Peripheral arterial disease (PAD), the narrowing of the blood vessels outside of the heart and brain, affects approximately 12 million Americans a year, mainly those who are older than 50 years.1 PAD is an indicator of systemic atherosclerosis, meaning that those with PAD are also at high risk for heart attack, stroke, and cardiovascular death.2 Statistics indicate that patients with PAD have a four- to fivefold higher risk of mortality resulting from a cardiovascular incident.3 The magnitude of PAD symptoms often vary along a spectrum, with 1% to 2% of patients developing severe critical limb ischemia (CLI), a constant state of lower extremity rest pain and/or nonhealing ulceration, a condition that results from advanced PAD retarding oxygen delivery to the affected extremity.4 Approximately 40% of patients with CLI require amputation of the affected limb, and approximately 150,000 amputations occur in the United States annually.5,6

The purpose of this article is to introduce a decision tree for treating arterial-insufficient CLI wounds (Figure 1). Amputation is the last resort when all other treatments have been exhausted.

SYSTEM OF CARE

CLI patients presenting with active wounds require a team approach to prevent amputation and reduce their risk of suffering an adverse cardiovascular event. The team is composed of wound care specialists (podiatrists, surgeons, and internal medicine physicians) and invasive vascular physicians (interventional cardiologists, interventional radiologists, and/or vascular surgeons).

Figure 1. A decision tree outlining the system of care that should be provided to patients with a CLI wound. Wound care is concurrent with vascular therapy, and the approach is a collaboration between both the wound care specialist and the vascular specialist.
Historically, collaboration among these differing medical specialties has been poor, resulting in adverse patient outcomes. Changing behaviors and working together as a team are imperative to developing standards of care for treating CLI patients.

**WOUND CARE**

When a patient is initially referred to a wound care specialist, certain steps are taken to promote healing of an arterial-insufficient CLI wound. First, transcutaneous oximetry is performed in all patients. A number of studies have shown that periwound transcutaneous oxygen tension (PtcO₂) below a cutoff of 40 mm Hg is associated with impaired healing due to inadequate oxygen supply. Thus, a PtcO₂ < 40 mm Hg should prompt a referral to an invasive vascular specialist for possible revascularization. Data suggest that PtcO₂ may be superior to Doppler in screening for vascular disease, predicting healing after amputation, and assessing the success after vascular intervention.

Necrotic tissue is laden with bacteria. Devitalized tissue impairs the body’s ability to fight infection and serves as a rich environment for bacterial growth. Therefore, removal of all necrotic or devitalized tissue by sharp, enzymatic, mechanical, or autolytic debridement leads to a more normal wound healing process. In arterial ulcers with dry gangrene or eschar, debridement should not be used until arterial flow has been reestablished. Restoration of blood flow is crucial to infection control in arterial ulcers.

In diabetic patients, the immune system is impaired, so infection may be present without obvious signs. As a result, tissue cultures should be taken, and short courses of systemic antibiotics should be considered even when clinical signs of infection are not present. However, chronic treatment with systemic antibiotics does not prevent infection and may worsen outcomes if infection develops. In a review of treatment for digital osteomyelitis, peripheral vascular occlusive disease and prolonged prehospital antibiotic use was associated with decreased wound healing compared with aggressive surgical debridement and selected use of arterial bypass.

Adequate tissue perfusion is essential in CLI wound care. Wound healing and infection prevention are more likely to occur in an environment that is adequately oxygenated. Revascularization is prudent, but adjuvant treatments such as hyperbaric oxygen (HBO) may help to maximize cutaneous flow and thus facilitate ulcer healing. HBO has been shown to accelerate the rate of healing, reduce amputation rates, and increase the number of wounds that are completely healed at long-term follow-up. Considering HBO therapy is an adjuvant treatment, it can be used at any stage of the wound care process. If amputation is contemplated, HBO therapy should be considered.

Finally, evidence suggests that autografts and allografts can accelerate the closure of wounds. In refractory ulcers, these grafts act as biological dressings, increasing the chance of wound healing. Skin graft survival depends on appropriate wound bed preparation and perfusion.

**MEDICAL THERAPY**

There are currently no class I or IIA recommended medical treatments for CLI to improve limb outcomes (ie, improve wound healing or amputation prevention). As a result, the majority of medical therapies focus on reducing cardiovascular and cerebrovascular mortality, as 20% of CLI patients will die 6 months after initial wound treatment. The American Heart Association and American College of Cardiology guidelines recommend the three following suggestions.

First, treatment of dyslipidemia should follow guidelines established by the National Cholesterol Education Program Adult Treatment Panel III guidelines, which classify CLI patients as very high risk. Treatment includes the use of hydroxymethylglutaryl coenzyme-A reductase inhibitor (statin) medication. A goal of < 70 mg/dL of low-density lipoprotein needs to be reached (class IIA, level B). Second, antihypertensive medical therapy should be employed with the goal of achieving < 140 mm Hg systolic over 90 mm Hg diastolic (nondiabetics) or < 130 mm Hg systolic over 80 mm Hg diastolic (diabetics and individuals with chronic renal disease) (class I, level A). Beta-adrenergic blockers (class I, level A) and/or angiotensin-converting enzyme inhibitors (class IIA, level B) can be used to reduce hypertension in affected individuals. Third, antiplatelet therapy, such as aspirin, in daily doses of 75 to 325 mg is recommended as a safe and effective antiplatelet therapy to prevent platelet aggregation and thrombus formation.

**ANGIOSOMES**

The initial vascular consultation uses the angiosome concept. This concept, described by Taylor and Palmer in 1987, divides the body into three-dimensional vascular territories supplied by specific source arteries and drained by specific veins. The lower leg is separated into five angiosomes and the foot and ankle into six angiosomes. The angiosomes of the lower leg are supplied by the medial sural artery, lateral sural artery, posterior tibial artery (PTA), anterior tibial artery (ATA), and peroneal artery (PA). The angiosomes of the foot and ankle are supplied by the PTA, ATA, and PA.
Angiosome mapping is an important noninvasive diagnostic tool used to localize the ischemic vessel(s) based on the location of the CLI wound.\textsuperscript{24,25} The angiosome method is particularly important when there are multiple occluded tibial arteries, and thus revascularization is catered to the artery supplying the wound. The angiosome model of reperfusion can also be applied to planning incisions and tissue exposures that preserve blood flow for surgical wounds to heal and predicting which pedicle flap can be successfully harvested or whether a particular amputation will heal.\textsuperscript{26}

**CONTRAST ANGIOGRAPHY**

After approved medical therapy and diagnostic angiosome mapping, referral to an invasive vascular specialist for anatomic roadmapping with contrast angiography is required. Contrast angiography identifies the level of arterial disease such that endovascular and/or surgical interventions and/or amputation can be appropriately planned.\textsuperscript{6} Endovascular therapy, such as atherectomy, angioplasty, and/or stenting, can be performed during contrast angiography, if warranted.

**ENDOVASCULAR THERAPY AND/OR SURGERY**

The goal of revascularization (endovascular intervention or vascular bypass surgery) is to restore in-line arterial blood flow to the ulcer. Without revascularization, the disease progresses, and the limb is eventually lost.

Percutaneous transluminal angioplasty (PTA) is the initial therapy of choice for CLI in patients who are candidates for either surgery or endovascular therapy to avoid the additional morbidity associated with vascular surgery.\textsuperscript{27} Endovascular intervention does not preclude the possibility of subsequent surgery. Often, there is a role for both modalities. In patients who are poor candidates for surgery, such as those with poor distal targets, those who lack adequate saphenous vein for bypass grafting, and those with severe comorbidities, endovascular therapy may offer the only opportunity for limb salvage.

The Bypass Versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial compared PTA to surgery in 452 patients with rest pain, ulceration, or gangrene of the leg secondary to infrainguinal disease.\textsuperscript{28} The primary endpoint, amputation-free survival, was similar for patients who underwent PTA and surgery at 1 year (71\% vs 68\%; \(P = \text{NS}\)) and 3 years (52\% vs 57\%; \(P = \text{NS}\)). Although there was no significant difference in mortality rates between the groups at 30 days, surgery was associated with higher postprocedure morbidity. During the initial hospitalization, almost three times as many patients who were treated with surgery required admission to the intensive care or high-dependency unit compared to those who were treated with angioplasty (27\% vs 7.5\%), which resulted in the cost of hospitalization being higher in the surgical group.

Additionally, PTA was associated with higher immediate failure rates and 12-month reintervention rates in the BASIL study. This did not affect the patients’ candidacy for a second percutaneous procedure or subsequent surgery. BASIL showed that endovascular therapy and surgery were comparable as first-line therapies for CLI but that PTA was less expensive and did not preclude subsequent treatment with surgery.

CLI wounds typically warrant multilevel arterial occlusive treatment. Below-the-knee angioplasty has generally been reserved for cases of threatened limb loss CLI because of the technical difficulty of using conventional peripheral angioplasty equipment in these vessels and the fear of potential limb loss should a complication occur. Two recent trials have shown the efficacy and attractiveness of an initial percutaneous approach for selected patients with CLI and infrapopliteal vascular disease.\textsuperscript{29,30} The limb salvage rate in these patients who were treated with PTA range from 85\% to 91\% after 2 to 5 years. This evidence supports the contention that angioplasty of the tibioperoneal vessels should not necessarily be reserved for limb salvage situations; however, caution is still advised in patient selection because the surgical options are limited if angioplasty fails.

Patients with CLI need to be followed closely after therapy. Not only does close follow-up provide the interventionist or surgeon an opportunity to monitor the patient’s response to revascularization, it also allows for the early identification of recurrent problems and treatment failure.\textsuperscript{31} This is particularly important in patients who are likely to require multiple procedures for sustained benefit (ie, diabetics, patients with multivessel disease, and those who have undergone prior procedures).\textsuperscript{6}

**AMPUTATION**

Primary amputation should be considered in certain clinical situations in which limb salvage is not a practical solution. For example, significant necrosis in weight-bearing areas of the foot, previously nonambulatory patients (bedridden or wheelchair bound), and those with noncorrectable flexion contractures will usually benefit more from early primary amputation.

Otherwise, if a patient has a nonhealing wound and endovascular therapy, surgery, and HBO therapy have
failed, amputation should be considered. Amputation can help alleviate pain and prevent death from systemic infection. The level of amputation should be based on angiography such that (1) there is adequate blood supply to the amputation flap and (2) the lowest level of amputation is performed. The lower the level the amputation, the more functional the patient remains and the less amount of energy is needed to walk. Compared to a patient who has not undergone amputation, below-the-knee amputees consume 9% to 20% more energy, bilateral below-the-knee amputees consume 33% to 46% more energy, above-the-knee amputees require 45% to 70% more energy, and bilateral above-the-knee amputees require up to 300% more energy. At the same time, if a toe is amputated while a below-the-knee amputation is needed, the psychological impact of multiple amputations cannot be overstressed as being potentially harmful.

The prognosis after amputation is even worse. In most series, the perioperative mortality rate is 5% to 10% for below-the-knee amputees and 15% to 20% for above-the-knee amputees. Even when the patients survive, nearly 40% will die within 2 years of the first major amputation. A second amputation is required in 30% of cases, and full mobility is achieved in only 50% of patients who have below-the-knee amputation and in 25% of those who have above-the-knee amputation.

CONCLUSION

Approximately 30,000 to 40,000 Americans undergo amputation annually. In 2008, an estimated 1.6 million Americans were living with an amputation, and it is estimated that by 2050, 3.6 million will be living with an amputation. This epidemic of uncontrolled proportion should be tamed by changing behavior of both patients and physicians. Amputation should be the treatment of last resort when all other modalities have been exhausted.

Limb salvage is a team endeavor. Historically, physicians have not consistently provided a collaborative multidisciplinary team approach to CLI wound care. This lack of collaboration has been a limiting factor to reaching optimal care and has resulted in unnecessary amputations. Using a team approach, the wound should be treated by both an “outside-in” as well as an “inside-out” approach. A wound care specialist takes care to use debridement, topical antimicrobials, systemic antibiotics, and HBO therapy to form the “outside-in” approach. The invasive specialist uses the necessary diagnostic angiography and endovascular/surgical approach to provide an “inside-out” approach to restoring blood flow to the affected wound. Angiography is absolutely necessary and is a crucial precursor step to amputation. After angiography and/or endovascular therapy/surgical intervention, amputation is the last option considered. In the ideal system of care, assessments provided by the wound care specialist and the invasive specialist drive the decision process of the amputating surgeon.

Programs emphasizing this multidisciplinary team approach (ie, Save a Limb, Save a Life and Amputation Prevention) have recently gained notoriety and will hopefully decrease the number of Americans who undergo amputation annually.

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