CLI: Overview of Incidence and Impact

Understanding the importance of taking a multidisciplinary approach to treating CLI.

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Critical limb ischemia (CLI) is defined by the TransAtlantic Inter-Society Consensus (TASC) as persistent recurring ischemic rest pain requiring opiate analgesics for at least 14 days, ulceration or gangrene of the foot or toes, ankle-brachial index (ABI) <0.4, toe pressure <30 mm Hg, systolic ankle pressure <50 mm Hg, flat pulse volume waveform, and absent pedal pulses.[1,2] The two most popular systems for classifying the symptoms of peripheral artery disease (PAD) and the effects of any intervention are the Fontaine stages and the Rutherford categories. The TASC guidelines classify CLI as Fontaine[3] class III or IV and Rutherford class 4, 5, and 6.[2] This article discusses the epidemiology, natural history, diagnosis, and state-of-the-art treatment options of chronic CLI.

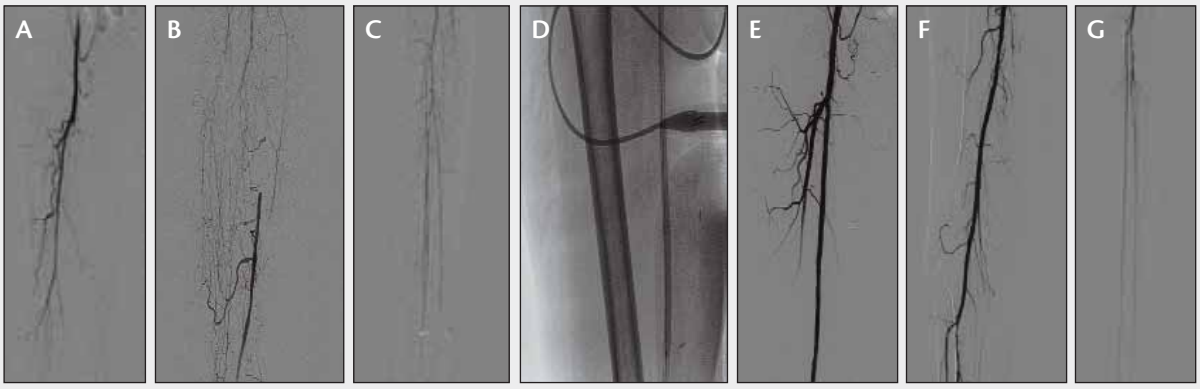
EPIDEMIOLOGY AND NATURAL HISTORY

The incidence of CLI is 1% to 2% of patients with PAD who are older than 50 years of age.[4] The risk factors for CLI are >65 years of age, smoking, diabetes mellitus, ABI <0.7, and hyperlipidemia.[5] Patients with CLI face a high risk of limb loss—between 10% to 40% at 1 year, and at 5 years, the mortality rate reaches 50%.[6] The major

Figure 1. Arterial ulcers.

CASE 1

A 46-year-old woman with hypertension, diabetes mellitus, hypercholesterolemia, tobacco and cocaine abuse, and coronary artery disease after coronary artery bypass graft presented with nonhealing ulcers in the right foot. The patient had a right leg ABI of 0.6. A bilateral lower extremity arteriography was performed to delineate anatomy.



Case 1. An occluded superficial femoral artery (SFA) and reconstitution of the distal SFA via collaterals (A through G). Angioplasty and stenting of SFA; final two-vessel runoff (D through G).

cause for mortality and morbidity[4] in patients with CLI is cardiovascular and cerebrovascular events such as myocardial infarction and stroke. Patients with CLI have multivessel disease, and ABI is generally <0.4.[6] CLI patients should be considered as having a systemic disease. Treatment of CLI should be centered to include maximal medical therapy with endovascular and/or surgical procedures for limb salvage.[7]

CLI patients who are at high risk for amputation (diabetes mellitus, neuropathy, renal failure, and infection) should inspect their feet carefully for any skin breakdown. Such patients need early referral to specialists in treating vascular disease.

DIAGNOSIS

CLI is mostly diagnosed by history and physical examination. Classic rest pain is described as redness and a burning sensation on the dorsum of the feet upon elevation in the bed at nighttime. This pain is severe in the supine position due to reduced blood supply to the legs. The relief for rest pain is noted when the patient gets up from a supine position to walk or dangle his feet on the ground. Some patients with CLI will give a history of sleeping in a chair due to fear of pain upon leg elevation. These patients may also have dependent edema. A thorough inspection of the feet by the physician is imperative to look for limb ulcers or tissue breakdown, especially between the toes. A leg elevation test can elicit rest pain and/or pallor upon limb elevation for 2 to 3 minutes and slow return of rubor and decreased pain upon return to the dependent position.

Typically, CLI patients will have multivessel disease involving the aortoiliac arteries, superficial femoral arteries, and tibioperoneal vessels. Examination should be focused on findings of bruit, absent or weak pulses, palpable aneurysm, and evaluation of limb ulcers. An example of typical arterial ulcers is depicted in Figure 1. Baseline ABI, toe brachial index, and ankle pressure measurement are useful for the assessment of ischemia. An ABI of <0.4, toe brachial index <0.7, and ankle pressure index <40 mm Hg aid in diagnosis of CLI.[8] Arteriography is the most definitive test to precisely define the anatomy of the inflow and outflow to help determine a treatment plan. Noninvasive tests such as magnetic resonance angiography, arterial duplex ultrasound, and computerized tomography are all complementary.[9] These noninvasive tests can provide a road map to treatment options.

TREATMENT

A multidisciplinary effort among wound care experts, endovascular interventionists, and vascular surgeons must concurrently exist for optimal outcomes.

Medical Treatment

Patients with CLI should be treated for aggressive risk factor reduction aimed at antiplatelet therapy, angiotensin-converting enzyme inhibitor therapy, and lipid therapy to treat the comorbid conditions of car-

diac and cerebrovascular disease. However, medical therapy alone may be insufficient for limb salvage and should be complemented with patient-appropriate revascularization procedures.[10]

Endovascular Approach

Innovative technologies currently being used for limb salvage include laser atherectomy, excisional atherectomy, cryoplasty, cutting-balloon angioplasty, and stents (bare metal, balloon expandable, self-expanding, and drug eluting). The limb salvage rates with the use of laser and adjunctive therapies in the LACI trial were promising.[11] The procedural success rate in the LACI trial was 88%, and the 6-month limb salvage rate was 93%. Stents for total occlusions in superficial femoral artery disease have a better patency rate than balloon angioplasty. Plaque excision for CLI as reported by Kandzari et al[12] 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.[13]

The endovascular approach is less invasive, quicker, and requires a shorter hospitalization, but the patency rate of the treated artery is lower than that of a surgical approach. At the end of percutaneous revascularization, a patient with CLI must have restoration of flow to the pedal arch via at least one vessel.[14] Despite a high long-term failure rate, short-term establishment of improved perfusion is sufficient to allow 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%.[15-18] The recent BASIL (Bypass versus Angioplasty in Severe Ischemia of the Leg) trial randomized patients with CLI to surgery versus angioplasty.[19] This landmark study for CLI demonstrated some key findings:

(1) Higher failure rates for angioplasty (20%) versus surgery (3%)
(2) Amputation-free survival was similar between surgery and angioplasty at 1 year
(3) After 2-year follow-up, total survival and amputation-free survival rates were higher in surgery compared to angioplasty
(4) The cost was cheaper with angioplasty compared to bypass

Endovascular approaches represent an innovative field with the advent of revolutionary technology. CLI patients who have significant comorbidities of cardiopulmonary disease, are elderly, and have limited life expectancy should be considered strongly for the endovascular approach first. The outcomes of endovascular approach depend on physician expertise, renal function, patient cooperation, interventional device availability, and imaging facilities.

Surgical Approach

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%.[20] 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 patients with CLI.

Surgical bypass for limb salvage is an effective strategy and can improve the quality of life in patients with CLI.[21] A healthy patient with low risk for cardiopulmonary events and with a suitable vein for bypass should be considered for a surgery-first approach. PREVENT III (Project of Ex Vivo Vein Graft Engineering via Transfection)[22] is a prospective, multicenter study of quality of life before and after lower extremity vein bypass in 1,404 CLI patients. This study showed that patients with CLI have a low quality of life at baseline, and it improved at 3 months and 1 year after surgery with vein bypass. Diabetic patients who suffer from graft-related events tend to have low quality of life. Improvement in quality of life is directly related to success of the procedure, and these benefits persisted at 1 year. Surgical success for CLI depends on the comorbidities, presence of usable vein for bypass, surgical expertise, inflow disease, and number of runoff vessels.

CONCLUSION

If left untreated, CLI carries a high morbidity and mortality rate. A multidisciplinary approach with aggressive risk factor reduction should be initiated early in the course. An endovascular approach versus surgical approach should be tailored based on a patient's comorbidities and anatomical factors. ■

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