Critical Limb Ischemia

Understanding the scope of the problem.

BY ARAVINDA NANJUNDAPPA, MD, AND JOHN R. LAIRD, JR, MD

Critical limb ischemia (CLI) is defined by Transatlantic Inter Society Conference (TASC) as persistent recurring ischemic rest pain requiring opiate analgesics for at least 14 days, ulceration or gangrene of the foot or toes and ankle-brachial index (ABI) <0.40, toe pressure <30 mm Hg, systolic ankle pressure <50 mm Hg, flat pulse volume waveform, and absent pedal pulses.[1] CLI has traditionally been categorized as stage III or IV of the Fontaine classification[2] or Rutherford classification[3] 4, 5, and 6. Most patients with CLI have multilevel, multivessel disease, often with three-vessel tibioperoneal occlusive disease. Limb loss and cardiovascular mortality and morbidity ensue rapidly if CLI is not treated.[4] Treatment options include surgical revascularization, amputation, and endovascular intervention. The main treatment goals for CLI are limb preservation, quality-of-life improvement, and a reduction in cardiovascular complications from the underlying diffuse atherosclerosis. Risk factors[5] that contribute to the development of CLI are listed in Table 1.

Elderly patients (octogenarians in particular) are at high risk for CLI. Diabetes mellitus accentuates the risk of CLI by four times, while continued tobacco abuse triples the risk.[6] Diabetes mellitus leads to rapid progression of atherosclerosis at a premature age and preferentially affects distal calf vessels. This diffuse distal disease that is associated with diabetes poses challenges for the surgeon or endovascular specialist. It has been estimated that 40% to 45% of all amputees are diabetic.[7] A diabetic patient with CLI is 10 times more likely to need amputation compared to a nondiabetic. Uncommon causes of CLI include thromboangiitis obliterans, vasculitis, and arteritis.[8]

PRESENTATION

Ischemic rest pain is characterized by discomfort in the toes, forefoot, or heel that is not relieved with the use of simple analgesics.[9] Ischemic rest pain is predominantly nocturnal, and patients will often need to dangle their feet over the side of the bed to get relief. Minor trauma to the skin or nails usually precedents a poor-healing ulcer. An ulcer is classified as nonhealing when 8 to 12 weeks of wound dressings and wound care fail to result in complete healing. Gangrene can ensue when

TABLE 1. RISK FACTORS FOR CLI

- Diabetes mellitus
- Neuropathy
- Renal failure
- Age >80 years
- Smoking
- Peripheral arterial disease
- Hypertension
- Hypercholesterolemia
- Infection

TABLE 2. DIAGNOSTIC CRITERIA FOR CLI

- ABI <0.4
- Toe-brachial index <0.7
- Ankle pressure <50 mm Hg
- Toe pressure <30 mm Hg
- Flat waveform by pulse volume recording
- Absent pedal pulses
- Non-Dopplerable pedal pulse
- Transcutaneous oxygen measurement

the reduced arterial supply to the limb does not meet with the metabolic demands of the ischemic leg. Late stages of CLI are characterized by sensory loss and muscle weakness. Infection may precede or may complicate the nonhealing ulcer.

NATURAL HISTORY

If not promptly diagnosed and intervened upon, CLI can lead to limb loss, gangrene, sepsis, myocardial infarction, and death. Studies have shown that within the first several months of the diagnosis of CLI, death occurs in 9%, myocardial infarction in 1%, stroke in 1%, amputation in 12%, and persistent CLI in 18% of patients.[10] One- and 2-year mortality rates are noted to be 21% and 31.6%, respectively.

DIAGNOSIS

History and physical examination plays a pivotal role in the diagnosis of CLI. A good history should include all the relevant risk factors and a physical examination must document pulses, ulcers, and infection. Sensory loss and loss of muscle power in later stages of CLI needs to be identified. An array of simple diagnostic tools[11] can assist in the diagnosis of CLI (Table 2).

TREATMENT

All patients must receive aggressive medical management, including antiplatelet therapy. A case can be made for the use of dual antiplatelet therapy with aspirin and clopidogrel in this high-risk patient population. Angiotensin-converting enzyme inhibitors should be considered for hypertension treatment and for their potential to reduce cardiovascular events. Aggressive

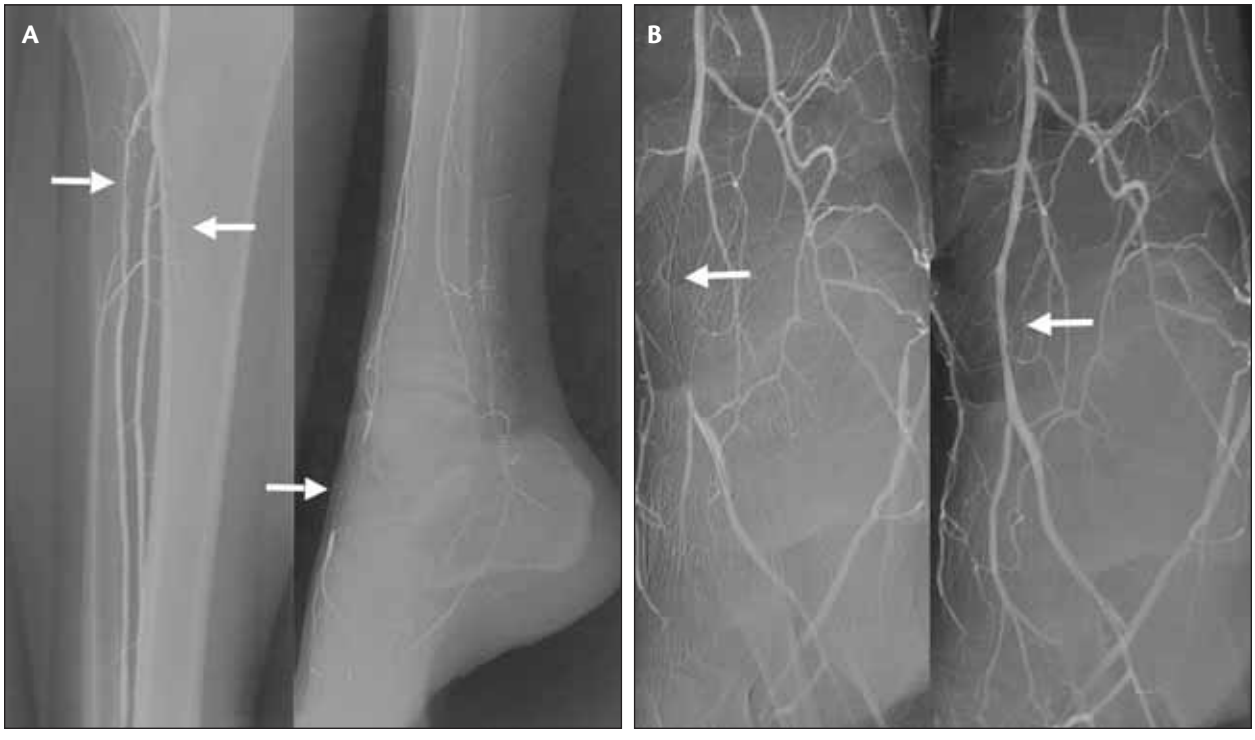

Figure 1. A diabetic patient with an infected foot ulcer. There is a stenosis of the proximal anterior tibial artery and occlusion of the posterior tibial artery. Importantly, there is also occlusion of the dorsalis pedis (arrows) (A). PTA of the proximal anterior tibial artery and dorsalis pedis was performed with good results (arrows) (B).

lipid-lowering therapy and optimal blood glucose control are critically important.[12] Adjunct wound care, antibiotics, partial debridement, and analgesics are also essential in CLI management. If imminent limb loss is suspected, immediate hospital admission is required, and anticoagulation with fractionated or unfractionated heparin can be considered.

> "The imperative for the endovascular specialist is to reduce the mortality and morbidity associated with revascularization . . ."

Delineation of the arterial anatomy to define the extent of arterial occlusive disease is quintessential. Angiography remains the gold standard; however, noninvasive evaluation with duplex vascular ultrasound may be a useful starting point. In recent years, MRA and CTA image quality has improved to the point where they can be very helpful in guiding revascularization strategies.[13]

Amputation can be life saving in cases of extensive tissue necrosis, a nonviable limb, or occlusive disease that cannot be revascularized. It is important to recognize, however, that amputation is not a benign procedure in this patient population. The periprocedural mortality rate has been reported to range from 5% to 17%.[14] Up to 10% of above-the-knee amputations and 20% of below-the-knee amputations will need surgical revision of nonhealing stumps. Amputation carries a higher mortality rate in diabetics. Subsequent contralateral limb amputation and early death are dreaded downsides of amputation for CLI.

Surgical bypass for limb salvage is an effective strategy and can improve the quality of life in patients with CLI.[15] This approach is associated with a prolonged recovery, potential loss of saphenous vein (which might be needed for future CABG), chronic lower-extremity edema,[16] and worsened symptoms when the graft fails. Complications of infrainguinal bypass include death in 1.3% to 6%, myocardial infarction in 1.9% to 3.4%, wound complications in 10% to 30%, and vein infection in 1.4%.[17] Despite a successful bypass, amputation is still needed in 5% to 10% of patients.

KEYS TO THE ENDOVASCULAR APPROACH

The imperative for the endovascular specialist is to reduce the mortality and morbidity associated with revascularization in this high-risk patient population. A cadre of highly skilled endovascular specialists who can treat CLI in a less-invasive manner offers the promise of improving outcomes in CLI.[18] Optimal utilization of newer therapeutic modalities and a multidisciplinary approach to the treatment of CLI are essential.

Restoration of "straight-line flow" to the pedal arch in one or more tibial arteries is necessary for clinical success.[19] Dilatation of a proximal lesion in the setting of a distal occlusion will not be adequate for wound healing. The status of the pedal arch is very important and needs to be defined with a high-quality angiogram (Figure 1). Success of therapy is measured by relief of rest pain, healing of ulcers, and avoidance of major amputation. Because treatment of CLI is largely linked to the quality-of-life issue of being able to walk, the most important aspect of life quality for CLI patients is preservation of the limb.[20] The primary goal, above all others, is to leave the patient with an ambulatory foot, so the patient can walk without a prosthesis. An increase in blood flow is required to result in wound healing, yet this need not be permanent; it must last only long enough for the limb to heal. Less blood flow is required to keep tissues healed than to achieve healing. Restenosis or vessel patency is a less relevant endpoint in this patient population.

After revascularization, the patient must have straight-line flow to the foot, and the ABI should ideally be >0.7 with an ankle pressure >50 mm Hg. A combined, multidisciplinary approach to the treatment of the patient including podiatry, an infectious disease specialist, and a plastic surgeon (along with the endovascular specialist) will assist in wound healing. Endovascular approaches to the treatment of CLI have been shown to have procedural success rates of 92% to 96% with 3-year limb salvage rates from 77% to 94%.[19-22]

Dorros et al successfully treated 270 of 284 critically ischemic limbs (95%) using tibioperoneal angioplasty with resultant relief of rest pain and/or improved flow. Clinical 5-year follow-up revealed a limb salvage rate of 91%.[22] Among this group, 8% required surgical bypass, and 9% required significant amputation.

The results with endovascular therapies will, of course, vary widely depending upon comorbid conditions within the patient population being studied, lesion length, lesion complexity, etc. Long-segment arterial occlusions have traditionally not responded well to percutaneous transluminal angioplasty.

Innovative technologies currently being used for limb salvage include laser atherectomy, excisional atherectomy, cryoplasty, cutting-balloon angioplasty, and stents (bare metal, balloon-expandable, self-expandable, and drug-eluting). The limb salvage rates with the use of

laser and adjunctive therapies in the LACI trial were promising.[23] The procedural success rate in the LACI trial was 88%, and the 6-month limb salvage rate was 93%. Plaque excision for CLI as reported by Kandzari[24] et al had a procedural success rate of 99% with a 1% major adverse event rate and no unplanned amputations. Heparin-coated, small-diameter, balloon-expandable stents were used for the treatment of tibial disease by Feiring and colleagues with good results.[25] Recent results from the BASIL trial demonstrated that compared to traditional bypass surgery, an endovascular approach to the treatment of CLI had comparable results and is a cost-effective strategy.[26]

> "Excellent limb-salvage rates are now being achieved with a variety of endovascular therapies."

CONCLUSION

If untreated, CLI carries a high risk of limb loss, mortality, and morbidity. Excellent limb-salvage rates are now being achieved with a variety of endovascular therapies. The guiding principle is to establish straight-line flow to the foot in one or more of the tibial arteries. Innovative techniques offer the potential to further improve upon the results with endovascular therapies and provide patients with a better chance for limb salvage and an improved quality of life. ■

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