The burden of critical limb ischemia (CLI) is staggering—for the individual patient, for providers, on the health care system, and on society as a whole. Individuals with CLI represent the most challenging patients for those clinicians who treat peripheral arterial disease (PAD). Yet, these patients also stand to benefit the most from proper and effective management. CLI is characterized by intractable foot or ankle pain at rest and/or the presence of ischemic ulcerations or gangrene. Without successful revascularization, up to 40% of patients will require limb amputation. The annual incidence of CLI in the United States is 500 to 1,000 per million and is expected to grow due to the impact of diabetes, dietary indiscretion, tobacco abuse, and the aging population.

Medical therapy is generally ineffective in CLI: resolution of rest pain or tissue loss requires successful revascularization to improve limb perfusion. Over the last 2 decades, the widespread adoption of endovascular techniques for PAD has extended to patients with CLI in whom reduced periprocedural morbidity and mortality compared to open surgery has created a paradigm shift away from surgical bypass toward an endo-first approach. Yet, evidence regarding effectiveness, durability, cost, and appropriate case selection for initial treatment with endovascular intervention versus open surgery is lacking. There is general agreement that poor surgical candidates are appropriate for endo-first, but in patients who are candidates for both open and endovascular treatment, it remains to be defined which therapy is most effective (and cost-effective).

BEST-CLI is a prospective, randomized, multicenter (and multispecialty), controlled trial comparing Best Endovascular versus Best Surgical Therapy in patients with Critical Limb Ischemia, designed to evaluate these issues. Funded by the National Institutes of Health (NIH), it will enroll 2,100 patients with CLI at 120 North American sites over the course of 4 years. The aim of BEST-CLI is to compare treatment efficacy, functional outcomes, and cost in patients who are candidates for both infrainguinal open surgical and endovascular revascularization. The design is pragmatic: once randomized, the definition of best endovascular or surgical therapy is left to the individual investigator. Investigators may use virtually any commercially available endovascular therapy, as well as all surgical bypass techniques and types of conduit.

The national Principal Investigators are Drs. Alik Farber, Matthew Menard, and Kenneth Rosenfield. The Executive Committee and investigators represent all disciplines involved with CLI collaboration among specialties will be mandated. BEST-CLI will examine two cohorts of patients: 1,620 patients with adequate single segment great saphenous vein (SSGSV) and 480 patients without adequate SSGSV. Within each group, patients will be randomized 1:1 between open surgical bypass and endovascular therapy. Groups will also be stratified based on clinical presentation and anatomy.

The BEST-CLI trial incorporates novel endpoints and a robust cost-effectiveness component. The primary endpoint is major adverse limb event (MALE)—free survival. This aggregate measure captures the main goals of treatment, namely, survival with an intact, functional limb without a major reintervention (eg, repeat bypass graft, thrombectomy or thrombolysis, major surgical graft revision) that might significantly impact quality of life (QoL). Minor reinterventions (eg, surgical patch angioplasty or percutaneous intervention without lysis) are captured as secondary endpoints, as are amputation-free survival, reintervention- and amputation-free survival, freedom from MALE perioperative death, and freedom from myocardial infarction or stroke. BEST-CLI will also provide a comprehensive assessment of patient functional status, QoL, and cost-effectiveness, capturing resource utilization throughout the continuum of care.

The BEST-CLI trial and NIH leadership acknowledge the importance of participation of all relevant specialties at each trial site in promoting the concept of CLI teams. CLI teams are intended to promote enrollment of all eligible patients, ensure standard-of-care treatment for each patient, and create a collaborative environment with ongoing communication, collegiality, and information exchange among investigators. BEST-CLI promises to answer many questions that remain regarding the management of patients with CLI and infraguinal PAD, and to help define best practice in these challenging patients.

The BEST-CLI Trial: A Multidisciplinary Effort to Identify What’s BEST for Patients With Critical Limb Ischemia

BY ALIK FARBER, MD; MATTHEW MENARD, MD; AND KENNETH ROSENFIELD, MD