significant upstream disease. When limited inflow disease (eg, iliac stenosis) is present, it can be corrected first or simultaneously in a hybrid procedure, where angioplasty or stenting of the iliac artery is combined with a downstream cross femoral bypass. Multiple groups have reported satisfactory outcomes with this technique.55

In contrast to the in-line AFB, the durability of extra-anatomic bypasses does not fare nearly as well although it does have acceptable mid-term results for patients who otherwise have a limited life expectancy.51 The 5-year patency rates for femorofemoral bypasses average ≈65%.56,57 Patency rates are most strongly influenced by outflow disease. Results of hybrid endovascular iliac revascularization combined with femorofemoral bypass have acceptable short- and mid-term results, with no apparent difference in patency when compared against historical controls.55 As is
the case with most retrospective single center surgical series, a selection bias may be at least partially attributable to these results.

**Axillofemoral Bypass**

The axillofemoral bypass is well suited for patients with limb-threatening ischemia because of advanced AIOD who would otherwise be considered high risk for direct aortic reconstruction. Other indications include patients with hostile abdomens, such as those with extensive previous surgical history, previous radiation therapy, intestinal stomas, or intra-abdominal sepsis. As the source of inflow pedicles on a long graft from the axillary artery, the amount of hemodynamic improvement for the lower extremities is limited and the maximum flow provided from the graft may be inadequate to fully relieve symptoms of IC. For this reason, this operation is limited to patients with limb-threatening ischemia.

Although the original report describes the procedure performed entirely under local anesthesia, it is typically performed under general anesthesia as 3 distinct and remote surgical fields are exposed. Typically, the right axillary artery is used as a source of inflow, as the left subclavian artery is athero-prone; however, a simple blood pressure measurement is sufficient to determine laterality (Figure 3). As with all aortoiliac reconstructions, optimizing the outflow is key to maintaining the durability of the procedure.

Of the various surgical revascularization options for severe AIOD, the axillofemoral bypass has the lowest 5-year primary patency, with modern series reporting rates averaging 50% to 70%. Outflow through both femoral arteries, rather than a unilateral axillofemoral bypass, has been shown to increase flow in the graft adjacent to the axillary artery and improves the long-term patency of the procedure. Nevertheless, many of these patients have shortened life expectancy and the long-term outcome data are biased by survivors with a lesser burden of disease. Even so, stratifying results by indication shows that results are inferior to aortofemoral grafting.

The surgical morbidity of extra-anatomic bypasses are similar to those of other bypass procedures with prosthetic. There are risks of hemorrhage, wound complications, hematoma, graft infection, and pseudoaneurysm formation. The femorofemoral bypass graft has the unique complication of tunneling subfascial with subsequent bowel and bladder perforation. For axillofemoral grafts, trauma to the brachial plexus, atheroemboli to the hand, and graft avulsion during arm abduction has been reported.

**Femoropopliteal Disease**

Because the first femoral–popliteal bypass with a saphenous vein was performed in 1949 by French surgeon Dr Kunlin, technical advances have broadened the application of the technique to a variety of clinical and anatomic scenarios (Figure 4). In appropriately selected patients, femoropopliteal bypass has proven not only effective but also the most durable intervention for advanced occlusive disease of the femoropopliteal segment. To maximize performance and to minimize infectious complications, the saphenous vein is the preferred conduit. The application of the graft in a reversed or nonreversed orientation, or left in situ, is largely a matter of surgeon preference with no significant impact on surgical outcomes. Up to 40% of patients will not have adequate ipsilateral saphenous vein for use as conduit. Contralateral GSV should be considered next unless the donor limb also has evidence of advanced PAD by either clinical or hemodynamic assessment.

For patients without adequate autologous conduit, prosthetic grafts can be used depending on the indication and pattern of disease. Unlike autologous grafts, there seems to be a significant decrease in patency rates by distal target vessel location, with a progressive decline from the above knee to the below knee location, and an even larger reduction in long-term patency for distal bypass. Only subtle differences in outcomes have been observed among different prosthetics grafts in the below knee popliteal position, whether using Dacron, PTFE, ringed PTFE, and more recently, heparin bonded PTFE.

Short-term results with bypass surgery are also excellent, with early graft failure occurring in ≈5% of vein bypass procedures, largely a result of technical errors. Virtually all patients develop lower extremity edema postoperatively with symptoms that may last for several months. The putative pathogenesis of angioedema is autonomic dysfunction from chronic ischemia, inflammation, and interruption of lymphatics during surgical exposure. Compliance with leg elevation is typically enough to keep lower leg edema in control. Wound complications, although usually minor, are common and can be seen in ≤15% of patients.

Although vein grafts have intrinsic antithrombotic properties, low-dose aspirin therapy is continued through the perioperative period. The effect of antiplatelet therapy on patency is marginal and the benefits are derived from lowering peri-procedural cardiac events. Both dual antiplatelet therapy and anticoagulation have been rigorously studied without any meaningful improvement on patency of vein grafts. The addition of dual antiplatelet therapy or anticoagulation for prosthetic grafts has not been shown to unequivocally improve patency and its use is somewhat controversial. In patients with prior graft failure, poor runoff or with those other features placing the graft at high risk, additional anticoagulation may be considered, but at risk of adding to the 15% of patients who develop wound complications. There is some suggestion that statins may improve long-term outcomes, in both patient who develop wound complications. There is some suggestion that statins may improve long-term outcomes, in both patient survival and graft patency, although definitive studies are pending.

Vein graft stenosis is a common occurrence, being detected in as many as 40% of vein bypasses, typically observed within the first 18 postoperative months. Although a change in symptoms or a change in the ABI of >0.2 should warrant further investigation, ultrasound surveillance is a more sensitive method of detection and early intervention can prolong the longevity of the graft. A surveillance program consisting of a duplex ultrasound at 1, 3, 6, and 12 months after surgery, then every 6 months thereafter is suggested. Changes in the peak systolic velocity (>300 cm/s),
a change in the velocity ratio (>3.5) or a low velocity with blunting of waveforms (<40 cm/s) should prompt a diagnostic angiogram with possible reintervention, even in the absence of a change in the clinical examination. A successful surveillance program will prolong the primary-assisted patency of vein grafts, which is particularly important as the long-term outcomes of a thrombosed vein graft that is salvaged yield poor results. As the modes of failure of prosthetic grafts are distinct, typically the result of anastomotic neointimal hyperplasia, surveillance has not been shown to prolong prosthetic graft patency.

**Tibial–Pedal Disease**

Infrageniculate revascularization is a durable and efficacious intervention for appropriately selected patients (Figure 5). When using high-quality autologous conduit, the level of the distal anastomosis does not affect long-term outcomes, with equivalency demonstrated between bypasses to the popliteal, tibial, or pedal level (Figure 4).

The most basic measure of surgical revascularization is patency. Contemporary results from carefully conducted surgical trials routinely report >80% 5-year patency for vein grafts to infrainguinal targets. By far the most important factor in determining the durability of the operation is the quality of the conduit used. High-quality vein grafts that comprised a single segment of saphenous vein >3.5 mm in diameter perform equally well over time irrespective of the level of the distal anastomosis, including popliteal, tibial, or pedal targets. Long-term results suffer with compromised conduit quality, such as vein grafts that are small in size (<3 mm), spliced vein grafts, and nonsaphenous vein grafts.

In addition, multiple studies have demonstrated that diabetes mellitus is not a risk factor for vein graft failure, including both single center series and prospective data accrued from multicenter trials. As diabetics have a pattern of disease that includes a heavy burden of disease in tibioperoneal arteries, the level of distal anastomosis has proved to be a much weaker predictor of graft failure than conduit quality.

Although graft patency by itself is unaltered in diabetics, amputation-free survival is lower in this patient population. Other nonmodifiable risk factors affecting amputation-free survival include race, sex, infection, and certain comorbid conditions. For example, chronic renal insufficiency is an independent risk factor for limb loss and mortality. Up to 15%
of lower extremity bypass patients with end-stage renal disease may go on to major amputation despite having a patent bypass graft.77 In fact, there is a nearly linear relationship between the degree of chronic renal insufficiency and mortality among patients undergoing lower extremity bypass surgery and the relationship develops well before the onset of end-stage renal disease.78

Finally, although improving ambulatory function is the ultimate goal for IC, it remains a distant goal for more than half the patients with CLI.79 The most important measure of success in CLI is functional outcomes such as ambulatory status, ability to live independently, improved quality of life, and complete wound healing. A minority of patients undergoing bypass for CLI meet all of these functional goals, underscoring the severity of the systemic disease in this patient population. The most predictive factor for high functional outcomes in these patients is preoperative ambulatory status.80 Successful bypass surgery has been shown to improve quality of life in CLI, but maintaining that benefit depends on avoiding reinterventions and achieving complete wound healing.81 This underscores the importance of selecting a durable and effective revascularization in this otherwise high-risk patient population.

Distal Origin Grafts
As the CFA is easily exposed surgically and the anterior surface is often spared of atherosclerotic changes, it is the typical source of inflow for lower extremity revascularization procedures. However, grafts originating more distally in the limb, such as the distal SFA, have been shown to fare equally well in well-selected patients.82,83 Shorter bypasses have higher patency rates than longer grafts, in part because the quality of the conduit improves as marginal segments are excluded. The progression of atherosclerosis proximal to the graft has not been shown to dramatically alter the fate of the bypass. The application of distal origin grafts is particularly well suited to diabetics, who have a pattern of atherosclerosis that spares the femoropopliteal segment and disproportionately involves the tibioperoneal vessels. In fact, distal origin grafts seem to have even better outcomes in diabetics than nondiabetics, even in the setting of more involved tissue loss. In a prospective study, no difference was seen between CFA-based and non-CFA-based bypasses and expectedly, shorter grafts had lower rates of reinterventions.82

A hybrid approach that combines endovascular treatment of proximal femoropopliteal occlusions with surgical bypass distally offers an appealing solution for patients with limited autologous conduit.84 As a general rule, proximal endovascular interventions fare better than distal interventions. The ideal patient for this type of intervention will have a heavy burden of disease in the tibial vessels, with limited short segment disease within the SFA (TASC A). The reverse situation, of bypassing proximal disease and using endovascular interventions for more distal lesions to treat CLI, should only be used in extreme cases.

Scientific Challenges and Major Unmet Needs
Control of Neointimal Hyperplasia
Neointimal hyperplasia is the end result of the prototypic response of blood vessels to injury. An inflammatory response, followed by activation of vascular smooth muscle cells, leads to a proliferative lesion with subsequent elaboration of extracellular matrix and fibrosis. When excessive, this scarring response leads to lumen narrowing (restenosis), the most common cause of failure of all types of endovascular and open vascular interventions. Prevention of restenosis remains the greatest unmet need in the vascular surgical patient. In vein bypass grafts, an early adaptive remodeling occurs in response to increased shear stress and wall tension, resulting in overall vessel enlargement and increased wall thickness.85,86 If the hyperplastic response continues, or is accompanied by a constrictive fibrosis, stenosis may ensue. Vein graft stenosis is most typically focal, for example, in the perianastomotic regions and at valve sites; more rarely it occurs diffusely throughout the graft. Prosthetic graft failure is commonly a result of progressive hyperplasia in the perianastomotic region of the native artery, typically at the outflow side. The process seems pathologically similar, but its course may also be influenced by the chronic host response to the artificial implant and the compliance mismatch across the anastomosis.
Despite progress in the use of antiproliferative drugs to limit restenosis after endovascular interventions (drug-eluting stents and balloons), there is as yet no proven approach to attenuate neointimal hyperplasia in the surgical setting. The Project of Ex vivo Vein graft Engineering via Transfection (PREVENT) trials tested a genetic strategy using a transcription factor (E2F) decoy to block proliferation in vein grafts. Two large randomized trials demonstrated no improvement in either lower extremity or coronary vein graft patency. Although a great deal of translational research continues in this arena, to date no other candidate therapy has reached the stage of advanced clinical testing. Vein grafts offer unique opportunity for targeted molecular/pharmacological intervention at the time of implantation, with the goal of promoting favorable remodeling and subsequent long-term patency.

Small Caliber Vascular Conduits

As previously mentioned, a significant numbers of patients with advanced PAD lack adequate autogenous conduit for infragenual revascularization. For these patients, prosthetics and other available conduits (eg, cryopreserved homografts) offer a compromised solution, with reduced patency particularly for tibial and pedal bypass grafts. The significant need for a small caliber arterial substitute has been a driver of bioengineering research for 2 to 3 decades. Many lessons have been learned and much progress has been made in the efforts to create an off-the-shelf tissue engineered vascular graft. The current favored approach uses human vascular cells to populate scaffolds, elaborate, and organize matrix during in vitro conditioning. Tissue engineered vascular graft have now been used in humans as patches, conduits, and for dialysis access. Two constructs are currently in early stage clinical investigation and are likely to be tested in patients with PAD in the near future. Other approaches being investigated include the use of stem/progenitor cells to populate scaffold constructs, with subsequent recruitment of host vascular cells after implantation. In the coming decade, it seems likely that a commercially available tissue engineered vascular graft will provide a useful new alternative for lower extremity reconstruction.

Adjuvant Medical and Biological Therapies

Optimal medical management of patients after revascularization has to date focused on prevention of major complications and cardiovascular events. After limb revascularization, inflammation, thrombosis, ischemia–reperfusion injury, and remote organ injury may all ensue to various subclinical and clinical degrees. There is considerable room for improved periprocedural interventions to attenuate these deleterious responses and to augment the local tissue response to revascularization. Anti-inflammatory, antithrombotic, and pro-resolving strategies could minimize injury, maintain vessel patency, and promote homeostasis and tissue repair. This could involve nutritional, pharmacological, cell- or even gene-based therapies applied in adjuvant fashion. Future research in this arena offers great opportunity to broadly improve clinical outcomes in vascular patients undergoing invasive treatments.

Conclusions

Surgical revascularization remains a cornerstone of treatment for advanced, symptomatic PAD. The emergence of percutaneous techniques has expanded the armamentarium but has not altered the fundamental principles of revascularization nor the indications for intervention. Rather, the emphasis is placed on patient selection for these complementary modalities. Patient-specific factors are critical in selecting the most efficacious and durable outcome, with particular importance placed on comorbid conditions, estimated life expectancy, functional status, pattern of disease, and availability of conduit.

Disclosures

None.

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Surgical Intervention for Peripheral Arterial Disease
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