Management of Critical Limb Ischemia

Scott Kinlay, MBBS, PhD

Abstract—Critical limb ischemia (CLI) is a clinical syndrome of ischemic pain at rest or tissue loss, such as nonhealing ulcers or gangrene, related to peripheral artery disease. CLI has a high short-term risk of limb loss and cardiovascular events. Noninvasive or invasive angiography help determine the feasibility and approach to arterial revascularization. An endovascular-first approach is often advocated based on a lower procedural risk; however, specific patterns of disease may be best treated by open surgical revascularization. Balloon angioplasty and stenting form the backbone of endovascular techniques, with drug-eluting stents and drug-coated balloons offering low rates of repeat revascularization. Combined antegrade and retrograde approaches can increase success in long total occlusions. Below the knee, angiosome-directed angioplasty may lead to greater wound healing, but failing this, any straight-line flow into the foot is pursued. Hybrid surgical techniques such as iliac stenting and common femoral endarterectomy are commonly used to reduce operative risk. Lower extremity bypass grafting is most successful with a good quality, long, single-segment autogenous vein of at least 3.5-mm diameter. Minor amputations are often required for tissue loss as a part of the treatment strategy. Major amputations (at or above the ankle) limit functional independence, and their prevention is a key goal of CLI therapy. Medical therapy after revascularization targets risk factors for atherosclerosis and assesses wound healing and new or recurrent flow-limiting disease. The ongoing National Institutes of Health–sponsored Best Endovascular Versus Best Surgical Therapy in Patients With Critical Limb Ischemia (BEST-CLI) study is a randomized trial of the contemporary endovascular versus open surgical techniques in patients with CLI. (Circ Cardiovasc Interv. 2016;9:e001946. DOI: 10.1161/CIRCINTERVENTIONS.115.001946.)

Key Words: angioplasty, balloon • drug-eluting stent • endarterectomy • endovascular techniques • peripheral arterial disease

Critical limb ischemia (CLI) is a clinical syndrome of ischemic pain at rest and ischemic tissue loss such as nonhealing ulcers or gangrene, related to peripheral artery disease (PAD) of the lower limbs. It differs from acute limb ischemia, which is a sudden loss of limb perfusion (defined as within 14 days) typically caused by embolus or in situ thrombus. In contrast, CLI occurs over several weeks to months, but is at the extreme end of the spectrum of chronic limb ischemia (Table, Rutherford classification 4–6, Fontaine III/IV). Its importance is because of the much higher risks of limb ischemia defined by the hemodynamic criteria of low ankle or toe pressures, or low transcutaneous oxygen (TcO2) values. Ankle pressure criteria range from <40 to 70 mm Hg, toe pressures <30 to 50 mm Hg, TcO2 <20 to 40 mm Hg. Higher cut points are often used for tissue loss on the assumption that greater perfusion is required for wound healing, but expert consensus on these hemodynamic criteria differs between guidelines.2,4–7 The original definitions were designed to standardize entry criteria for clinical trials of CLI in patients without diabetes mellitus to permit comparisons across studies6,6 or to assess the likelihood of wound healing.8 However, their value as diagnostic tests of CLI in clinical practice is more controversial.2,5,9 Defining specific cut points of toe pressure or TcO2 for the clinical diagnosis of CLI is difficult because of the considerable overlap in values among patients with CLI who do or do not progress to major amputation or cardiovascular events (Figure 1).10,11 One trial suggests that they do not impact the decision for revascularization.12 Other definitions of CLI incorporate wound infection and osteomyelitis in addition to ischemia.13

Definitions

Definitions of CLI aim to identify patients who are risk of major limb amputation without specific treatment such as revascularization or wound care. Traditionally, CLI is defined as rest pain or tissue loss (ulcers or gangrene) supported by ischemia defined by the hemodynamic criteria of low ankle or toe pressures, or low transcutaneous oxygen (TcO2) values. Ankle pressure criteria range from <40 to 70 mm Hg, toe pressures <30 to 50 mm Hg, TcO2 <20 to 40 mm Hg. Higher cut points are often used for tissue loss on the assumption that greater perfusion is required for wound healing, but expert consensus on these hemodynamic criteria differs between guidelines.2,4–7 The original definitions were designed to standardize entry criteria for clinical trials of CLI in patients without diabetes mellitus to permit comparisons across studies6,6 or to assess the likelihood of wound healing.8 However, their value as diagnostic tests of CLI in clinical practice is more controversial.2,5,9 Defining specific cut points of toe pressure or TcO2 for the clinical diagnosis of CLI is difficult because of the considerable overlap in values among patients with CLI who do or do not progress to major amputation or cardiovascular events (Figure 1).10,11 One trial suggests that they do not impact the decision for revascularization.12 Other definitions of CLI incorporate wound infection and osteomyelitis in addition to ischemia.13
For clinical purposes rest, pain or nonhealing wounds may suffice as a definition to justify the use of expensive technology (angiography and revascularization), which are fundamental to the clinical treatment of this condition.

Natural History of CLI
Patient outcomes in CLI are largely determined by morbidity and mortality caused by cardiovascular events and functional impairment caused by limb loss. Although, over the whole spectrum of PAD, cardiovascular events such as myocardial infarction and stroke occur in 30% to 50% of subjects over a 5-year period, patients with CLI face this risk over a 1-year period—an outcome worse than many cancers or severe heart failure. Similarly, although the risk of major amputation (at or above the ankle) is <5% in the following 5 years in patients with claudication, it is at least 30% to 50% in the first year in patients with CLI who do not have revascularization.

Assessment and Initial Treatment
The clinical presentation of CLI depends on the degree of ischemia, the presence of infection, and coexisting neuropathy. Ischemic pain is usually worse when the patient is supine and often requires narcotics for analgesia. It may waken patients from sleep and prevent them from walking. Infection can increase pain even without severe ischemia. Neuropathy can contribute to tissue injury or mask pain from an ulcer.

Current guidelines recommend measuring the ankle pressure or ankle brachial index although medial calcinosis may yield artificially high values in which case toe pressures may indicate arterial obstruction. TcO₂ or skin perfusion pressures may indicate the likelihood of wound healing.

The primary goal is to preserve limb function. Revascularization is a fundamental strategy to limb preservation, but in some patients, this does not improve limb function and mobility. For example, cognitive impairment, nonambulatory status before CLI, and severe comorbidities portend a poor prognosis even with revascularization.15 When revascularization is considered, arterial imaging identifies the targets and mode of revascularization.

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Duplex ultrasound, and noninvasive angiography with computerized tomographic angiography (CTA) or magnetic resonance angiography, can demonstrate arterial obstruction. Duplex ultrasound does not require contrast but requires specific training and may not image the tibial arteries easily. In infrainguinal disease, vein mapping is required to determine the feasibility of surgical bypass with autogenous vein.

CTA requires iodinated contrast and may cause contrast nephropathy in patients with impaired renal function. Heavily calcified arteries can create artifacts that limit CTA particularly in distal disease. Noncontrast time-of-flight magnetic resonance angiography is prone to artifact with nonlaminar flow typical of atherosclerotic plaque, and concerns of nephrogenic systemic fibrosis from gadolinium contrast limit its

Table. Rutherford and Fontaine Classifications of Chronic Peripheral Arterial Disease Severity

<table>
<thead>
<tr>
<th>Symptom Complex</th>
<th>Rutherford Classification</th>
<th>Fontaine Classification</th>
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</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>Stage 0</td>
<td>Stage I</td>
</tr>
<tr>
<td>Intermittent claudication</td>
<td>Stage 1</td>
<td>Stage IIA (symptoms with &gt;200-m walking)</td>
</tr>
<tr>
<td>Moderate claudication</td>
<td>Stage 2</td>
<td>Stage IIB (symptoms with &lt;200-m walking)</td>
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<tr>
<td>Severe claudication</td>
<td>Stage 3</td>
<td></td>
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<tr>
<td>Critical limb ischemia</td>
<td>Stage 4</td>
<td>Stage III</td>
</tr>
<tr>
<td>Rest pain</td>
<td>Stage 5</td>
<td>Stage IV</td>
</tr>
<tr>
<td>Ischemic ulceration (limited to digits)</td>
<td>Stage 6</td>
<td></td>
</tr>
<tr>
<td>Severe ischemic ulceration or frank gangrene</td>
<td>Stage 6</td>
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use in advanced kidney disease. CTA and magnetic resonance angiography are sometimes inadequate to assess the smaller tibial arteries. Nevertheless, CTA and magnetic resonance angiography can help localize disease targets and help plan the mode and approach to revascularization.

Because of limitations in imaging distal arteries noninvasively, invasive angiography is often used to clarify the potential for revascularization and should be considered before major amputation. Invasive angiography uses iodinated contrast and provides the highest spatial resolution. Diagnostic cases can use as little as 30 mL of contrast for both legs with conventional and digital subtraction angiography.

Initial treatments include control of pain, which may require narcotics, pressure relief of ulcers, sheepskin boots to increase superficial collateral supply, and tilting the bed downward to increase limb dependency and perfusion. Pain relief may reverse sympathetic-mediated vasoconstriction. Although some of these measures only marginally improve perfusion, they may reduce the discomfort associated with CLI while planning definitive treatment.

**Endovascular Revascularization**

In many centers, endovascular revascularization is the favored approach to CLI because of lower morbidity and mortality than open surgery (Figure 2). The optimal treatment strategy (endovascular versus open surgery) will depend on anatomic factors, comorbidities, patient preference, and operator experience and skill. Although claudication can be relieved by inflow revascularization (aorto-iliac and femoral), CLI is often associated with multilevel disease and usually requires outflow (tibial) revascularization as well as treating inflow disease. Much of the evidence for endovascular treatment of inflow disease is based on studies of patients with claudication or a mix of claudication and CLI.

**Inflow and Femoral-Popliteal Disease**

Aorto-iliac disease can be approached from the ipsilateral or contralateral common femoral arteries or brachial and radial arteries. Rarely, a retrograde approach from the popliteal artery can assist crossing superficial femoral artery (SFA) occlusions, which cannot be traversed antegrade (Figure 3). The retrograde popliteal approach requires access from above from the contralateral or antegrade common femoral artery, and then turning the patient prone on the table and using ultrasound with a micropuncture needle to access the popliteal artery at or just above the knee joint. Small sheaths (4–5F) provide access for a wire, which can be snared from above once it traverses the occlusion. A wire that is exteriorized above and below occlusion provides a rigid rail to assist pushing catheters and balloons through an occlusion (the dental floss technique).

A variety of systems are used to cross lesions including 0.035″, 0.025″, 0.018″, and 0.014″ diameter wires and balloons. Concerns of recoil of ostial lesions and dissections associated with occluded or calcified disease has led to the almost universal practice of primary stenting in iliac disease. Balloon expandable stents offer greater radial force and a more precise deployment (especially useful in ostial locations), whereas nitinol self-expanding stents may be useful in long tapered lesions. Covered stents are useful for life-threatening perforations of the iliac artery during endovascular treatment. Their value in preventing restenosis is uncertain because of concerns of increased rates of stent thrombosis and the potential to jail and occlude branch vessels.

Common femoral disease often involves the profunda and SFA origins. Endovascular treatment alone can achieve durable results with acute dissection of the common femoral artery
from arterial closure devices. Stents are avoided in this region because of the repeated flexion and extension of this artery and potential for stent fracture, as well as jailing the profunda artery—an important collateral in the event of SFA occlusion. Preservation of both branches with balloon angioplasty alone can be difficult with complex calcified plaques, and often surgical endarterectomy with patch angioplasty offers a more durable result. Hybrid endovascular-surgical approaches using endovascular approaches for iliac or superficial femoral disease and endarterectomy for common femoral disease are increasingly used. New developments in atherectomy and drug-coated balloons have renewed interest in endovascular approaches for common femoral disease although this paradigm needs formal testing in clinical trials.

The SFA is the longest artery in the leg and subject to flexion, compression, and torsion. These forces are particularly important close to the knee and the common femoral artery. Balloon angioplasty offers similar results to stenting in short lesions (<100 mm) when there is good arterial expansion without flow-limiting dissections. Minor dissections often heal without long-term sequela. Nitinol self-expanding stents offer better long-term patency in longer lesions and re-expand after external radial compression. Stent fracture is thought to increase instent restenosis, but is much rarer with the newer self-expanding stent platforms. Recent drug-eluting stent designs offer a lower rate of restenosis than bare-metal self-expanding stents.

Drug-coated balloons offer lower rates of restenosis than balloon angioplasty alone in patients with SFA disease and claudication. Drug-coated balloons also prevent restenosis when used before bare-metal stent deployment and offer more durable treatment of instent restenosis of the femoral artery. The evidence supporting drug-eluting stents and drug-coated balloons requires further testing, particularly in areas where stents are avoided (over the knee and hip joints). Given the high risks of major amputation, stenting over the knee joint is sometimes required to maintain patency. Many specialty stents with greater durability to repeated flexion are designed for the popliteal artery in particular.

Tibial Disease

There is rarely a justification for tibial interventions in claudication. However, wound healing and relief of CLI is more dependent on establishing straight-line flow into the foot. Therefore, below-knee popliteal and tibial artery interventions are more commonly pursued in CLI.

Access is more limited for distal tibial disease as a contralateral common femoral approach or brachial approach are often too distant for most equipment based on 130- to 150-mm shaft lengths. An antegrade femoral approach also gives more pushability to drive through long occlusions. The retrograde tibial approach can be used for tibial and popliteal occlusions, which cannot be crossed antegrade (Figure 3), but if unsuccessful may create a nonhealing ulcer at the access site. The retrograde pedal or tibial artery approach uses ultrasound and a micropuncture needle for access and the dilator of the micropuncture kit or a small sheath for wire access. Access from above (eg, antegrade femoral) allows a retrograde wire to be snared and exteriorized above and below the tibial or popliteal occlusion to provide a rigid rail to drive catheters and balloons through an occlusion (Figure 5).

The value of angiosome-directed revascularization versus restoring any straight-line flow into the foot is debated. The former assumes that revascularization of a tibial artery supplying the angiosome of the ulcer or gangrenous region (Figure 6) is more likely to promote healing than nonangiosome revascularization, which relies on increased collateral flow to an ischemic region. In observational studies, wound healing was greater.
and amputation was lower with angiosome-directed than indirect (nonangiosome) tibial revascularization. However, these observations may be confounded. Indirect revascularization may be a marker for more complex tibial disease, which may be associated both with no option for angiosome-directed revascularization and poorer limb salvage. In 1 study, changes in foot microcirculation assessed by skin perfusion pressure improved regardless of whether the angiosome-related tibial artery or the nonangiosome-related artery was revascularized. Although it makes intuitive sense to use an angiosome-directed treatment wherever possible, if this is not successful, any straight-line flow should be better than none.

Primary balloon angioplasty of tibial disease provides a good response in most situations. Long balloons are specifically designed to treat the often diffuse tibial disease with prolonged inflations. Stents are reserved for poor balloon results (reocclusion, recoil to \(>50\%\) stenosis, flow-limiting dissection). Tibial arteries are \(\approx2.5\) to \(3.5\) mm in diameter and are usually treated with balloon expandable coronary stents with a spot-stenting philosophy. Proximal lesions are somewhat protected by the bulk of the calf muscle, but can theoretically be crushed by external compression. Stent crush is more likely with extensive stenting and stents in the distal calf. Poor outflow theoretically increases the risk of stent thrombosis and may reduce the enthusiasm for stenting. Randomized studies in tibial arteries show better patency and less need for reintervention with drug-eluting than with bare-metal coronary stents, with 1 trial showing lower rates of amputation.

Compared with conventional balloon angioplasty, drug-coated balloons for tibial interventions provided promising results in early series and single-center trials. However, restenosis rates were higher than drug-eluting stents in 1 small trial, and the multicenter randomized Amphirion Deep Drug Eluting Balloon vs Standard Percutaneous Transluminal Angioplasty for the Treatment of Below the Knee Critical Limb Ischemia (IN.PACT DEEP) study raised concerns because of a trend to more amputations in the drug-coated versus standard balloon angioplasty arms (8.8\% versus 3.6\%; \(P=0.08\)). Reasons for the lackluster results when compared with femoral-popliteal disease include reduced drug delivery because of drug coating after balloon wrapping and poor drug-release characteristics. Further randomized trials will explore their value in tibial arteries.

Atherectomy in tibial arteries is of uncertain value beyond balloon angioplasty and stenting. Long segment tibial atherectomy could cause embolization, which decreases outflow and distal perfusion. One recent report showed greater acute success, but no difference in amputation, repeat revascularization, or mortality with laser-assisted versus conventional angioplasty. Wire perforation of the tibial arteries is usually easily treatable by low-pressure balloon angioplasty, but larger perforations may require longer balloon inflations or covered stents to avoid a compartment syndrome, which can cause ischemic muscle and nerve injury and threaten the viability of the lower limb.

**Open Surgical Revascularization**

The goals of surgical revascularization are to provide straight-line flow into the foot, promote wound healing, and to limit the
level of amputation. Open surgery has higher risks of perioperative myocardial infarction, death, and stroke than endovascular revascularization. However, in CLI, the potential loss of limb and function may favor surgery when endovascular therapy is not possible or not successful and patients otherwise have a reasonable 2-year survival. Risk scores can help risk-stratify CLI patients having infragenual bypass surgery. For example, the Project of Ex-Vivo Graft Engineering via Transsection III (PREVENT III) risk score includes dialysis, tissue loss, age ≥75 years, and coronary artery disease. A higher score associates with a lower risk of survival free from amputation. In addition to patient risk, assessment includes vein mapping of saphenous vein to determine available autogenous conduit. This is particularly important in patients who may have had vein harvested for coronary artery bypass in the past.

Multilevel disease is often treated with hybrid revascularization using endovascular techniques to treat inflow disease (eg, iliac stenting) and surgical revascularization for femoral or infrainguinal disease (eg, common femoral endarterectomy and femoral popliteal bypass). Rarely, occlusion of the distal aorta and iliac disease may require aorto-bifemoral bypass, contralateral femoral to femoral bypass, or axillary-femoral bypass.

Common femoral endarterectomy may extend into the proximal SFA or profunda artery. Closure is usually achieved with a bovine or synthetic patch to reduce restenosis, or sometimes with primary closure without a patch. Complications include wound infection (particularly in patients with obesity), hematoma, and lymph leak. This procedure offers a high long-term patency rate (>90%) and considered superior to endovascular treatment particularly for heavily calcified disease involving the SFA and profunda origins.

As with endovascular treatment, infragenual bypass relies on good inflow and outflow. The 3 types of saphenous vein bypass are reversed (translocated) vein, nonreversed vein, and in situ bypass where vein branches are ligated and the distal ends mobilized and anastomosed to the artery. The latter 2 configurations require excision of the valves with a valvulotome, which can sometimes injure the vein conduit. Observational studies suggest similar outcomes with all 3 configurations. Limb salvage and graft patency are best with good quality, long, single-segment, autogenous vein with a diameter of at least 3.5 mm. In the PREVENT III trial, bypass grafts with these characteristics had a low 30-day failure rate (<2%) and high secondary patency and limb salvage at 1 year (>90%).

In pooled analyses, autogenous saphenous vein provided better long-term patency than prosthetic grafts for above- and below-knee grafts. Prosthetic grafts of heparin-bonded polytetrafluoroethylene may provide better outcomes than older prosthetic grafts with comparable results with autologous vein in a 1 retrospective study. Cryopreserved cadaveric vein has poorer long-term patency results.

Comparisons of Open Surgical Versus Endovascular Revascularization

The only randomized study comparing endovascular versus open surgical treatment of patients with CLI is the Bypass Versus Angioplasty in Severe Ischaemia of the Leg (BASIL) study. This trial published a decade ago, demonstrated no difference in major amputation or death >5 years. Rates of myocardial infarction, wound infection, pulmonary complications were higher in the surgical group, and repeat revascularization was higher in the endovascular arm. However, over the past 10 to 15 years, perioperative mortality from open surgery has improved, and there are more options for graft salvage with endovascular techniques. Similarly, endovascular options developed after the BASIL trial include bare-metal stents, drug-coated balloons and stents, and a variety of wires and devices to assist crossing long occlusions.

More recently, several proposals for end points important in CLI have converged on limb salvage (avoiding a major amputation) and the need for major reintervention (a new bypass graft, or thrombolysis of graft or treated segment). As a result of these developments, the National Institutes of Health sponsored the Best Endovascular Versus Best Surgical Therapy in Patients With Critical Limb Ischemia (BEST-CLI) study, a new randomized trial of open surgery versus endovascular revascularization in CLI.

BEST-CLI will assess open surgery or endovascular revascularization in patients who are acceptable candidates for both techniques. The primary end point of BEST-CLI includes major limb amputation, repeat major intervention (thrombolysis or new bypass graft), and mortality. These reflect life- and limb-threatening events that have major effects on quality and quantity of life, as opposed to minor procedures to treat restenosis, which are not included in the primary end point. BEST-CLI will also include assessments of quality-of-life and cost-effectiveness.

Amputation

Minor amputations such toe, ray (toe and metatarsal), or transmetatarsal amputations require an adequate blood supply into the foot to maximize healing and are usually a part of the treatment plan for gangrene or tissue loss after successful revascularization. Generally, minor amputation does not limit functional independence or require a prosthesis.

Major amputations (at or above the knee) limit functional independence and require a prosthesis to walk. Although preventing major amputation is a key goal, amputation may be indicated for failed revascularization, patients with extensive tissue loss or infection, patients unfit for surgical revascularization with no endovascular options, and potentially nonambulating patients. Up to one third of below-knee amputations may require further surgery or an above-knee amputation caused by poor healing. A patent popliteal pulse reduces the failure rate of healing to <10%. More than 90% of above-knee amputations heal, but only ≈20% of amputees regain full mobility with a prosthesis when compared with 60% with a below-knee prosthesis. Factors related to poor prosthesis use and function after major amputation include increasing age, bilateral or above-knee amputations, dementia, and poor function before amputation.

Wound Care

Wound care principles include improving perfusion into the limb, treating infection, avoiding pressure on a wound,
debridement, and adequate nutrition. Debridement of devitalized or infected tissue by scalpel, collagenases, or even maggots promotes wound healing. Antibiotics may be required to treat infection to prevent osteomyelitis. Avoiding pressure on the wound (eg, off-loading the foot) also assists wound healing. The local temperature of the limb can be increased using sheepskin (Rooke) boots and may improve superficial collateral flow to help perfuse a limb. Negative pressure dressings (eg, vacuum-assisted) increase capillary flow and help drain wounds. Hyperbaric oxygen therapy offers no advantages for amputation prevention, but may improve the more subjective end point of wound healing in diabetes mellitus.

In patients where there are no revascularization options, intermittent pneumatic compression may assist wound healing and prevent major amputation. To date, cell-based therapies such as infusion of bone marrow–derived mononuclear cells have not prevented major amputation in patients with no revascularization options.

Medical Therapy and Surveillance After Revascularization

Failure of endovascular and surgical treatment of CLI caused by thrombosis, neointimal proliferation, or progression in atherosclerosis demands close surveillance of patients by providers with vascular expertise. Surveillance also includes intensively treating risk factors for atherosclerosis to reduce the high risk of cardiovascular events.

Recurrent ischemic pain in the leg, lack of progression in wound healing, or a decline in ankle brachial indices are indicators of restenosis or occlusion. Duplex ultrasound of bypass grafts is commonly practiced to identify graft stenoses for revision and preserve long-term patency. However, this practice was not associated with lower amputation or better patency in 1 randomized trial, and there are no randomized trials of its value after endovascular therapy. Our practice after endovascular therapy includes a history and examination, and to use duplex ultrasound in the femoral artery particularly after treating long segment disease or when symptoms or poor wound healing raise concerns of patency.

Evidence for therapies to prevent thrombosis or restenosis after endovascular interventions is sparse and often extrapolated from studies of coronary artery interventions. Low-dose aspirin is usually given for life to prevent not only thrombosis of a treated segment but also other cardiovascular events. The duration of clopidogrel to prevent occlusion of segments treated by endovascular techniques is uncertain. Most clinical trials of bare-metal stenting use dual-antiplatelet therapy for 1 to 3 months, but data extrapolated from medical studies of patients with PAD could justify longer treatment. Clinical studies from Japan suggest that cilostazol may reduce instant restenosis, but this is not yet incorporated in recent guidelines of revascularization for CLI.

The value of anticoagulation for lower extremity bypass is conflicting with some trials showing benefit over aspirin for autogenous vein versus prosthetic conduit and vice versa. Given the increased risk of bleeding, most surgeons reserve anticoagulation for graft thrombosis or hypercoagulable disorders. There is no benefit of adding clopidogrel to aspirin for graft patency.

Evidence for the value of intensive atherosclerosis risk factor reduction is derived largely from observational studies and subgroups of patients with PAD in clinical trials. For example, patients with PAD who stop smoking have fewer cardiovascular events than those who continue smoking. Antiplaletel therapy with aspirin or clopidogrel and angiotensin-converting enzyme inhibitors decrease cardiovascular events in patients with PAD. Intensive statin therapy consistently lowers cardiovascular events in patients with PAD than no statin or low-intensity statins. In observational studies of patients receiving revascularization for PAD, statin therapy is associated with lower risks of cardiovascular events and limb loss. In population studies, intensive risk factor modification in patients with PAD is improving, but still lags behind its use in patients with symptomatic coronary disease.

Conclusions

Patients with CLI have a high risk of limb loss without revascularization and a high short-term risk of cardiovascular events when compared with less severe forms of chronic PAD. Revascularization is indicated if it will prevent limb loss and preserve ambulation and function, whereas intensive medical therapy targets the risk factors for atherosclerosis progression and cardiovascular events. Endovascular revascularization offers a lower initial risk than open surgery, but recurrent disease from restenosis or new de novo disease is common in patients with CLI. New drug-eluting balloons and stents offer better longer term outcomes after some endovascular revascularizations, but further long-term data on durability are required to assess their overall benefit given the increased costs of initial treatment. Close follow-up focusing on wound care and prevention, risk factor management, and surveillance for new and recurrent disease is required.

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