

Albeir Mousa, Mehiar El Hamdani, Raymond A. Dieter, Jr.,  
Aravinda Nanjundappa, Mohamed A. Rahman,  
David J. Leehey, Raymond A. Dieter, III, James S. Walter,  
Scott T. Sayers, Sanjay Singh, Morgan M. Meyer,  
Amit S. Dayal, Amir Darki, and Robert S. Dieter

---

## Introduction

Although intentionally brief, this chapter is to remind the clinician that the treatment of the patient with critical limb ischemia (CLI) is inherently multidisciplinary (Fig. 55.1). Depending on the type of lesion and the etiology, one, two, or more consultants will be required.

Arterial disease is the etiology of only about 50 % of foot ulcerations. The remainder is due to a variety of causes, including neuropathic/neuroischemic, rheumatological disorders, venous stasis disease, trauma, nutritional, etc.

Above the foot ulcers, the role of venous pathology contributing to the ulcer exceeds that of arterial insufficiency [1]. Furthermore, the complexity of the microcirculation and nutritional factors in the development and nonhealing of ulcerations highlights the complexity of these lesions.

It is naïve for the clinician to believe that they can act in isolation when caring for most of these patients. Accurate imaging, wound care, and risk factor modification are all required for the optimization of the limb and patient. Frequently, these patients will require the coordinate involvement of primary care and medical specialties—including endocrinology, nephrology, and rheumatology. Many patients

---

A. Mousa, MD, MPH, MBA  
Surgery, Charleston Area Medical Center,  
WVU Physicians of Charleston, Charleston, WV, USA

M. El Hamdani, MD  
Medicine, Marshall University School of Medicine,  
Huntington, WV, USA

R.A. Dieter, Jr., MD, MS  
Northwestern Medicine, At Central DuPage Hospital,  
Winfield, IL, USA

International College of Surgeons, Cardiothoracic  
and Vascular Surgery, Glen Ellyn, IL, USA

A. Nanjundappa, MD, RVT  
Medicine and Surgery, West Virginia University, Charleston,  
WV, USA

M.A. Rahman, MD  
Medicine, Nephrology, Hines VA Hospital, Loyola University,  
Hines, IL, USA

D.J. Leehey, MD  
Medicine, Loyola University Medical Center and Hines VA,  
Maywood, IL, USA

R.A. Dieter, III, MD  
Division of Cardiothoracic Surgery, The University of Tennessee  
Medical Center, Knoxville, TN, USA

---

J.S. Walter, PhD  
Research Service, Hines VA Hospital, Hines, IL, USA

S.T. Sayers, PhD  
Department of Thoracic and Cardiovascular Surgery, Loyola  
University Medical Center, Maywood, IL, USA

S. Singh, MS, PhD  
Research Service, Edward Hines Jr., VA Hospital, Hines, IL, USA

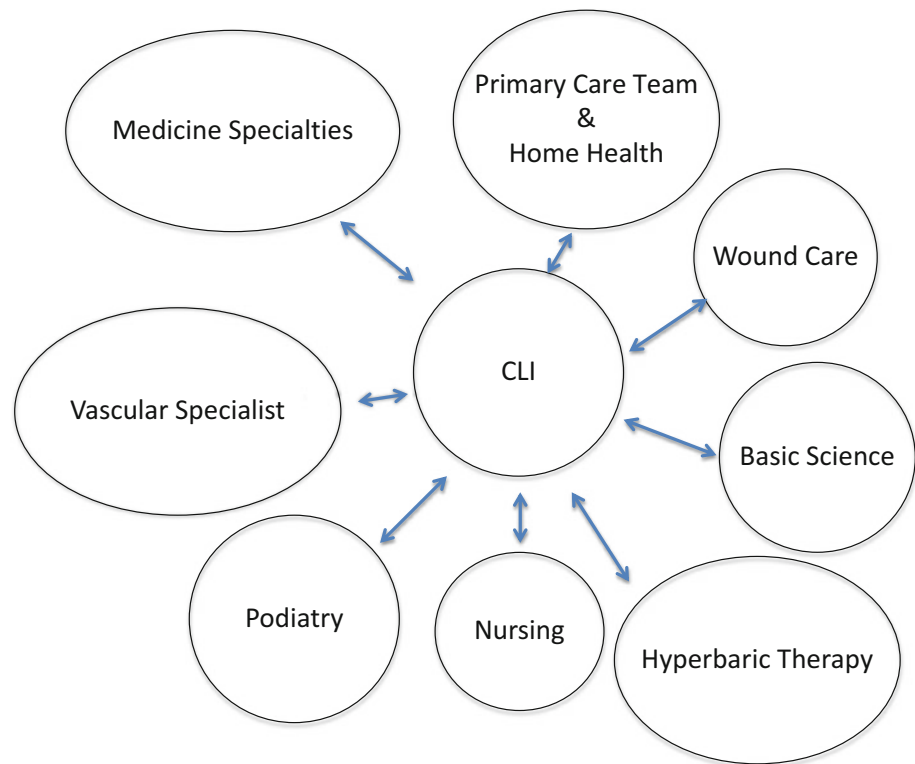
M.M. Meyer, MD  
Internal Medicine, Illinois State Medical Society,  
Lombard, IL, USA

A.S. Dayal, MD  
Medicine, Edward Hines Jr., Veterans Affairs Hospital,  
Hines, IL, USA

A. Darki, MD, MSc  
Medicine, Cardiology, Loyola University Medical Center,  
Maywood, IL 60153, USA

R.S. Dieter, MD, RVT (✉)  
Medicine, Cardiology, Vascular and Endovascular Medicine,  
Loyola University Medical Center, Maywood, IL, USA

**Fig. 55.1** Multidisciplinary approach to critical limb ischemia



will require endovascular or surgical revascularization. Endovascular therapies have epitomized the overlap of a therapy offered by different disciplines. Rather than interdepartmental conflicts, working together enhances patient care and creates a collaborative learning environment that benefits all. Critical limb ischemia is one end of the spectrum of cardiovascular disease—an extreme with incredibly sick patients. Rather than focusing on our differences, combined programs recognize our common grounds so that these patients are appropriately recognized and treated.

### Definition, Incidence, and Epidemiology of Critical Limb Ischemia

Critical limb ischemia may develop consequent to a number of acute or chronic processes including trauma, vascular, or malignant processes that endanger the viability of the extremity. Chronic limb ischemia contributes to significant morbidity and mortality; it is estimated to account for more than 400,000 hospitalizations in the United States every year. It also carries a 20% annual mortality [2]. The various degrees of limb ischemia—acute, subacute, or chronic—are a growing problem in United States secondary to an increase in the aging population who have many comorbidities such as diabetes mellitus, hypertension, atherosclerosis, and end-stage renal disease. The afflicted require appropriate and timely intervention to salvage the patient and the extremity after appropriate pre-intervention review.

### Multidisciplinary Approach for Treating Patients with CLI Secondary to Obstructive Arterial Disease

Ideal therapy for peripheral arterial occlusive disease is yet to be determined. Standard surgical therapy has been bypass for those patients who have tissue loss or rest pain. However, since the advent of endovascular therapy, minimally invasive therapy has been replacing open revascularization in most institutions. These interventions are only advised after initial noninterventional diagnostic approaches, treatment of any underlying processes (such as infection, edema, wound care, nutritional status, etc.), and appropriate consideration and treatment of non-arterial contributors to the CLI.

In a comparative study between open surgical revascularization and endovascular therapies for femoropopliteal occlusive disease in patients with no previous intervention, surgical bypass for the primary treatment of claudication showed improved freedom from restenosis and symptom relief despite treatment of more extensive disease, but was associated with increased length of stay and wound infection. Medical therapy with statins has shown improved freedom from restenosis and symptom recurrence overall [3].

Yet the only randomized controlled study comparing the bypass versus the angioplasty in patients with CLI is the “Bypass versus Angioplasty in Severe Ischemia of the Leg” [4]. This study concluded that there is no initial difference between angioplasty and open surgery arms regarding the

amputation-free survival or overall survival. However after 2 years, patients with surgery did better than angioplasty. Secondary analysis of the same study indicated that both failed endovascular and prosthetic bypass grafts were predictors of failure after intervention. This further points out the need to justify initial intervention and whether it should be delayed or performed as well as the need for further study.

In a retrospective study to evaluate the efficacy of endovascular therapies in recurrent femoropopliteal occlusive disease, this study concluded that second-time femoropopliteal angioplasty/stenting has excellent technical success but limited midterm primary and secondary patency. Early failure of the initial endovascular intervention strongly predicts poor outcome and in this cohort was more significant than comorbidities, anatomic factors, or procedural characteristics. These data suggest that after early endovascular failure, alternatives to a continued endoluminal strategy should be adopted [5]. Although endovascular therapy allows for a less invasive approach, the clinician must be open minded to surgical revascularization when symptoms warrant.

Flush ostial occlusion of the SFA may contribute to significant challenge to the vascular specialist; Hayes et al. found that a combined femoral endarterectomy and endovascular femoral-popliteal stent grafting provides a viable option for revascularization of flush SFA occlusions utilizing only a minimal groin incision [6]. This highlights the necessity to approach revascularization in an open-minded, multidisciplinary approach.

According to the Trans-Atlantic Inter-Society Consensus (TASC) II guidelines, lesions can be classified according to their complexity. These provide a common recommendation to confer endovascular treatment to TASC II A and B lesions. With increasing experience, there is an ongoing expansion of the indications and utilization of endovascular therapies in TASC II C and D. Sidhu et al. evaluated 120 patients with TASC II C/D lesions intervened upon and found the technical success was 91%. Primary patency at 6 and 12 months was 90% and 73%. Secondary patency at 6 and 12 months was 94% and 85%. The long-term amputation-free survival was 90% with limb salvage rate of 98% at 1 year. The authors concluded that endovascular treatment for TASC C/D lesions is a safe procedure and may be considered an alternative to bypass, especially in high-risk patients [7]. Once again, this highlights the necessity to look at patients in a cross-disciplinary manner to optimize patient care.

---

## Chronic Venous Ulceration

The prevalence of chronic venous ulcers (CVU) is underestimated. It affects more than 600,000 people annually in the United States. In the general population, the prevalence of CVU is estimated to be 2% and increasing, as it is more

common in the population >65 years [8]. In addition, it contributes to a significant socioeconomic burden in our society as it accrues treatment costs of US\$2.5–5 billion per year [8, 9].

Risk factors for CVU include age, heredity, female sex, and obesity [10]. The underlying pathophysiology of CVU is a complex interplay between many pathological factors such as chronic DVTs, venous hypertension (valvular dysfunction and varicosities), chronic dermal inflammation with subsequent lipodermatosclerosis, and cellular dysfunction secondary to cytokine and matrix metalloproteinase (MMP) activation [10].

Besides compression and elevation, the main therapy to treat venous hypertension is multidisciplinary. Patients require elevation, wound care, compression stockings, or Unna boots; some require venous ablation and nutritional support. For example, one of our patients was admitted to the hospital 6 times due to recurrent infected ulceration. Once she accepted periodic leg elevation and night time elevation of the foot of the bed, the ulcers never recurred.

Additionally, venous ablation helps with wound care and reduction in ulcer recurrence [11]. The long-term corner stone element of treating CVU is elevation and to maintain compression therapy to reduce venous stasis. The ESCHAR trial showed that superficial venous surgery and compression is equivalent to compression alone for wound healing but superior regarding CVU recurrence. In CVU, combined therapy achieved a 24-week healing rate of 65% and 12-month recurrence rate of 12% ( $p < 0.0001$ ) [12]. The same authors in another trial reported that superficial venous surgery also resulted in a significant hemodynamic benefit for limbs with CVU despite coexistent deep reflux and residual saphenous reflux being common [13]. Others have related CVU to an increase in the compartment pressure. Within a 4-year period, 58 patients with 70 CVU were evaluated with superficial venous ablation plus subcutaneous fasciotomy, and it was found that this approach can expedite ulcer healing and decrease recurrence especially in patients without the post-phlebotic syndrome [14]. Further, negative pressure wound therapy (NPWT) may play a role in wound healing, stimulation, and possibly preparing the ulcers for the next treatment therapy such as artificial or autogenous skin graft [15].

---

## Diabetic Ulcers/Diabetic Neuropathy

There is no doubt that diabetes mellitus with its possible complications is a major contributor to leg and foot ulcer formation. The natural history of diabetic neuropathy is a progressive and irreversible loss of sensitivity in the feet. As such, it is crucial to remember the multidisciplinary approach to the diabetic patient—to involve podiatry, endocrinology, and other disciplines, highlighting the fact that diabetic foot

ulcers are the consequence of multiple factors including peripheral neuropathy, decreased blood supply, and high plantar pressures. [16].

---

## Basic Science

Whatever the reasons for the development of the leg ulcer, continued study into causes and treatments is necessary. For example, better dietary treatment of diabetes and atherosclerotic risk factors is a cornerstone to nutritional support. The role of gene therapy and growth factors for angiogenesis and wound healing is evolving. It is through basic science and benchtop/translational research that we have a better understanding of how to treat our patients, ultimately in a less invasive and more efficient manner.

In conclusion, it is only through a multidisciplinary approach to the patient and the wound that the ulceration will be adequately healed and associated mortality reduced.

---

## References

- Serra R, et al. Low molecular weight heparin improves healing of chronic venous ulcers especially in the elderly. *Int Wound J.* 2013;12:150–3.
- Conrad MF, et al. Intermediate results of percutaneous endovascular therapy of femoropopliteal occlusive disease: a contemporary series. *J Vasc Surg.* 2006;44(4):762–9.
- Siracuse JJ, et al. Long-term results for primary bypass versus primary angioplasty/stent for intermittent claudication due to superficial femoral artery occlusive disease. *J Vasc Surg.* 2012;55:1001–7.
- Conte MS. Bypass versus angioplasty in severe ischaemia of the leg (BASIL) and the (hoped for) dawn of evidence-based treatment for advanced limb ischemia. *J Vasc Surg.* 2010;51(5):69S–75S.
- Robinson 3rd WP, et al. Results of second-time angioplasty and stenting for femoropopliteal occlusive disease and factors affecting outcomes. *J Vasc Surg.* 2011;53(3):651–7.
- Hayes Jr DJ, Dougherty MJ, Calligaro KD. Management of flush superficial femoral artery occlusions with combined open femoral endarterectomy and endovascular femoral-popliteal angioplasty and stent-grafting. *Ann Vasc Surg.* 2011;25(4):559.e19–23.
- Sidhu R, et al. Subintimal angioplasty for advanced lower extremity ischemia due to TASC II C and D lesions of the superficial femoral artery. *Vasc Endovascular Surg.* 2010;44(8):633–7.
- McDaniel JC, Roy S, Wilgus TA. Neutrophil activity in chronic venous leg ulcers—a target for therapy? *Wound Repair Regen.* 2013;21(3):339–51.
- Serra R, et al. Doxycycline speeds up healing of chronic venous ulcers. *Int Wound J.* 2013;12:179–84.
- Raffetto JD. Inflammation in chronic venous ulcers. *Phlebology.* 2013;28(1):61–7.
- Sufian S, Lakhnpal S, Marquez J. Superficial vein ablation for the treatment of primary chronic venous ulcers. *Phlebology.* 2011;26(7):301–6.
- Barwell JR, et al. Comparison of surgery and compression with compression alone in chronic venous ulceration (ESCHAR study): randomised controlled trial. *Lancet.* 2004;363(9424):1854–9.
- Gohel MS, et al. Randomized clinical trial of compression plus surgery versus compression alone in chronic venous ulceration (ESCHAR study)—haemodynamic and anatomical changes. *Br J Surg.* 2005;92(3):291–7.
- Christenson JT, Prins C, Gemayel G. Subcutaneous fasciotomy and eradication of superficial venous reflux for chronic and recurrent venous ulcers: mid-term results. *Phlebology.* 2011;26(5):197–202.
- Kieser DC, et al. Negative pressure wound therapy as an adjunct to compression for healing chronic venous ulcers. *J Wound Care.* 2011;20(1):35–7.
- Kavitha KV, et al. Choice of wound care in diabetic foot ulcer: a practical approach. *World J Diabetes.* 2014;5(4):546–56.