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Critical limb ischemia: medical and surgical management

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Abstract: Chronic critical limb ischemia (CLI), defined as > 2 weeks of rest pain, ulcers, or tissue loss attributed to arterial occlusive disease, is associated with great loss of both limb and life. Therapeutic goals in treating patients with CLI include reducing cardiovascular risk factors, relieving ischemic pain, healing ulcers, preventing major amputation, improving quality of life and increasing survival. These aims may be achieved through medical therapy, revascularization, or amputation. Medical therapy includes administration of analgesics, local wound care and pressure relief, treatment of infection, and aggressive therapy to modify atherosclerotic risk factors. For patients who are not candidates for revascularization, and who are unwilling or unable to undergo amputation, treatments such as intermittent pneumatic compression or spinal cord stimulation may offer symptom relief and promote wound healing. Revascularization offers the best option for limb salvage. The decision to perform surgery, endovascular therapy, or a combination of the two modalities ('hybrid' therapy) must be individualized. Patients who are relatively fit and able to withstand the rigors of an open procedure may benefit from the long-term durability of surgical repair. In contrast, frail patients with a limited life expectancy may experience better outcomes with endovascular reconstruction. Hybrid therapy is an attractive option for patients with limited autologous conduit, as it permits complete revascularization with a less extensive procedure, shorter duration of operation, and decreased risk of peri-operative complications. Amputation should be considered for patients who are non-ambulatory, demented, or unfit to undergo revascularization.

Key words: critical limb ischemia; medical therapy; revascularization

Introduction

Chronic critical limb ischemia (CLI), defined as > 2 weeks of rest pain, ulcers, or tissue loss attributed to arterial occlusive disease, is associated with great loss of both limb and life.[1] At 1 year following presentation, 25% of patients have resolved CLI, 20% have ongoing CLI, 30% are alive with amputation, and 25% are dead.[1] Therapeutic goals in treating CLI patients include reducing cardiovascular risk factors, relieving ischemic pain, healing ulcers, preventing major amputation, improving quality of life and increasing survival. These aims may be achieved through medical therapy, revascularization, or amputation.[1]

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Pathophysiology of critical limb ischemia

Under normal circumstances, healing of ulcers occurs unless wound repair mechanisms are altered; this may include diminished arterial perfusion, infection, or repeated trauma. In the insensate foot, repeated trauma (especially shear force) results in ulceration. Non-healing wounds occur as the result of arterial insufficiency, neuropathy, musculoskeletal abnormalities, or a combination thereof.[2] Decreased perfusion is most commonly due to atherosclerotic occlusive disease of major arterial conduits. Patients with relatively mild symptoms of arterial insufficiency may develop non-healing ulcers if other factors are involved, as the blood supply needed to heal an ulcer is greater than that needed to maintain an intact integument. Another frequent risk factor for foot ulceration is neuropathy, both sensory and autonomic. In addition to reducing sensation to pain and thermal stimuli, neuropathy involving motor fibers leads to ataxic gait and weakness of the foot muscles. High stress loads in areas not typically used to weight-bearing, accompanied by loss of protective sensation, leads

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to increased shear stress, repetitive trauma, and skin breakdown. Foot ulcers in diabetic patients tend to have a mixed ischemic and neuropathic etiology.

CLI occurs when arterial lesions impair blood flow to such an extent that the nutritive requirements of the tissues cannot be met.[1] Ordinarily, the skin microcirculation is involved in skin tissue nutrition and heat exchange during thermal stress.[3] In patients with CLI, compensatory mechanisms of skin perfusion are exhausted; the skin fails to receive adequate nutrition.[3] Inadequate perfusion leads to a host of microcirculatory defects including endothelial dysfunction, altered hemorrheology, inflammation, and loss of sympathetic autoregulatory response to alteration in posture.[1] Rheologic disturbances are present as well, including decreased erythrocyte fluidity, blood viscosity, and erythrocyte volume fraction.[4] The net effect of these derangements is rest pain, trophic changes, and impaired wound healing.

Non-invasive evaluation of CLI

Multiple tests have been devised to confirm the diagnosis of limb-threatening ischemia, assess foot perfusion, and predict wound healing (Table 1). The ankle–brachial index (ABI) provides key prognostic and diagnostic information for patients with CLI.[5] In patients with incompressible lower limb arteries, an ABI > 1.3 represents an independent predictor of major amputation.[6] In patients with a falsely elevated ABI, the toe–brachial index (TBI) or toe pressure may be diagnostic. However, based upon results from a recent randomized trial, even where the diagnosis of CLI is uncertain, the addition of toe pressures and $TcPO_2$ (see below) does not alter the number of diagnostic studies or therapeutic interventions.[7]

Skin microcirculation may be assessed using capillary microscopy, laser Doppler perfusion, or transcutaneous oxygen pressure ($TcPO_2$). Nailfold capillary microscopy of the great toe enables visualization of capillary morphology, density, and erythrocyte velocity at rest and during reactive hyperemia. The use of dyes such as sodium fluorescein permits the study of microvascular dynamics, flow distribution, and microvascular permeability.[3] Laser Doppler perfusion is used to provide information about flow in capillaries, deeper vessels, and arteriovenular anastomoses that are involved in thermoregulation.[8] $TcPO_2$, a non-invasive measure of skin oxygenation, is reduced in the presence of impaired blood flow. Measures of skin microcirculation were used prospectively to predict amputation in 111 CLI patients with unreconstructable vascular disease.[9] Microcirculation was classified as 'good', 'intermediate', or 'poor' according to a combination of cut-off values (poor: capillary density < 20/mm^2, absent reactive hyperemia in capillary microscopy and laser Doppler, $TcPO_2$ < 10 mmHg; good: capillary density > 20/mm^2, reactive hyperemia in capillary microscopy and laser Doppler, $TcPO_2$ > 30 mmHg). Limb survival at 1 year was 15% in the poor group, 63% in the intermediate group, and 88% in the good group. Patients who are not candidates for revascularization and who have poor skin microcirculation may be best served by undergoing amputation rather than aggressive local therapy.

Table 1 Features of critical limb ischemia

Physical exam
Dry skin, thickened nails, loss of hair, loss of subcutaneous fat or muscle atrophy
Coolness to palpation
Decreased or absent pulses
Elevation pallor or dependent rubor
Non-healing wound or ulcer, especially over bony prominences, distally, and on the plantar surface of the foot
Non-invasive vascular laboratory
Ankle–brachial index ≤ 0.4
Ankle systolic pressure ≤ 50 mmHg
Toe systolic pressure ≤ 30 mmHg
Measures of skin microcirculation
Capillary density ≤ 20 mm^2
Absent reactive hyperemia on capillary microscopy
$TcPO_2$ < 10 mmHg

Therapy for patients with critical limb ischemia

Risk factor modification

Medical therapy for CLI patients includes pain relief, local ulcer care and pressure relief, treatment of infection, and modification of atherosclerotic risk factors.[1] Most CLI patients have concomitant cerebrovascular and coronary disease, which accounts for mortality rates of 13.4% at 6 months, 19–25% at 12 months,[10,11] and > 60% at 5 years.[12] Yet, with distressing frequency, these patients are not given aspirin, beta-blockers, or statins – agents that have been shown to reduce cardiovascular morbidity and mortality.[13–15] PREVENT III (PRoject of Ex-Vivo vein graft ENgineering via Transfection III) examined the treatment regimens of 1404 patients who required infrainguinal bypass for limb salvage.[16] Only 67% of the patients were taking an antiplatelet drug (aspirin in 50% and a thienopyridine in 17%), only 46% were receiving lipid-lowering therapy, and despite facing major vascular surgery, only 49% were prescribed a beta-blocker.[16] Among the patients not receiving a beta-blocker at trial entry, the adjusted odds ratio of an event was 3.9 times higher in those with a prior history of advanced coronary artery dis-

ease compared with those without such a history. In the Coronary Artery Revascularization Prophylaxis (CARP) trial, 80% of CLI patients received an antiplatelet agent, 46% a statin, and 77% a beta-blocker.[17]

Mechanical devices

For CLI patients who are not candidates for vascular reconstruction, several therapeutic options are available, including intermittent pneumatic compression, spinal cord stimulation, lumbar sympathectomy, hyperbaric oxygen, and ultrasound. In a series of 101 CLI patients with non-healing wounds, intermittent pneumatic compression (IPC) led to complete wound healing and limb preservation in 40% of patients with $TcPO_2$ levels < 20 mmHg, 48% of patients with osteomyelitis, and 46% of patients with insulin-dependent diabetes mellitus.[18] Kavros and colleagues conducted a retrospective study to examine the efficacy of IPC on patients with chronic non-healing amputation wounds of the foot and tissue loss attributable to CLI on whom all means of additional revascularization had been exhausted.[19] Controls received standard wound care. Patients in the active treatment group received 6 hours of IPC (ArterialFlow; DJO, Vista, CA, USA) in addition to standard wound care. At 18 months follow-up, wound healing and limb salvage were significantly better for patients who received IPC. The below-knee amputation rate for IPC patients was 42% versus 83% for controls.

A prospective 17-center European trial found that compared with controls, patients who received spinal cord stimulation showed improved microcirculation, Fontaine Class at 12 months, limb survival at 12 months (78% vs 50%), and pain relief.[20] A Cochrane review concluded that spinal cord stimulation was superior to medical management for treating CLI patients with unreconstructable disease.[21] Another option for selected patients is surgical or chemical lumbar sympathectomy, which improves skin blood flow in the leg and foot[22] and is associated with 1-year limb salvage rates of 58–61%.[23]

Prostaglandins

Iloprost – an analogue of prostacyclin I_2 that acts as an arterial vasodilator, promotes angiogenesis, decreases inflammation, and inhibits platelets – has been studied for treating CLI. Results have been mixed. A meta-analysis of five placebo-controlled, randomized prospective trials of intravenous iloprost in patients with CLI found a significantly decreased incidence of major amputations in patients who received iloprost.[24] These findings have not been replicated by more recent studies using oral iloprost[25] or parenteral lipo-ecraprost as destination therapy[26] or as adjunctive therapy immediately following distal revascularization.[27] Based on available data, prostaglandins cannot be recommended as therapy for patients with CLI.

Therapeutic angiogenesis

Therapeutic angiogenesis using stem cells,[28] autologous progenitor cells,[29,30] growth factors such as basic fibroblast growth factor (bFGF),[31] and transcription factors such as hypoxia-inducible factor-1 alpha that induce synthesis of angiogenic cytokines [32] have been utilized in CLI patients who lack options for endovascular or surgical revascularization. For example, in one randomized, placebo-controlled study, bone marrow-mononuclear cells were injected into the gastrocnemius muscle in 45 critically ischemic limbs.[29] Significant improvement in ABI, $TcPO_2$, rest-pain scale, and pain-free walking time was noted at 4 weeks and sustained at 24 weeks in treated patients. Angiographic evaluation showed that 27 of 45 patients developed a striking increase in the number of visible collaterals compared with baseline. The preliminary results of this and other studies of novel therapeutic approaches for CLI patients appear promising. As yet, however, none of these therapies has been tested in a large-scale, randomized trial.

Wound care

The basic tenets of wound healing include assurance of adequate perfusion to the ischemic limb, adequate nutrition, and absence of infection or mechanical features that might inhibit healing. To this end, surgical debridement of infected wounds is often required before healing can be expected to occur. In addition, debridement by hydrotherapy, negative pressure therapy, and wound dressings can assist in preparing wounds with less severe degrees of infection and necrosis. Finally, biosurgery (myiasis) with sterile maggots has been shown of benefit in debriding a variety of wounds.[33]

Vacuum-assisted closure is a negative-pressure healing technique that uses subatmospheric pressure to remove excess fluid from the wound, which leads to improved oxygenation and blood flow. The technique is particularly useful to expedite healing large wounds. It is contraindicated in patients with thin, friable skin and in those with wounds secondary to neoplasm.[34] The addition of non-contact, low-intensity, low-frequency ultrasound therapy to standard wound care leads to more rapid wound healing than standard wound care alone.[35] Hyperbaric oxygen therapy has been recommended for a variety of non-healing wounds. A systematic review of the available literature, however, failed to find evidence that hyperbaric therapy was efficacious in healing chronic wounds. It may have a role in reducing the

risk of major amputation in patients with diabetic foot ulcers.[36] A variety of topical therapies are available for use in chronic wounds, including platelet-derived growth factor, which has been shown to be safe and effective in the healing of chronic, full-thickness neurotrophic ulcers.[37]

Revascularization

Even with aggressive local wound care, patients with severe limb ischemia and chronic ulceration who do not undergo revascularization often progress to amputation, with the likelihood of amputation increasing as the ABI decreases. In a series of 142 patients (169 limbs) with arterial insufficiency and full thickness ulcers who did not undergo an attempt at revascularization, the 12-month amputation rate for limbs with ABI 0.5–0.7 was 15%, for limbs with ABI < 0.5 it was 32%, and for limbs with ABI < 0.4 it was 43%.[38] Revascularization to reestablish continuous in-line flow to the pedal arch represents the preferred treatment for patients with limb-threatening ischemia.[1] Options for revascularization include surgery, endovascular intervention, and 'hybrid therapy', a combination of surgical and endovascular therapy.

Surgical revascularization

Surgical revascularization is warranted for patients with complex lesions that are not amenable to catheter-based intervention, and for younger patients with prolonged life expectancy who require a more durable revascularization. Surgery represents the optimal revascularization strategy for patients who are relatively fit, can withstand the rigors of an open procedure, and have a life expectancy greater than 2 years. Aortoiliac disease may be treated with anatomic or extra-anatomic bypass (e.g. axillofemoral, axillobifemoral, or femorofemoral bypass). Patients who undergo extra-anatomic repair are generally older, more likely to have advanced ischemia, previous aortofemoral inflow operation, renal insufficiency, and severe chronic obstructive pulmonary disease (COPD).[39] A meta-analysis of 95 articles revealed a late patency of 82–92% for aortofemoral grafts, 52–83% for femorofemoral grafts, and 45–62% for axillofemoral grafts.[40] Similar patency rates have been observed in more contemporary series.[39,41] At 5 years, limb salvage rates following surgical revascularization for aortoiliac occlusive disease are 90–94% for anatomic bypass procedures and 60–90% for extra-anatomic procedures.[40] Mortality and systemic morbidity for anatomic bypass have decreased over time, even as the complexity of cases has increased.[42,43] Aortobifemoral bypass may be performed laparoscopically, but this approach does not appear to alter overall morbidity and mortality.[44,45] Despite the superior durability of anatomic bypass compared with angioplasty and stenting,[46] there has been an 850% increase in utilization of iliac artery angioplasty and stenting, and a decrease of 15% in aortobifemoral bypass from 1996 to 2000.[47]

Bypass for infrainguinal occlusive disease is associated with limb salvage rates > 80%[48] and mortality rates of 0.97–2.0%.[49–51] To date, the Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial remains the only prospective, randomized trial to compare outcome of a surgery-first with an angioplasty-first strategy in patients with severe limb ischemia due to infrainguinal disease.[52] Based on the need for aorto-iliac intervention, inability to revascularize the ischemic limb, significant co-morbidity precluding surgery, or a pattern of disease that was technically unsuitable for angioplasty or surgery, 90% of patients screened were excluded from the trial. In the short-term, the surgery-first strategy was associated with higher morbidity, longer hospital stay, and greater utilization of the intensive care unit than the angioplasty-first strategy. Of patients assigned to angioplasty, 20% were immediate technical failures. Angioplasty was also associated with a markedly higher rate of reintervention than surgery. Although the 30-day mortality rate was similar between groups, surgery was associated with a significantly higher rate of early morbidity, including a twofold greater incidence of myocardial infarction and threefold greater rate of stroke. However, medical therapy was suboptimal: 33% of patients were not receiving an antiplatelet drug and 66% were not taking a statin. Quality of life and amputation-free survival in the 2 years following revascularization were similar between groups. Beyond 2 years, *post hoc* analysis showed a survival advantage for patients who underwent surgery first.

Whenever possible, autologous vein should be used as conduit for infrainguinal bypass. A meta-analysis comparing outcomes for infrainguinal bypass in CLI patients showed that above-knee vein and below-knee vein performed better than above-knee prosthetic grafts.[50] The primary patency at 1 year was 83.4% for above-knee vein, 84.3% for below-knee vein, and 76.3% for above-knee prosthetic. Secondary patency rates followed a similar pattern. At 5 years, the difference in patency between vein and prosthetic graft was even more pronounced. Greater saphenous vein is also the optimal conduit for infrapopliteal reconstruction. For example, in diabetics with limb-threatening ischemia, primary patency, secondary patency, and limb salvage rates for dorsalis pedis artery bypass were 56.8%, 62.7%, and 78.2%, respectively.[51] In patients with limited autologous

conduit, the superficial femoral or popliteal artery may be used as inflow without compromising outcome.[53] Alternative autologous vein yields superior primary patency, secondary patency, and foot preservation compared to polytetrafluoroethylene, umbilical cord vein, and cryopreserved vein.[54] Limb salvage rates with prosthetic femorotibial bypass were 72.5% at 1 year and 61.9% at 5 years.[55] In the most severe cases, CLI patients may lack a patent outflow vessel for distal anastomosis. In this situation, 'blind bypass' to a collateral artery may be performed, although the limb salvage rates are lower than the rates when bypass is performed to a patent outflow vessel.[56] Despite superior patency and limb salvage rates, surgical revascularization for infrainguinal disease is associated with postoperative thrombosis in 5% and wound complications in nearly 20% of patients, especially those who are diabetic and obese. Functional outcome is largely dependent on the patient's pre-operative status. Abou-Zamzam and colleagues found that in patients with limb-threatening ischemia, postoperative independence was maintained in more than 90% of their patients.[57] Only 4% who were not living independently became independent postoperatively, and only 21% who were non-ambulatory became so following operation. In addition, only 45% of patients reported being 'back to normal' at 6 months.

Endovascular revascularization

In the past decade, angioplasty has supplanted surgery as the first-line therapy for patients with CLI in many centers.[11,58–62] Endovascular revascularization is appealing as it is minimally invasive, associated with low morbidity and mortality, reduced hospital costs, and decreased length of hospitalization; the tradeoff is poorer durability when compared with the surgical alternative.[52] Endovascular therapy represents the optimal revascularization strategy for patients who are elderly, ill-suited to withstand an open surgical procedure, and have a life expectancy less than 2 years. The companion article by Arain and White[63] examines endovascular therapy for patients with limb-threatening ischemia.

Hybrid revascularization

An increasing number of CLI patients undergo a combination of endovascular and open surgery to achieve complete revascularization with a less extensive operative procedure, shorter duration of operation, and decreased risk of peri-operative complications.[59,64] Hybrid therapy represents an attractive revascularization option in patients who are older, frail, or have limited autologous conduit for bypass (Figure 1). In a hybrid procedure, the endovascular portion may consist of inflow,[65–67] outflow,[67] a combination of inflow and outflow,[68] or revision of a bypass graft.[68] Endovascular repair may be performed percutaneously using the cross-over technique from the contralateral common femoral artery or via cut-down over the ipsilateral common femoral artery, which permits reconstruction of the femoral artery with an interposition graft or endarterectomy with patch angioplasty.[69,70] The use of an endovascular inflow procedure – whether of the aortoiliac segment[65,69–71] or the superficial femoral artery[66] – does not appear to compromise long-term patency of the downstream bypass graft. In one of the largest series to date, 125 patients underwent hybrid therapy for *de novo* arterial reconstruction or revision of a bypass graft.[68] Overall, the peri-operative mortality was < 1%, and morbidity was 15.4%. The primary patency was 39.6%, primary assisted patency 65.1%, and secondary patency 73.5% over a mean follow-up of 27.6 months. Other investigators have reported excellent limb salvage rates using hybrid therapy.[64,65,67] Postoperative duplex surveillance is essential for maintaining long-term patency of the arterial reconstructions.

Outcomes following revascularization

The investment of time and resources to restore CLI patients to their premorbid state is immense. In one series, 48.9% of CLI patients who underwent infrainguinal bypass required at least one additional operation within 3 months, 49.3% were readmitted to hospital within 6 months, and 54% required more than 3 months to heal their wounds.[72] In PREVENT III, patients presenting with tissue loss who experienced early graft complications had a longer initial hospitalization, greater number of readmissions to hospital, and increased total days in hospital in the year following bypass than patients who presented with rest pain and maintained patent grafts.[73]

The unfortunate reality is that many patients with CLI will spend a significant portion of their remaining life tending to the needs of their ischemic limb.[72–74] A retrospective examination of 133 patients who underwent infrainguinal bypass for limb salvage showed that only 14% of patients had an 'ideal' surgical result, defined as an uncomplicated operation with long-term symptom relief, maintenance of functional status, uncomplicated wound healing, and no recurrence or repeat operations regardless of postoperative survival time.[75] A subsequent report found that an even smaller number of patients – only 5.6% – achieved an ideal result following infrainguinal bypass for limb salvage.[74] The definition of success in these reports was strict, with anything short of primary patency considered an adverse event. In contrast, Taylor and colleagues proposed a less severe definition of clinical success

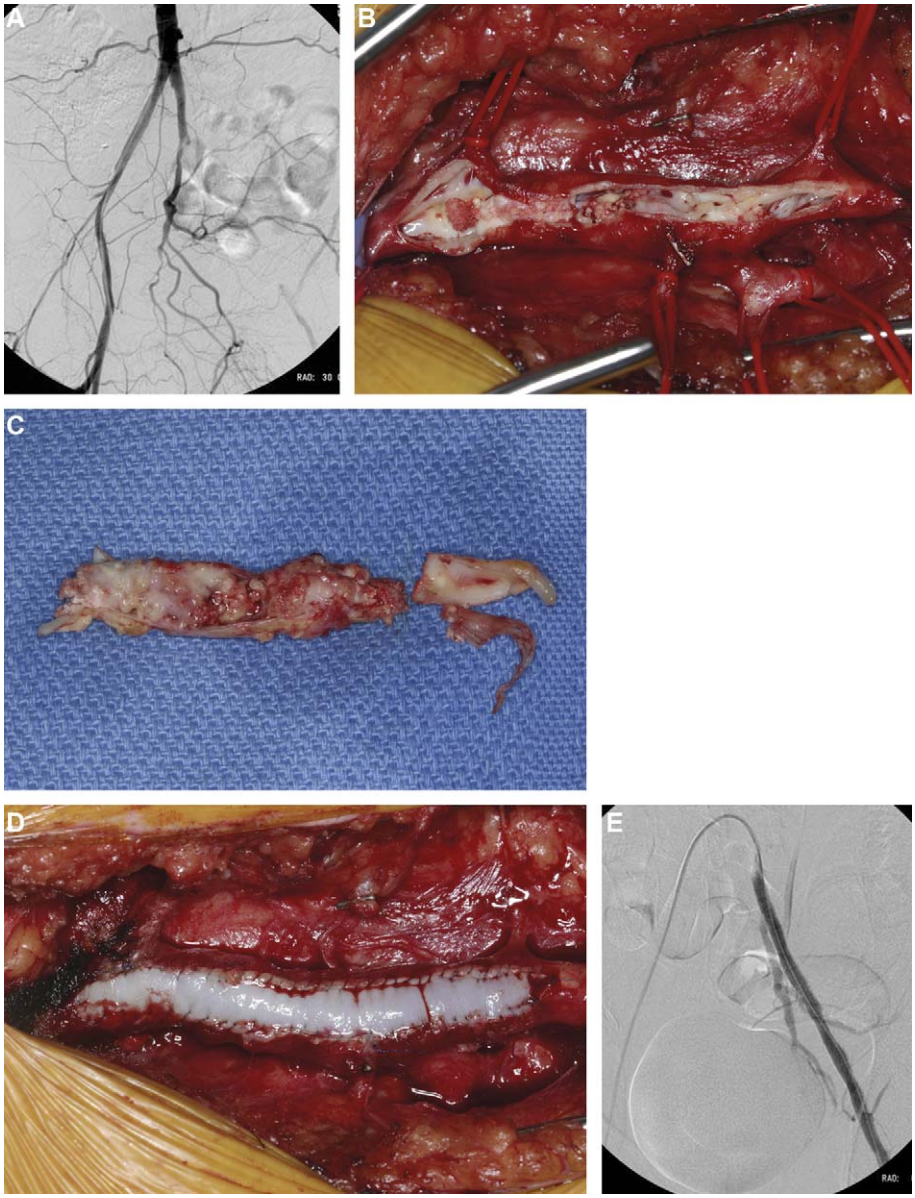

Figure 1 An elderly woman presented with ischemic rest pain. Angiography revealed total occlusion of the left external iliac artery and common femoral artery (A). Hybrid revascularization was performed. Using the cross-over technique, the left external iliac artery was treated with percutaneous transluminal angioplasty and stent placement. Surgical exploration of the left common femoral artery demonstrated dense, atherosclerotic plaque (B), which was treated with endarterectomy (C) and patch angioplasty (D). Completion arteriography showed a widely patent left iliofemoral system (E). The patient's rest pain resolved and her ankle–brachial index increased from 0.42 to 0.92.

following revascularization – one that shifts away from outcome measures of graft patency and limb salvage proposed by Rutherford, *et al.*[76] and moves towards four measures of greater importance to the patient: graft patency to the point of wound healing; limb salvage for 1 year; maintenance of ambulatory status for 1 year; and survival for 6 months.[77] The authors examined outcomes for 331 consecutive patients who underwent bypass for ischemic ulcers or gangrene. At 36 months, the secondary graft patency and limb salvage rates were 72.7% and 73.3%, respectively. When all four parameters of an ideal outcome were combined, only 44% of patients achieved clinical success. Independent predictors of failure included impaired ambulation at presentation, infrainguinal level of disease, end-stage renal disease, and the presence of gangrene at presentation.[77] The likelihood of success in the presence of multiple adverse predictors was dismal (< 10%).

Despite the limited number of CLI patients who experience an ideal outcome, successful revascularization – whether surgical or endovascular – leads to a sense of improved quality of life.[52,78–80] For example, following infrainguinal bypass for limb salvage, mean global quality of life scores increased signifi-

cantly at 3 months and 1 year.[78] The results may be biased, however, as patients with a patent graft who remained amputation-free were more likely to respond to follow-up surveys than patients who had loss of primary-assisted patency, loss of secondary patency, or amputation. Not surprisingly, patients who developed graft stenosis or occlusion were found to have a markedly reduced quality of life.[78] In BASIL, patients in both the bypass and angioplasty arms of the trial demonstrated low quality of life at baseline followed by a small but significant improvement 3 months after revascularization.[52] Little further improvement in quality of life scores was observed beyond 3 months.

Primary amputation

Selecting patients who should undergo primary limb amputation rather than revascularization remains daunting. Frequently, intense efforts are made to salvage the ischemic limb using surgery or endovascular techniques prior to concluding that major amputation is required. For example, Jamsen and colleagues reported that 32% of patients who underwent infrainguinal angioplasty subsequently progressed to major amputation.[81] In BASIL, 16% of patients in both the surgery-first and angioplasty-first group underwent repeated procedures only to eventually die or lose their leg (or both) within the first 12 months.[52]

Amputation is indicated after failed attempts at revascularization, if the patient is unfit or unable to undergo revascularization, in the presence of extensive tissue loss or infection, and in patients who do not ambulate. According to the TASC guidelines, "… amputation may offer an expedient return to a useful quality of life, especially if a prolonged course of treatment is anticipated with little likelihood of recovery".[1] Amputation level is determined clinically, although objective data such as transcutaneous oxygen pressure, fluoroscein angiography, or skin thermography may supplement the surgeon's judgment. Efforts are made to preserve the knee joint, as the lower energy expenditure required for ambulation after below-knee amputation (BKA) makes it easier to walk independently. The 30-day mortality for BKA is 5% and for above-knee amputation (AKA) 16%.[82,83] In many reports, it is unclear whether patients undergoing limb amputation received appropriate therapy (i.e. beta-blockers, anti-platelet agents, and statins) to decrease cardiovascular mortality. Short-term complication rates following amputation range between 13% and 22%.[82,84] Long-term survival is markedly reduced with a higher amputation level (1-year survival after AKA 50.6% vs BKA 74.5%), diabetes, end-stage renal disease, decreased serum albumin, advanced age, and no prior coronary artery bypass surgery.[82,83] A non-randomized, retrospective study in patients with limb-threatening ischemia suggested that compared with primary amputation, angioplasty was associated with a mortality hazard.[85] Although the study was flawed because of marked differences between the angioplasty and primary amputation groups, it nevertheless supports the notion that revascularization should not be offered indiscriminately to all patients with CLI.

Few studies have examined the effects of amputation on functional outcomes. Following surgical or endovascular revascularization, the leading determinants of poor functional outcome were impaired ambulatory status at time of presentation (70% 5-year mortality; 39.5% failure to eventually walk; 30% loss of independent living status) and dementia (73% 5-year mortality; 41.2% failure to eventually walk; 46.4% loss of independent living status).[86] Older age (> 70), limited preoperative functional ability, and AKA were associated with failure to wear a prosthesis, failure to ambulate, and failure to maintain independent living status following major lower extremity amputation.[87] However, failure to wear a prosthetic limb after amputation does not guarantee loss of independent living status. Of surviving patients who underwent amputation in a Veterans Hospital or university setting, fewer than half (42%) used a prosthetic limb, and the majority of these patients had undergone BKA.[84] Interestingly, despite the failure to use a prosthesis following amputation, only 8% of patients moved from the community to a care facility. It is possible that increased community wheelchair access in the past decade may have enabled more amputees to remain at home.

Towards a more consistent method of choosing therapy

Given the number of different specialists involved in caring for CLI patients, it is not surprising that treatment approaches vary amongst providers: interventionalists may be predisposed to recommending endovascular therapy, while surgeons may be inclined to recommend open bypass. The Lower Extremity Grading System (LEGS), which is calculated based on arteriographic findings, presentation, functional status, co-morbidities, and technical factors, was devised to standardize treatment for patients with CLI.[80] The LEGS score was used to prospectively guide therapy for 227 CLI patients. Surgery was performed in 34%, endovascular repair in 61.5%, and primary amputation in 4.5%. At 6-month follow-up, patency, limb salvage, survival, ambulatory status, living status, and health assessment were similar between patients

undergoing either surgery or endovascular revascularization. Although the LEGS scheme requires further validation, it appears to be a promising means of allocating therapy to CLI patients.

Conclusion

The care of patients with limb-threatening ischemia is complex. Whenever possible, ambulatory and functional patients with CLI should undergo revascularization. The decision to perform surgery, endovascular therapy, or a combination of the two modalities must be individualized. Patients who are relatively fit and able to withstand the rigors of an open procedure may benefit from the long-term durability of surgical repair. In contrast, frail patients with a limited life expectancy may experience better outcomes with endovascular reconstruction. Amputation should be considered for patients who are non-ambulatory, demented, or unfit to undergo revascularization. For patients who are not candidates for revascularization, or who are unwilling or unable to undergo amputation, medical therapy such as intermittent pneumatic compression or spinal cord stimulation may offer symptom relief and promote wound healing. Regardless of which treatment strategy is employed, clinicians must redouble their efforts to place patients with limb-threatening ischemia on appropriate cardioprotective medication regimens.

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