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Clinical outcomes of bypass-first versus endovascular-first strategy in patients with chronic limb-threatening ischemia due to infrageniculate arterial disease

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Abstract

Background: Chronic limb-threatening ischemia (CLTI), defined as ischemic rest pain or tissue loss secondary to arterial insufficiency, is caused by multilevel arterial disease with frequent, severe infrageniculate disease. The rise in CLTI is in part the result of increasing worldwide prevalence of diabetes, renal insufficiency, and advanced aging of the population. The aim of this study was to compare a bypass-first with an endovascular-first revascularization strategy in patients with CLTI due to infrageniculate arterial disease.

Methods: We reviewed the American College of Surgeons National Surgical Quality Improvement Program targeted lower extremity revascularization database from 2012 to 2015 to identify patients with CLTI and isolated infrageniculate arterial disease who underwent primary infrageniculate bypass or endovascular intervention. We excluded patients with a history of ipsilateral revascularization and proximal interventions. The end points were major adverse limb event (MALE), major adverse cardiovascular event (MACE), amputation at 30 days,

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AUTHOR CONTRIBUTIONS

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Analysis and interpretation: SK, NM, MH
Data collection: AD
Writing the article: AD, MH
Critical revision of the article: AD, NT, SK, NM, MH
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reintervention, patency, and mortality. Multivariable logistic regression was used to determine the association of a bypass-first or an endovascular-first intervention with outcomes.

Results: There were 1355 CLTI patients undergoing first-time revascularization to the infrageniculate arteries (821 endovascular-first revascularizations and 534 bypass-first revascularizations) identified. There was no significant difference in adjusted rate of 30-day MALE in the bypass-first vs endovascular-first revascularization cohort (9% vs 11.2%; odds ratio [OR], 0.73; 95% confidence interval [CI], 0.50-1.08). However, the incidence of transtibial or proximal amputation was lower in the bypass-first cohort (4.3% vs 7.4%; OR, 0.60; CI, 0.36-0.98). Patients with bypass-first revascularization had higher wound complication rates (9.7% vs 3.7%; OR, 2.75; CI, 1.71-4.42) compared with patients in the endovascular-first cohort. Compared with the endovascular-first cohort, the incidence of 30-day MACE was significantly higher in bypass-first patients (6.9% vs 2.6%; adjusted OR, 3.88; CI, 2.18-6.88), and 30-day mortality rates were 3.23% vs 1.8% (adjusted OR, 2.77; CI, 1.26-6.11). There was no difference in 30-day untreated loss of patency, reintervention of treated arterial segment, readmissions, and reoperations between the two cohorts. In subgroup analysis after exclusion of dialysis patients, there was also no significant difference in MALE or amputation between the bypass-first and endovascular-first cohorts.

Conclusions: CLTI patients with isolated infrageniculate arterial disease treated by a bypass-first approach have a significantly lower 30-day amputation. However, this benefit was not observed when dialysis patients were excluded. The bypass-first cohort had a higher incidence of MACE compared with an endovascular-first strategy. These results reaffirm the need for randomized controlled trials, such as the Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL-2) trial and Best Endovascular vs Best Surgical Therapy in Patients with Critical Limb Ischemia (BEST-CLI), to provide level 1 evidence for the role of endovascular-first vs bypass-first revascularization strategies in the treatment of this population of challenging patients.

Keywords

Critical limb ischemia/chronic limb-threatening ischemia; Infrapopliteal/infrageniculate arterial disease; Endovascular intervention; Open bypass

Chronic limb-threatening ischemia (CLTI) is a subset of peripheral arterial disease characterized by varying degrees of foot pain at rest or the presence of ischemic ulcerations and tissue loss. The incidence of CLTI in the United States is estimated to be between 500 and 1000 per million persons per year.[1] The incidence of CLTI is rising worldwide because of the aging population, increasing rates of metabolic syndrome, and continuing high rates of smoking.[2] CLTI is associated with significant disability, morbidity, and mortality.[3] At 1 year after the development of CLTI, it is estimated that up to 30% of patients have an amputation, and 25% of patients die.[1,3] The decision to recommend surgical or endovascular revascularization for CLTI patients varies substantially among providers. The United Kingdom multicenter Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial remains the only randomized controlled trial (RCT) to compare a bypass-first with an endovascular-first revascularization strategy for infrainguinal arterial occlusive disease; however, this study did not specifically address the effectiveness of treatment for the infrageniculate arteries.[4] In this study, we used the American College of Surgeons

National Surgical Quality Improvement Program (ACS NSQIP) targeted lower extremity revascularization data to provide short-term contemporary data on the effectiveness of a bypass-first vs endovascular-first strategy for revascularization in patients with CLTI due to infrageniculate arterial disease.

METHODS

Data source.

The ACS NSQIP and targeted lower extremity revascularization NSQIP are risk-adjusted procedure-based data sets for analysis of clinical outcomes. Participating hospitals use their collected data to develop quality initiatives that improve surgical care and to identify elements in health care that can be improved compared with other institutions. The ACS NSQIP collects data on a variety of clinical variables, including preoperative risk factors, intraoperative variables, and 30-day postoperative mortality and morbidity outcomes, for patients undergoing major surgical procedures in both the inpatient and outpatient settings. The targeted vascular module includes additional disease- and procedure-specific characteristics as well as procedure-related outcomes chosen by vascular surgeons. Each site has trained surgical clinical nurse reviewers (SCNRs) who capture outcomes data by medical record extraction. To ensure that the data collected are of high quality, the NSQIP has developed different training mechanisms for the SCNRs and conducts an inter-rater reliability audit of participating sites. The processes of SCNR training, inter-rater reliability auditing, data collection, and sampling methodology have been previously described in detail.[5]

Data selection and outcomes.

The Institutional Review Board approved this project and waived the need for informed consent for the use of deidentified data. We reviewed the lower extremity revascularization-targeted ACS NSQIP and the ACS NSQIP data sets from 2012 to 2015 for this study. This data source contains prospectively collected information on perioperative variables, including indication for index operation, procedure technique (endovascular vs bypass), type of conduit (single-segment great saphenous vein or prosthetic or spliced/composite vein conduit), symptoms (claudication, rest pain, tissue loss), level of revascularization (femoral endarterectomy, femoral-popliteal bypass, femoral-popliteal angioplasty/atherectomy/stenting, profundaplasty, popliteal distal, tibial angioplasty/stenting), preoperative medications (statins, beta blockers, and antiplatelet agents), and other preoperative comorbidities. We included all patients treated for CLTI with infrageniculate arterial disease. We excluded patients with missing information about the lower extremity revascularization technique, patients with an above-knee arterial intervention, patients with symptoms of claudication, and patients with a history of prior endovascular or bypass ipsilateral arterial revascularization. We restricted the study period from 2012 to 2015 because details of unplanned readmissions and reoperations to any hospital within 30 days of the index bypass were not collected before 2012 and the ACS did not release the data beyond 2015 at the time of the study. The lower extremity revascularization-targeted data set and general ACS NSQIP records of the patients meeting the inclusion criteria were merged to capture additional perioperative variables.

The primary intervention for our analysis was infrageniculate arterial intervention, which was considered a binomial categorical variable (endovascular vs bypass). Other predictive variables included patients' sex, race/ethnicity (white, black, Hispanic, or other/unknown), age, diabetes mellitus (none, non-insulin requiring, or insulin requiring), ongoing tobacco use, chronic obstructive pulmonary disease, congestive heart failure, hypertension requiring medication, disseminated cancer, chronic steroid use, weight loss >10% within 6 months before the index operation, bleeding disorder, body mass index, operative time, American Society of Anesthesiologists class, symptoms (rest pain and tissue loss), and preoperative medication (statin, beta blocker, and aspirin or clopidogrel).

The outcomes for our analysis were 30-day perioperative incidences of a major adverse limb event (MALE) and a major adverse cardiovascular event (MACE), composite variables endorsed by the Society for Vascular Surgery's objective performance goals.[6] MALE was defined as major amputation (below-knee or more proximal amputation) or reintervention (new or revision lower extremity bypass operation, jump or interposition graft revision, bypass graft thrombectomy or thrombolysis) of the index limb. MACE included death from any cause, myocardial infarction, and stroke. Other included outcomes variables were wound infection (superficial, deep, and organ/space surgical site infections), postoperative renal insufficiency (acute renal insufficiency or the need for dialysis), reoperation, and readmission. The *Current Procedural Terminology* codes for unplanned reoperations and *International Classification of Diseases, Ninth Revision* codes for readmission are detailed in Supplementary Tables I and II (online only). We also performed secondary analyses to evaluate the outcomes of each treatment strategy (bypass-first vs endovascular-first revascularization) in a subgroup after excluding patients with end-stage renal disease (ESRD) as multiple studies have demonstrated that ESRD has a negative impact on limb salvage and survival in patients undergoing lower extremity open and endovascular surgical revascularization.[7-9]

Statistical analysis.

We described categorical data as absolute numbers and percentage prevalence in the study cohort and continuous variables as means ± standard deviation. Categorical variables were compared by use of the χ^2 test or Fisher exact test for discrete values. Independent two-sample *t*-tests were used for normally distributed continuous variables, and the Wilcoxon rank sum test was used for nonparametric data. Multivariable logistic regression modeling was used to assess the effect of bypass-first vs endovascular-first revascularization while controlling for possible confounders. Adjusted multivariable models were created by including candidate covariates with a P value ≤ .2 among the bypass-first cohort vs the endovascular-first cohort on univariable analysis and demographic variables like race, sex, and age. Candidate covariates were included in the adjusted models using forward selection with the PIN $\alpha = .05$ (with POUT $\alpha = .1$) as the criterion. The model selection was based on a stepwise procedure that alternates between dropping the least significant variable from the model and then reconsidering all potential variables for reintroduction into the model until no more variables can be added. The Hosmer-Lemeshow goodness-of-fit test and the Pearson χ^2 statistics were used for the calibration of the logistic model. We analyzed data using SPSS software (version 21.0; IBM Corp, Armonk, NY).

RESULTS

Study population characteristics.

A total of 1355 patients underwent first-time infrageniculate arterial revascularization for CLTI; 821 (60.6%) underwent endovascular-first revascularization, and 534 (39.4%) underwent bypass-first revascularization. Among the patients undergoing bypass-first revascularization, single-segment saphenous vein conduit was used in 439 (32.4%) patients, and prosthetic/composite or spliced vein conduit was used in 95 (7%) patients. Comorbidities, demographics, and characteristic data of the two cohorts are summarized in Table I. The mean age at presentation was significantly higher in the endovascular-first cohort compared with the bypass-first cohort (68.61 ± 11.42 years vs 66.64 ± 12.20 years; $P < .01$). There were 379 (71.0%) men in the endovascular-first cohort compared with 548 (66.7%) men in the bypass-first cohort ($p = .10$). Compared with endovascular-first treatment, patients who underwent bypass-first treatment were more likely to be smokers (127 [23.8%] vs 110 [13.4%]; $P < .01$), less likely to be partially dependent for activity of daily living (55 [10.3%] vs 138 [16.8%]; $P < .01$), and less likely to have ESRD (12.4% vs 21.78%; P value < .01). In terms of other comorbidities (obesity, diabetes, dyspnea, chronic obstructive pulmonary disease, congestive heart failure, and hypertension), there was no difference between the two cohorts. There was no difference in preoperative treatment with antiplatelet, statin, and beta blocker between the two cohorts. Compared with the endovascular-first cohort, patients in the bypass-first cohort were more likely to present with a rest pain (114 [21.3%] vs [14.7%]; $P < .01$) and less likely to have tissue loss (420 [78.7%] vs 700 [85.3%]; $P < .01$).

Unadjusted outcomes.

The mean operative time for the bypass-first cohort was 260.69 ± 102.44 minutes compared with 109.24 ± 71.69 minutes ($P < .01$). The unadjusted rate of 30-day MALE was 48 (9.0%) in the bypass-first cohort compared with 92 (11.2%) in the endovascular-first cohort ($P = .19$; Table II). Breakdown of MALE shows that the incidence of proximal amputation was 61 (7.4%) in the endovascular-first cohort compared with 23 (4.3%) in the bypass-first cohort ($P = .02$). There was no difference in the untreated loss of patency between the two groups (endovascular, 17 [2.1%]; bypass, 10 [1.9%]; $P = .79$) or major reintervention (endovascular, 25 [3.0%]; bypass, 23 [4.3%]; $P = .22$). There was no significant difference in the incidence of 30-day amputation in the rest pain patients (4.7%) compared with the patients who presented with tissue loss (6.5%; $P = .28$). The unadjusted rate of 30-day MACE was 21 (2.6%) in the endovascular-first cohort and 37 (6.9%) in the bypass-first cohort ($P < .01$). Breakdown of MACE showed that patients in the endovascular-first cohort were less likely to have a postoperative cardiovascular event (7 [0.9%]) compared with the bypass-first cohort (20 [3.7%]; $P < .01$). There was no difference in the 30-day unadjusted mortality rate between the two cohorts (bypass-first cohort, 3.23%; endovascular-first cohort, 1.8%). Compared with the endovascular-first cohort, patients in the bypass-first cohort were more likely to require a blood transfusion or secondary procedure because of bleeding (130 [24.3%] vs 59 [7.2%]; $P < .01$), were more likely to develop wound complication (52 [9.7%] vs 30 [3.7%]; $P < .01$), and had a longer hospital stay (11.87 ± 9.52 days vs 7.17 ± 11.60 days; $P < .01$). There was no difference in the rate of readmission

and unplanned reoperation between the two cohorts (Tables III and IV). However, the rate of unplanned reoperation related to the principal procedure in the endovascular-first cohort was significantly lower compared with the bypass-first cohort (endovascular-first cohort, 65 [7.9%]; bypass-first cohort, 62 [11.6%]; $P = .02$). Wound infection complications were primarily responsible for the higher rate of unplanned reoperation related to the primary procedure, with 18 (3.4%) bypass patients requiring wound incision and drainage or debridement vs 14 (1.7%) endovascular-first patients ($P = .04$). The main cause of unplanned readmission was for nonhealing or open surgical wounds in 10 (1.2%) patients in the endovascular-first cohort compared with 19 (3.6%) patients of the bypass-first cohort ($P < .01$). Restenosis or occlusion of treated arterial segment or complication of bypass graft was responsible for readmissions in 22 (2.7%) patients in the endovascular-first cohort compared with 7 (1.3%) patients of the bypass-first cohort. There was no difference in 30-day MALE (38 [8.7%] vs 10 [10.5%]; $P = .56$) and MACE (31 [7.1%] vs 6 [6.3%]; $P = .80$) outcomes in single-segment saphenous vein graft vs spliced vein/composite/prosthetic conduit, respectively, in CLTI patients (Supplementary Table III, online only).

Adjusted outcomes.

On multivariable logistic regression analysis, we adjusted for age, sex, race, smoking, American Society of Anesthesiologists class, dyspnea, preoperative functional status, congestive heart failure, ESRD, bleeding disorder, type of procedure, rest pain, tissue loss, preoperative treatment with beta blocker, and diabetes (Table V). We found that the bypass-first strategy was associated with MACE (adjusted odds ratio [OR], 3.8; confidence interval [CI], 2.18-6.88) compared with the endovascular-first strategy. There was no statistically significant association between the endovascular-first or bypass-first strategy and MALE; however, the bypass-first strategy was associated with lower major amputation at 30 days (OR, 0.60; CI, 0.36-0.98) compared with the endovascular-first strategy (the amputation rate was 4.3% in the bypass-first cohort compared with 7.4% in the endovascular-first cohort; $P = .02$). The bypass-first strategy was associated with significantly higher odds of 30-day mortality (OR, 2.77; CI, 1.26-6.11) and higher wound complications (OR, 2.75; CI, 1.71-4.42). There was no association between the types of procedure (endovascular-first or bypass-first revascularization) and readmission (OR, 0.89; CI, 0.67-1.17). A trend was seen toward the positive association between the bypass-first strategy and unplanned reoperation, but this did not reach significance (OR, 1.18; CI, 0.98-1.58; $P = .2$).

Subgroup analysis.

After the patients with ESRD were excluded, a total of 1111 patients were identified; 643 (57.9%) underwent endovascular-first revascularization, and 468 (42.1%) underwent bypass-first revascularization. The rate of 30-day MALE was 38 (8.1%) in the bypass-first cohort compared with 63 (10%) in the endovascular-first cohort ($P = .33$). Breakdown of MALE shows that the incidence of proximal amputation was 40 (6.2%) in the endovascular-first cohort compared with 19 (4.1%) in the bypass-first cohort ($P = .1$). There was no difference in the untreated loss of patency and major reintervention between the two groups. The rate of 30-day MACE was 8 (1.2%) in the endovascular-first cohort and 24 (5.1%) in the bypass-first cohort ($P < .01$). Breakdown of MACE shows that patients in the endovascular-first cohort were less likely to have a postoperative cardiovascular event (4 [0.6%])

compared with the bypass-first cohort (16 [3.4%]; $P < .01$). There was no difference in the 30-day mortality rate between the two cohorts (bypass-first cohort, 1.7%; endovascular-first cohort, 0.8%; $P = .1$). In multivariable subgroup analysis after exclusion of ESRD patients, we found no association of treatment strategy (bypass-first vs endovascular-first revascularization) with MALE, 30-day amputation, or major reintervention. However, bypass-first revascularization was associated with 30-day MACE (OR, 4.7; CI, 2-10.70) compared with the endovascular-first cohort. Similarly, bypass-first revascularization was independently associated with the 30-day cardiovascular event (OR, 6.41; (CI, 2.12-19.37). There was no association between treatment strategy (bypass-first vs endovascular-first revascularization) and 30-day mortality.

DISCUSSION

This study used a national, clinical database to report contemporary outcomes of a bypass-first vs an endovascular-first strategy for revascularization in patients with CLTI due to infrageniculate arterial disease. Our findings suggest that patients undergoing bypass-first revascularization are younger, are more current smokers, and have less comorbidity. The bypass-first strategy was associated with a lower 30-day amputation rate compared with the endovascular-first strategy. However, this benefit is not observed when ESRD patients are excluded. We also observed a higher incidence of MACE in the bypass-first cohort compared with the endovascular-first cohort.

In our study, we saw no difference in 30-day unadjusted mortality rates between the two cohorts in the univariable analysis. However, after adjusting for confounding factors, 30-day mortality, cardiovascular events, and wound complications were independently associated with the bypass-first strategy compared with the endovascular-first strategy. This was in line with the study conducted by Darling et al[10] that evaluated the outcomes of bypass-first vs endovascular-first revascularizations in infrainguinal arterial disease patients suffering from CLTI. It showed no difference in perioperative mortality between procedure types; the rate of mortality was 3.3% in the bypass-first group and 2.8% in the endovascular-first group ($P = .63$), but bypass patients had higher wound complications (10%) and hematoma (7.9%). In our practice, frail patients or patients with an unsuitable conduit or focal occlusive disease would typically undergo an endovascular-first strategy.

Endovascular interventions have significantly evolved during the past decades, and many vascular surgeons and interventionists have adopted an endovascular-first approach in peripheral arterial disease patients even in the absence of level 1 evidence because it is less invasive and therefore associated with less perioperative risk, as observed in our study. The only randomized controlled clinical trial directly comparing open bypass surgery with endovascular therapy in patients with severe limb ischemia, mainly due to femoropopliteal disease (in the thigh), is the BASIL trial, which overall showed no differences between the treatment groups with respect to amputation-free survival at 1 year and 3 years of follow-up.[4] However, a recent subgroup analysis of patients from the original BASIL trial with infrapopliteal disease randomized to vein bypass (56 patients) or balloon angioplasty (48 patients) showed clinically important trends in favor of the bypass-first strategy, with amputation-free survival 32% lower in the endovascular group than in the bypass group

(hazard ratio [HR], 0.68; CI, 0.42-1.10).[11] Although this study was underpowered, it provides some thought-provoking evidence. Similarly, Spillerova et al[12] showed that bypass surgery is associated with a significantly better rate of wound healing ($P = .014$; HR, 1.536; 95% CI, 1.091-2.162). In this study, angioplasty and bypass surgery achieved similar limb salvage rates (HR, 0.791; 95% CI, 0.437-1.434). A similar pattern was seen in our study with transtibial or proximal amputation of 7.4% in the endovascular-first cohort compared with 4.3% in the bypass-first cohort. We believe the patients with a bypass-first strategy for revascularization in infrageniculate arterial disease have better outcomes in wound healing or lower amputation rate because patients after bypass have a good-diameter neoarterial line to perfuse the distal part of the lower limb compared with a diseased native arterial line treated with endovascular interventions, which is smaller and allows only limited revascularization, leading to suboptimal results in infrageniculate arterial disease. However, in our study, there was no difference in the primary outcome variable MALE; this could be due to the fact that MALE is a composite variable of amputation, major reintervention of the treated arterial segment, and untreated loss of patency. There was a statistical difference only in an individual component ("amputation") of the composite variable but not in the other components of the MALE, like "major reintervention of the treated arterial segment and untreated loss of patency"; therefore, this could have resulted in no significant difference in the overall composite variable MALE. In subgroup analyses after exclusion of ESRD patients, we found no evidence of a benefit for MALE 30-day amputation rate with bypass-first revascularization; however, the bypass-first strategy was significantly associated with 30-day cardiovascular events. These results reaffirm the need for RCTs such as BASIL-2 and Best Endovascular vs Best Surgical Therapy in Patients with Critical Limb Ischemia (BEST-CLI) to provide level 1 evidence for the role of endovascular-first vs bypass-first revascularization strategies in treatment of this population of challenging patients. The BASIL-2 trial, an RCT to compare a vein bypass-first with a best endovascular-first revascularization strategy for severe limb ischemia due to infrapopliteal arterial disease, is enrolling patients.[13] The BEST-CLI trial is an ongoing North American RCT comparing a best endovascular vs best surgical therapy in CLTI patients eligible for both treatments.[14]

This study provides robust national results and sets the national benchmark of postoperative quality outcomes after bypass-first and endovascular-first revascularization in CLTI patients. These results can aid vascular surgeons in planning revascularization strategies for this population of challenging patients. The findings of this study must be interpreted in the context of the study design. The lower extremity revascularization-targeted ACS NSQIP data set has numerous advantages for this study as it includes a sample of patients from >200 hospitals contributing targeted vascular data across the nation. Because of the diversity of the hospitals that contribute data to the targeted ACS NSQIP, this study is representative of "real-world" outcomes. The data are collected prospectively with rigorous attention to details and with standardized definitions for preoperative variables and complications.

Limitations.

This data set is not without limitations. The variables that were analyzed were limited to those that could be captured by the ACS NSQIP data set; specifically, the outcomes beyond 30 days, variables regarding a cost of care, whether a patient had an attempted endovascular

intervention before undergoing open bypass, and the surgeon's rationale behind clinical decision-making for an endovascular-first vs bypass-first strategy were not captured. The NSQIP registry also lacks details on types of endovascular interventions (atherectomy, angioplasty, stenting, or combination of therapies), graft configuration (in situ vs transposed/reversed anatomically tunneled graft), and information on the Wound, Ischemia, and foot Infection (WIfI) classification system that predicts amputation rates, all of which could have added further detail to our comparison. In this study, we have attempted to control for confounding variables using robust multivariable analysis. However, it is retrospective; it is likely that not all confounders were measured or controlled for, and also multivariable analysis cannot account for sampling error. Therefore, the multivariable results cannot be interpreted to show a causal effect of the procedure on the outcomes. It is likely that some residual confounding still exists, which may explain some of the associations that were observed between procedure and outcomes, which could only be explained after the RCT.

CONCLUSIONS

This study reports the real-world outcomes of a bypass-first strategy vs an endovascular-first strategy in patients with CLTI due to infrageniculate arterial disease. The risk of 30-day mortality, morbidity, and reoperation rate in this population is considerable. However, the amputation rate is significantly better for the bypass-first strategy. However, this benefit was not observed when dialysis patients were excluded. For the patient who is able to tolerate surgery, the bypass-first strategy appears to perform favorably with respect to 30-day amputation in CLTI due to infrageniculate arterial disease. These data should be considered in the context of the study design in planning the revascularization strategy for infrageniculate arterial disease while awaiting further evidence from the BASIL-2 trial and the BEST-CLI trial.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective analysis of prospectively collected data of the American College of Surgeons National Surgical Quality Improvement Program
- **Key Findings:** In patients with chronic limb-threatening ischemia (CLTI) and infrageniculate arterial disease, a bypass-first strategy (534 patients) resulted in lower rates of major amputation (4.3% vs 7.3%) but higher 30-day mortality rates (3.2% vs 1.8%) compared with an endovascular-first strategy (821 patients). The difference in amputation rates was lost when patients with end-stage renal disease were excluded.
- **Take Home Message:** This study suggests that the reduction in 30-day amputation rates observed with a bypass-first strategy in patients with CLTI and infrageniculate disease may be limited to patients with end-stage renal disease.

Table I.

Characteristics of bypass-first and endovascular-first cohorts

Characteristics	Bypass-first cohort	Endovascular-first cohort	*P* value
Age, years	66.64 ± 12.20	68.61 ± 11.42	<.01
Male	379 (71.0)	548 (66.7)	.10
BMI, kg/m^2	27.71 ± 8.20	27.54 ± 8.54	.70
Race			
White	334 (69.9)	491 (68.3)	.52
Black	131 (27.4)	200 (27.8)	
Other (Asian, Pacific Islander, and Native American)	13 (2.7)	28 (3.9)	
Diabetes			
Insulin dependent	246 (46.1)	424 (51.6)	.10
Non-insulin dependent	108 (20.2)	160 (19.5)	
Current smoker	127 (23.8)	110 (13.4)	<.01
Dyspnea			
At rest	1 (0.2)	5 (0.6)	.10
Moderate exertion	42 (7.9)	88 (10.7)	
Functional health before surgery			
Totally dependent	3 (0.6)	20 (2.4)	<.01
Partially dependent	55 (10.3)	138 (16.8)	
History of COPD	36 (6.7)	68 (8.3)	.29
CHF	18 (3.4)	45 (5.5)	.07
Hypertension	445 (83.3)	703 (85.6)	
Dialysis	66 (12.4)	178 (21.78)	<.01
Preoperative bleeding disorder	103 (19.3)	218 (26.6)	<.01
ASA class			
≤3	372 (69.7)	510 (62.1)	<.01
4	160 (30.0)	211 (25.7)	
Symptoms			
Tissue loss	420 (78.7)	700 (85.3)	<.01
Rest pain	114 (21.3)	121 (14.7)	

Characteristics	Bypass-first cohort	Endovascular-first cohort	*P* value
Preoperative aspirin or clopidogrel	401 (75.0)	627 (76.4)	.74
Preoperative statin	347 (65)	526 (64.1)	.89
Preoperative beta blocker	327 (61.2)	533 (64.9)	.19
Operative time, minutes	260.69 ± 102.44	109.24 ± 71.69	<.01

ASA, American Society of Anesthesiologists; *BMI*, body mass index; *CHF*, congestive heart failure; *COPD*, chronic obstructive pulmonary disease. Categorical variables are presented as number (%). Continuous variables are presented as mean ± standard deviation.

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Table II.

Postoperative outcomes of bypass-first vs endovascular-first strategy

Characteristics	Bypass-first cohort	Endovascular-first cohort	*P* value
MALE	48 (9.0)	92 (11.2)	.19
Untreated loss of patency	10 (1.9)	17 (2.1)	.79
Major reintervention of treated arterial segment	23 (4.3)	25 (3.0)	.22
Transtibial or proximal amputation	23 (4.3)	61 (7.4)	.02
MACE	37 (6.9)	21 (2.6)	<.01
30-Day mortality	17 (3.2)	15 (1.8)	.10
MI or stroke	20 (3.7)	7 (0.9)	<.01
Other outcomes			
Bleeding requiring transfusion or secondary procedure	130 (24.3)	59 (7.2)	<.01
Wound complication	52 (9.7)	30 (3.7)	<.01
Readmission	97 (18.2)	173 (21.1)	.19
Length of stay, days	11.87 ± 9.52	7.17 ± 11.60	<.01
Unplanned reoperation	102 (19.1)	141 (17.2)	.36

MACE, Major adverse cardiovascular event; *MALE*, major adverse limb event; *MI*, myocardial infarction.

Categorical variables are presented as number (%). Continuous variables are presented as mean ± standard deviation.

Table III.

Unplanned reoperations and indications for reoperation in patients undergoing primary bypass-first vs endovascular-first revascularization

	Bypass-first cohort, No. (%)	Endovascular-first cohort, No. (%)	*P* value
Related to principal procedure			
1 Unplanned reoperation	102 (19.1)	141 (17.2)	.36
>1 Unplanned reoperation	19 (3.6)	32 (3.9)	.74
Unplanned reoperation related to principal procedure	62 (11.6)	65 (7.9)	.02
Indications for unplanned reoperation related to principal procedure			
Incision and drainage or debridement	18 (3.4)	14 (1.7)	.04
Major or minor amputation	43 (8.1)	69 (8.4)	.81
Open or endovascular revascularization	26 (4.9)	24 (2.9)	.06
Other vascular	3 (0.6)	4 (0.5)	.85
Other reoperations	4 (0.7)	14 (1.7)	.13

Table IV.

Unplanned readmission and indications for readmission in patients undergoing primary bypass-first vs endovascular-first revascularization

	Bypass-first cohort, No. (%)	Endovascular-first cohort, No. (%)	*P* value
Related to principal procedure			
1 Unplanned readmission	91 (17.0)	157 (19.1)	.33
1 Unplanned readmission related to primary procedure	48 (9.0)	71 (8.6)	.82
>1 Unplanned readmission	3 (0.6)	12 (1.5)	.12
Limb-related readmissions			
Nonhealing or open surgical wound	19 (3.6)	10 (1.2)	<.01
Restenosis, occlusion, or complication of bypass	7 (1.3)	22 (2.7)	.08
Hemorrhage or seroma	6 (1.1)	4 (0.5)	.18
Pain complications	0	5 (0.6)	—
Other readmissions			
Diabetes mellitus	0	2 (0.2)	—
Sepsis, septic shock, or hypotension	7 (1.3)	9 (1.1)	.72
Acute respiratory failure or pneumonia	1 (0.2)	2 (0.2)	.82
Cardiac event	3 (0.6)	4 (0.5)	.85

Table V.

Adjusted[a] associations between revascularization techniques and perioperative outcomes in patients with chronic limb-threatening ischemia (CLTI)

Operation	OR	% CI	*P* value
MALE	0.73	0.50-1.08	.17
MACE	3.88	2.18-6.88	<.01
Major amputation	0.60	0.36-0.98	.04
Mortality	2.77	1.26-6.11	.01
Wound complication	2.75	1.71-4.42	<.01
Readmission	0.89	0.67-1.17	.41
Reoperation	1.18	0.98-1.58	.23

CI, Confidence interval; *MACE*, major adverse cardiovascular event; *MALE*, major adverse limb event; *OR*, odds ratio.

Bypass-first revascularization compared with endovascular-first revascularization (reference).

[a]Adjusted for age, sex, race, smoking, American Society of Anesthesiologists class, dyspnea, preoperative functional status, congestive heart failure, end-stage renal disease, bleeding disorder, type of procedure, symptoms, preoperative treatment with beta blocker, and diabetes.