Failure to achieve clinical improvement despite graft patency in patients undergoing infrainguinal lower extremity bypass for critical limb ischemia

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Objective: **Studies of infrainguinal lower extremity bypass for critical limb ischemia (CLI) have traditionally emphasized outcomes of patency, limb salvage, and death. Because functional outcomes are equally important, our objectives were to describe the proportion of CLI patients who did not achieve symptomatic improvement 1 year after bypass, despite having patent grafts, and identify preoperative factors associated with this outcome.**

Methods: **The prospectively collected Vascular Study Group of Northern New England database was used to identify all patients with elective infrainguinal lower extremity bypass for CLI (2003 to 2007) for whom long-term follow-up data were available. The primary composite study end point was clinical failure at 1 year after bypass, defined as amputation or persistent or worsened ischemic symptoms (rest pain or tissue loss), despite a patent graft. Variables identified on univariate screening (inclusion threshold, $P < .20$) were included in a multivariable logistic regression model to identify independent predictors.**

Results: **Long-term follow-up data were available for 1012 patients who underwent infrainguinal bypasses for CLI, of which 788 (78%) remained patent at 1 year. Of these, 79 (10%) met criteria for the composite end point of clinical failure: 21 (2.7%) for major amputations and 58 (7.4%) for persistent rest pain or tissue loss. In multivariable analysis, significant predictors of clinical failure included dialysis dependence (odds ratio [OR], 3.74; 95% confidence interval [CI], 1.84-7.62; $P < .001$) and preoperative inability to ambulate independently (OR, 2.17; 95% CI, 1.26-3.73; $P = .005$). A history of coronary artery bypass graft or percutaneous coronary intervention was protective (OR, 0.52; 95% CI, 0.29-0.93; $P = .03$).**

Conclusions: **After infrainguinal lower extremity bypass for CLI, 10% of patients with a patent graft did not achieve clinical improvement at 1 year. Preoperative identification of this specific patient subgroup remains challenging. To improve surgical decision making and the overall care of CLI patients, further emphasis needs to be placed on functional outcomes in addition to traditional surgical end points. (J Vasc Surg 2010;51:1419-24.)**

The management of patients with critical limb ischemia (CLI) remains complex, with several factors contributing to the treatment decision-making process. Traditional study end points for these patients have included graft patency,[1,2] limb salvage,[3,4] or death.[5,6] More recently, however, alternative end points have emerged that include amputation-free survival,[7-9] major adverse cardiovascular events,[9] target limb revascularization,[10] quality of life,[11] and functional outcomes such as the ability to ambulate or to live independently after surgery.[6,11,12] Although these findings, interpreted in aggregate, do suggest an association between graft patency and quality of life, most clinicians would acknowledge that patency does not always equate with symptom resolution and functional improvement.

The proportion of patients that does not experience clinical improvement at 1 year postoperatively, despite infrainguinal graft patency, has not been well delineated. Therefore, the objective of the current investigation was to use the prospectively collected Vascular Study Group of Northern New England (VSGNNE) database to address this question. In addition, we sought to identify preoperative factors associated with persistent ischemic symptoms or ipsilateral amputation, despite graft patency, to improve preoperative patient counseling.

METHODS

Cohort assembly. The VSGNNE is a regional cooperative quality improvement initiative that was developed in 2002 to prospectively evaluate outcomes in patients undergoing vascular surgery. Eleven teaching and nonteaching hospitals with 59 vascular surgeons (community and academic) currently participate in this program by reporting data into the registry. All data are self-reported and sent to a central data repository where they are aggregated and reviewed. Research analysts are blinded to patient, surgeon, and hospital identity.

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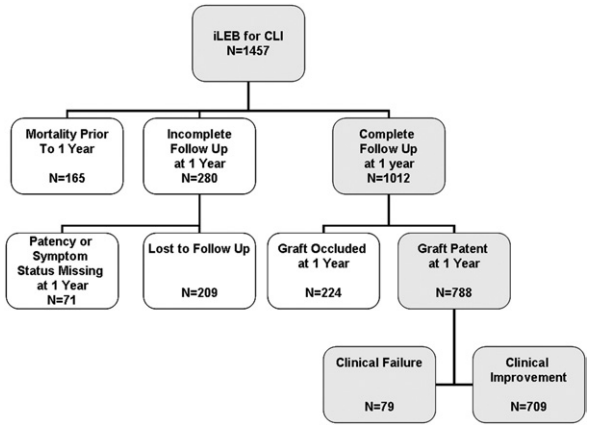

Fig 1. Flowchart shows cohort selection for primary analysis of clinical failure, defined as persistent rest pain, tissue loss, or ipsilateral major amputation at 1 year, despite a patent graft. *CLI,* Critical limb ischemia; *iLEB,* infrainguinal lower extremity bypass.

At the time of discharge after the index operation, a perioperative data sheet containing preoperative, intraoperative, and postoperative data is completed and submitted to the VSGNNE. The VSGNNE does not mandate a specific protocol for graft surveillance or medical or wound therapy after lower extremity bypass. These specific management decisions are left to the discretion of the operating surgeon.

The study design for the VSGNNE registry emphasizes the importance of collecting follow-up data at 1 year for all patients with procedures entered into the registry. To facilitate compliance with this requirement, the central site sends an electronically automated follow-up form for each operation to each surgeon in advance of the expected 1-year office visit. Accordingly, at the approximate 1-year follow-up, this data sheet is completed and submitted to the VSGNNE (acceptable window for the current analysis was 6 to 18 months). Data pertaining to ambulation status, symptom status, patency, ankle-brachial index, bypass graft revisions, or amputations are recorded on this form. Since the inception of the study, a claims-based audit system has been used that has demonstrated 99% accuracy in capturing consecutive operations performed at each center. Details relating to the VSGNNE study design have been published previously[13] and are available at the VSGNNE Web site (www.vsgnne.org).

For the purpose of this study, the VSGNNE database was queried for patients undergoing elective and urgent infrainguinal lower extremity bypass (iLEB) performed between January 1, 2003, and December 31, 2007, for an indication of CLI (defined as tissue loss or ischemic rest pain). To assess outcomes at 1 year, patients were excluded if they did not have a completed 1-year follow-up form that included all data pertaining to symptom status and patency, resulting in 445 of the 1457 patients being excluded (Fig 1). All infrainguinal bypass configurations were included for analysis, regardless of the specific inflow site, outflow site, or conduit.

Covariates examined. Patient information for >70 clinical and demographic variables (available at www.vsgnne.org) was collected. Comorbidities examined included coronary artery disease (history of myocardial infarction or angina), chronic obstructive pulmonary disease (COPD, medication-dependent or home oxygen-dependent), congestive heart failure (by history), diabetes mellitus (insulin-dependent or controlled by oral medication or diet), hypertension (history of hypertension or blood pressure ≥140/90 mm Hg on the preoperative evaluation), and history of tobacco use (never, <1 year prior, or current). Renal disease was categorized in three strata: normal (serum creatinine ≤1.8 mg/dL), renal insufficiency (serum creatinine >1.8 mg/dL), and dialysis-dependent.

Variables related to surgical history included previous coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI), as well as previous carotid, aortic, peripheral bypass or stent, and major extremity amputation. Medication variables included preoperative use of antiplatelet agents, statins, or β-blockers. Functional variables included preoperative living status (home or nursing home) and ambulation status (independent, with assistance, wheelchair-bound, and bed-bound).

Also evaluated were procedural details, such as urgency, bypass conduit, and bypass target vessel. Bypass conduit was considered a preoperatively available variable, based on an assumption that most patients undergoing bypass surgery receive vein mapping, allowing for a preoperative determination of conduit availability. Long-term follow-up data included vital status, patency of the graft (whether primary or secondary by duplex graft surveillance scan), amputation status, and symptoms (asymptomatic, claudication, rest pain, or tissue loss). Vital status was confirmed for all patients using follow-up visit notes and a current version of the Social Security Death Index.

Primary end point. Clinical failure, which was the primary end point, was defined as rest pain, tissue loss, or ipsilateral amputation (major amputation is defined as above- or below-knee [loss of foot] amputation) at long-term follow-up, despite a patent graft. The study excluded four patients who did not undergo amputation but were missing information on their symptoms at follow-up.

Statistical analysis. Baseline characteristics were compared between groups using Pearson χ^2 analysis for categoric variables and the *t* test for continuous variables. Those variables with a value of $P < .2$ were entered into a logistic regression model for the primary outcome of clinical failure. Significance was accepted at the $P < .05$ level. All analyses were conducted using SAS 9.1 software (SAS Institute, Cary, NC).

RESULTS

Cohort characteristics. Between 2003 and 2007, 1457 patients underwent elective or urgent iLEB for CLI at 11 participating centers. The perioperative death rate, defined as 30-day mortality, was 2.2%. After excluding 445 patients who did not specifically have patency or symptom status information at the 1-year follow-up, 1012 patients