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Outcomes after first-time lower extremity revascularization for chronic limb-threatening ischemia between patients with and without diabetes

Jeremy D. Darling, BA,[a] Thomas C. F. Bodewes, MD,[a,b] Sarah E. Deery, MD,[a,c] Raul J. Guzman, MD,[a] Mark C. Wyers, MD,[a] Allen D. Hamdan, MD,[a] Hence J. Verhagen, MD,[d] *and* Marc L. Schermerhorn, MD,[a]
Boston, Mass; and Utrecht and Rotterdam, The Netherlands

ABSTRACT

Objective: The effect of diabetes type and insulin dependence on short- and long-term outcomes after lower extremity revascularization for chronic limb-threatening ischemia (CLTI) warrants additional study and more targeted focus. We sought to address this paucity of information by evaluating outcomes in insulin-dependent and noninsulin-dependent patients after any first-time revascularization.

Methods: We reviewed all limbs undergoing first-time infrainguinal bypass grafting (BPG) or percutaneous transluminal angioplasty with or without stenting (PTA/S) for CLTI at our institution from 2005 to 2014. Based on preoperative medication regimen, patients were categorized as having insulin-dependent diabetes (IDDM), noninsulin-dependent diabetes (NIDDM), or no diabetes (NDM). Outcomes included wound healing; major amputation; RAS events (reintervention, major amputation, or stenosis); major adverse limb events; and mortality. Outcomes were evaluated using χ^2, Kaplan-Meier, and Cox regression analyses.

Results: Of 2869 infrainguinal revascularizations from 2005 to 2014, 1294 limbs (646 BPG, 648 PTA/S) fit our criteria. Overall, our analysis included 703 IDDM, 262 NIDDM, and 329 NDM limbs. IDDM patients, compared with NIDDM and NDM patients, were younger (69 vs 73 vs 77 years; $P < .001$) and more often presented with tissue loss (89% vs 77% vs 67%; $P < .001$), coronary artery disease (57% vs 48% vs 43%; $P < .001$), and end-stage renal disease (26% vs 13% vs 12%; $P < .001$). Perioperative complications, including mortality (3% vs 2% vs 5%; $P = .07$), did not differ between groups; however, complete wound healing at 6-month follow-up was significantly worse among IDDM patients (41% vs 49% vs 61%; $P < .001$). IDDM patients had significantly higher 3-year major amputation rates (23% vs 11% vs 8%; $P < .001$). Multivariable analyses illustrated that compared with NDM, IDDM was associated with significantly higher risk of both major amputation and RAS events after any first-time intervention (hazard ratio, 2.0 [95% confidence interval, 1.1-4.1] and 1.4 [1.1-1.8], respectively). Similar associations between IDDM and both major amputation and RAS events were found in patients undergoing a PTA/S-first intervention (4.1 [1.3-12.6] and 1.5 [1.1-2.2], respectively), whereas IDDM in BPG-first patients was associated with only incomplete wound healing (2.0 [1.4-4.5]). Last, compared with NDM, NIDDM was associated with lower late mortality (0.7 [0.5-0.9]).

Conclusions: Compared with NDM, IDDM is associated with similar perioperative and long-term mortality but a higher risk of incomplete wound healing, major amputation, and future RAS events, especially after a PTA/S-first approach. NIDDM, on the other hand, is associated with lower long-term mortality and few adverse limb events. Overall, these data demonstrate both the importance of distinguishing between diabetes types and the potential long-term benefit of a BPG-first strategy in appropriately selected IDDM patients with CLTI. (J Vasc Surg 2017;■:1-10.)

Despite advances in the management of diabetes, the profound effect of the estimated growth is still likely to yield a tremendous escalation in end-stage peripheral artery disease (PAD).[1] Chronic limb-threatening ischemia (CLTI), broadly defined as the most advanced stages of PAD and demarcated by ischemic rest pain, nonhealing ulcer, or gangrene, is significantly more likely in diabetic patients and is often a debilitating condition.[2] Ultimately,

From the Division of Vascular and Endovascular Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School,[a] and the Department of Surgery, Massachusetts General Hospital,[c] Boston; the Department of Vascular Surgery, University Medical Center, Utrecht[b]; and the Department of Vascular Surgery, Erasmus University Medical Center, Rotterdam.[d]

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Correspondence: Marc L. Schermerhorn, MD, Division of Vascular and Endovascular Surgery, Beth Israel Deaconess Medical Center, 110 Francis St, Ste 5B, Boston, MA 02215 (e-mail: mscherm@bidmc.harvard.edu).

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the diagnosis of PAD in patients with diabetes is often delayed because of the presence of neuropathy, as PAD-related symptoms go unnoticed until more severe CLTI symptoms develop.[3] Given the prevalence and severity of such events, nonoperative wound management and care may not be sufficient to avoid limb loss.

Although open surgical bypass grafting (BPG) has been shown to have excellent results in patients with diabetes and PAD, contemporary management of CLTI has gradually favored the use of minimally invasive techniques that offer lower periprocedural morbidity and mortality, reduced costs, faster procedural times, and shortened hospital stay.[4] Several studies have compared the utility of both BPG and percutaneous transluminal angioplasty with or without stenting (PTA/S) in varying degrees of lower extremity limb ischemia and in patients with and without diabetes; however, in the current endovascular era, few studies have evaluated the degree to which these subsets of patients fare in regard to procedure type.[5-13] In this study, we sought to describe our institution's long-term experience with BPG-first and PTA/S-first repair in insulin-dependent, noninsulin-dependent, and nondiabetic patients.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective review of a prospectively maintained single-center database
- **Take Home Message:** In 1294 limbs undergoing a first-time infrainguinal revascularization for chronic limb-threatening ischemia, insulin-dependent diabetes was associated with poorer wound healing, more major amputations, and more frequent reinterventions and restenosis than noninsulin-dependent diabetes or no diabetes at all.
- **Recommendation:** This study suggests that increased attention should be paid to insulin dependency in diabetics with chronic limb-threatening ischemia as it is associated with poorer outcomes after first-time revascularization compared with noninsulin-dependent diabetics or nondiabetics.

METHODS

Subjects and settings. We performed a retrospective review of all patients with CLTI undergoing a first-time lower extremity intervention at Beth Israel Deaconess Medical Center. Medical records of all BPG and PTA/S interventions from January 2005 to October 2014 were individually reviewed. Patients were categorized as having insulin-dependent diabetes (IDDM), noninsulin-dependent diabetes (NIDDM), or no diabetes (NDM). IDDM was defined as preoperative or at-home reliance on insulin administration to control diabetes at baseline. Patients with diabetes who were not prescribed insulin were categorized as having NIDDM. Importantly, for the purposes of this study, insulin dependence is not considered tantamount to type 1 diabetes, as it describes the patient-level pattern of insulin use at the time of revascularization. Patients who received previous interventions on the ipsilateral limb (whether at Beth Israel Deaconess Medical Center or at an outside institution) or interventions solely at or proximal to the iliac arteries were excluded. Patients undergoing a concomitant procedure, including endarterectomy, profundaplasty, thrombectomy, atherectomy, and patch, were included and adjusted for in our multivariable analyses. The interval for typical patient follow-up was every 3 to 4 months for 2 years and every 6 months afterward; the modality of follow-up was arterial duplex ultrasound imaging and ankle-brachial indices with forefoot pulse volume recordings or toe pressures.

Our analysis included patients whose disease severity was distinctly classifiable as CLTI and who underwent either first-time BPG or first-time PTA/S. Indications for intervention included tissue loss (ie, gangrene and ulcer) and rest pain. Patients presenting with more than one indication were assigned hierarchically, with gangrene constituting the most severe indication, followed by ulcer, and then rest pain. Femoropopliteal lesion anatomy and severity were defined according to the modified TransAtlantic Inter-Society Consensus II (TASC II) classification. As there was no updated TASC class for tibial lesions included in the modified TASC II classification, tibial lesion information was defined by TASC I.[14,15]

Measurements and outcome variables. Primary outcomes included perioperative complications, wound healing, major amputation, RAS events (a composite variable denoted by reintervention, major amputation, or stenosis), major adverse limb events (MALE; a composite variable denoted by any major amputation or any major reintervention, defined as creation of a new bypass graft, a jump graft revision, surgical thrombectomy with or without surgical patch angioplasty, and thrombectomy of an occluded graft or arterial segment using pharmacologic or mechanical thrombolysis), and mortality.[16] Demographics, comorbidities, Society for Vascular Surgery Wound, Ischemia, and foot Infection (WIfI) information, restenosis, and reintervention were also recorded.[17] Perioperative complications included hematoma, acute myocardial infarction, and death. Cardiac enzymes and electrocardiograms were not routinely obtained after revascularization. If patients developed chest pain, dyspnea, hemodynamic instability, or other concerning signs or symptoms, an electrocardiogram was obtained with cardiac enzymes (if the patient had electrocardiographic changes or strong history of coronary disease). The criterion for restenosis was at least 75% stenosis by angiographic measurement or a >3.5-fold increase in peak systolic velocity by duplex ultrasound. Reinterventions included any ipsilateral surgical or