Cost-effectiveness of Revascularization for Limb Preservation in Patients with Marginal Functional Status

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Background: Revascularization and limb salvage attempts are often offered to patients with foot wounds and chronic limb ischemia who are thought to be good-risk candidates, but some skepticism remains about the utility of these efforts for elderly patients with marginal functional status. We sought to determine whether limb preservation efforts in this population could be justified from a patient-centered, cost-effectiveness perspective.

Methods: A probabilistic Markov model was used to simulate the clinical outcomes, health utilities, and costs over a 10-year period with various management strategies. Clinical parameter estimates were obtained from previous clinical trials and large observational series. Cost estimates were obtained from cost literature and also a single-center study that reviewed total costs accumulated (including secondary amputations, wound care, outpatient nursing care, and nursing home costs). Cost (in 2011 U.S. dollars) per year of ambulation (with limb preservation or with a prosthesis after amputation) was the primary measure of cost-effectiveness.

Results: The total 10-year costs of revascularization—either endovascular or surgical—were lower than the costs of either local wound care alone or primary amputation. Revascularization strategies also produced more health benefits as measured in terms of years of ambulatory ability, years of limb salvage, or quality-adjusted life-years. In none of the scenarios modeled in deterministic sensitivity analyses did primary amputation prove to be cost-effective.

Conclusions: Revascularization and limb preservation attempts appear less costly and provide more health benefits than wound care alone or primary amputation, even among patients with marginal functional status at baseline.

INTRODUCTION

Nonhealing wounds of the foot represent a limb-threatening problem, especially when associated with chronic limb ischemia. The natural history of this problem is not favorable for the limb,[1] and revascularization and subsequent soft tissue/bony reconstruction of the foot—so-called ''limb salvage'' or limb preservation efforts—are offered to good-risk patients to reduce the risk of limb loss. These limb preservation efforts have repeatedly been shown to be highly effective and durable in minimizing the risk of limb loss.[2–4] Furthermore, limb preservation preserves ambulatory function and ability to live independently much more often than major amputation (see review[1]). Revascularization and limb preservation efforts can also be justified from an economic perspective using formal

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cost-effectiveness analyses addressing long-term outcomes, costs, and health utilities.[5]

There remains some degree of skepticism about the utility of these efforts among patients with marginal functional status—even among vascular surgeons.[6–9] Patients who have previously had a contralateral amputation, for example, have a higher prevalence of systemic comorbidities that affect perioperative morbidity, and they less often remain ambulatory without assistance after revascularization than patients with an intact contralateral limb.[10] Similarly, elderly patients have higher perioperative mortality and decreased long-term survival, and are less likely to remain mobile and independent after revascularization than younger patients.[11,12] These risks make the optimal management strategy for this population unclear.

Our goal in this study was to evaluate the management options for foot wounds associated with chronic limb ischemia among patients with marginal functional status, advanced age, and/or systemic comorbidities that denote increased perioperative risks for the perspective of costs and health benefits using a formal cost-effectiveness analysis.

METHODS

Overall Study Design and Definitions

The primary objective of this study was to assess the long-term cost-effectiveness of various contemporary management options used in the setting of nonhealing foot wounds and critical limb ischemia (i.e., Rutherford category 5 ischemia) in patients who were independently living at baseline but had marginal functional status. The management strategies investigated included: (1) local wound care, with selective major amputation as needed; (2) primary amputation; (3) revascularization with *infrainguinal surgical bypass* using an autologous vein conduit, followed by *endovascular intervention* as needed to maintain or restore patency of the bypass graft; (4) revascularization with infrainguinal surgical bypass using an autologous vein conduit, followed by *open surgical intervention* as needed to maintain or restore patency of the bypass graft; (5) initial revascularization with endovascular intervention, followed by surgical bypass and possible endovascular revisions as needed for failure of the initial endovascular intervention; and (6) revascularization achieved purely through an initial endovascular intervention, then further endovascular reintervention(s) as needed.

Clinical Parameters Used

Clinical parameters used in this model were largely based on those used in the Model to Optimize Value in Ischemic Extremities (MOVIE) study.[1,5] Estimates of certain clinical parameters were then modified to simulate an older, frailer patient population with a poorer baseline functional status. Specifically, the estimates of clinical outcomes were based on patients who were >80 years old and/or had a prior major amputation of the contralateral lower limb, as these two patient subsets have been consistently shown to have poorer postoperative clinical and functional outcomes than the typical chronic limb ischemia (CLI) population undergoing revascularization.[10,12–15] Therefore, the following modifications of the baseline MOVIE study parameters were made:

- The probability of remaining ambulatory after revascularization was decreased from 97%[11,16] to 72%.[10] (D.T. Baril, personal communication, 2012). The probability of remaining ambulatory after major (transtibial or transfemoral) amputation was decreased from 55%[1] to 38%.[17]
- The probability of independence (i.e., maintaining the ability to live independently) after revascularization was decreased from 98%[11] to 83%.[10] The probability of independence after major amputation was decreased from 92%[11] to 64%.[10]
- The proportion of patients needing a temporary stay in a skilled nursing facility after revascularization was increased from 29% to 70%.
- The annual baseline mortality rate was increased from 12% to 18%, and the perioperative mortality rate was increased from 2.6% to 5.2% to reflect an older patient cohort with an increased prevalence of systemic comorbidities.[10,18]
- The limb salvage rate was not modified from the MOVIE study estimate of 90% at 1 year for the ‘‘base case’’ scenario, as baseline marginal functional status did have a significant impact on major amputation rates in the multivariate model presented by Baril and colleagues.[10] To determine the potential impact of poorer limb salvage rates in this population, however, a deterministic sensitivity analysis was performed in which the limb salvage rate at 1 year was decreased from 90% to 83%.[10]

The estimates of direct and indirect inpatient costs were based on previous work by our group.[5] Estimates of outpatient costs were based on a literature review.[1] Some of the major cost estimates used in the model are included in Table I. All costs estimates were converted to 2011 U.S. dollars (USD) based on inflation data from the U.S. Bureau of Labor Statistics.

Model Design and Analysis

Cost-effectiveness was assessed using a probabilistic Markov model that simulated the long-term (10-year) costs and health benefits associated with the aforementioned management strategies. The analysis was performed with 1000 trials of cohorts having 1000 hypothetical patients. Costs and utilities were discounted at a standard 3.5% annual rate.[19]

RESULTS

Base Case Scenario: Clinical Outcomes, Health Benefits, and Costs

The four revascularization strategies produced similar limb salvage rates, ranging from 79.8% to 80.5% at 5 years (Table II). The 5-year limb salvage rate with wound care only was 27.9%. The overall survival rates were very similar for all management strategies, ranging from 33.7% to 34.9% at 5 years. The long-term total costs for primary amputation were 185,955 USD, the highest for any of the management strategies. Wound care with amputation as needed had a median total long-term cost of 129,651 USD. The revascularization strategies had lower long-term total costs, ranging from 104,118 to 113,944 USD. The total long-term total costs figure for purely endovascular intervention (strategy 5) was lower than the long-term total costs of wound care alone (strategy 1) in 915 of the 1000 simulations (Fig. 1).

The endovascular intervention strategies produced the highest median years of limb preservation: 3.031 years for purely endovascular intervention (strategy 5) and 3.015 years for endovascular intervention with bypass for failure (strategy 6). These were slightly higher than the median years of limb preservation associated with surgical revascularization—2.941 years for bypass with endovascular or surgical revisions (strategies 4 and 5, respectively)—and much higher than the 1.473 years of median limb preservation associated with wound care alone (strategy 1). Thus, when considering limb preservation as main health outcome of interest, endovascular intervention dominated other strategies (i.e., was both more effective and less costly).

Similarly, endovascular intervention (strategies 5 and 6) produced slightly more ambulatory years (2.468 and 2.459 ambulatory years, respectively) than surgical revascularization (2.410 ambulatory years for strategies 3 and 4), and much more than either primary amputation (strategy 2, 1.585 ambulatory years) or wound care (strategy 2, 0.834 ambulatory years). Using ambulatory years as the main health outcome of interest, endovascular intervention also dominated other strategies.

Deterministic Sensitivity Analysis: Decreased Limb Salvage Rates

To determine the potential impact of decreased patency/decreased limb salvage rates in this population compared with the typical critical limb ischemia population, a deterministic sensitivity analysis was performed in which the rates of limb loss after both endovascular intervention and surgical bypass were increased by 57%.[10] The results of model simulations using this elevated limb loss rate were largely similar to those in the base case scenario (Table III). Specifically, endovascular intervention (strategies 5 and 6) still dominated the other management strategies, with higher median years of limb salvage, higher median ambulatory years, and lower total long-term costs. The median cost differences between revascularization (strategies 3—6) and wound care (strategy 1) were smaller, however. The total long-term total costs of purely endovascular intervention (strategy 5) was lower than the long-term total costs of wound care alone (strategy 1) in only 64.4% of the 1000 simulations (Fig. 2). Primary amputation (strategy 2) remained much more costly and much less effective than other strategies and was thus dominated by these.

DISCUSSION

In spite of the wealth of data on patency and limb salvage rates after various forms of revascularization, few data are available to support the cost-effectiveness of such strategies. The cost-effectiveness is often called into question, sometimes even by experienced vascular surgeons with a focus on lower extremity revascularization and preservation.[6—9] Our study has evaluated the costs and health outcomes of various contemporary strategies to manage limb-threatening foot ulcers associated with chronic limb ischemia in patients who might be considered ‘‘marginal’’ because of advanced age or poor baseline functional status. The median total 10-year costs associated with the revascularization strategies (endovascular and surgical) ranged from 105,000 to 115,000 USD approximately 15,000—35,000 USD more the

Table I. Major parameters included in the model (see Barshes and Belkin[1] for review)

Parameter	Point estimate	Range[a]
Clinical events		
Annual (baseline) mortality	18.0%	14.5−21.9%
Excess mortality rate associated with:		
Major amputation	8.0%	4.0−17.8%
Surgical bypass	5.2%	2.9−7.5%
Endovascular intervention	3.9%	1.8−7.6%
Annual rate of major amputation during year 1 after:		
Local wound care	38.0%	27.9−48.1%
Surgical bypass	10.8%	8.4−13.2%
Endovascular intervention	12.2%	6.9−17.5%
Annual rate of major amputation during years 2−10 after:		
Local wound care	38.0%	27.9−48.1%
Surgical bypass	2.6%	2.0−3.0%
Endovascular intervention	2.6%	2.0−3.0%
Wound healing at 1 year after:		
Local wound care	41.0%	24.8−57.2%
Surgical bypass	95.0%	90.0−100.0%
Endovascular intervention	60.3%	53.6−67.0%
Probability of reintervention (endovascular or surgical) after:		
Surgical bypass	22.7%	20.5−24.9%
Endovascular intervention	26.0%	23.8−28.2%
Probability of ambulation after:		
Major amputation	38.2%	17.9−57.3%
Surgical bypass	72.0%	62.9−80.0%
Endovascular intervention	72.0%	62.9−80.0%
Probability of living independently after discharge:		
Major amputation	36.1%	19.5−55.2%
Surgical bypass	82.4%	73.0−89.8%
Endovascular intervention	82.4%	73.0−89.8%
Utilities		
Utility associated with a unhealed wound (foot or amputation stump) after:		
Local wound care	0.42	0.28−0.52
Major amputation	0.48	0.30−0.58
Surgical bypass	0.50	0.57−0.67
Endovascular intervention	0.50	0.59−0.69
Utility associated with healed wound after:		
Local wound care	0.64	0.59−0.69
Primary amputation	0.54	0.32−0.65
Surgical bypass	0.62	0.54−0.70
Endovascular intervention	0.62	0.54−0.70
Costs		
Wound care, USD per year	$23,065	$19,967−27,128
Procedures and associated hospitalization		
Major amputation	$40,541	$17,143−88,018
Surgical bypass	$49,228	$30,368−72,945
Endovascular intervention	$29,297	$18,748−43,542
Reintervention and associated hospitalization		
Operative reintervention	$30,910	$15,794−54,643
Endovascular reintervention	$14,449	$6870−24,162
Inpatient rehabilitation and/or home health nursing	$12,048	$1364−44,895
Residence in a nursing home, per year	$67,878	$35,235−83,898
Limb prosthesis		
Initial purchase	$10,000	$6057−14,573
Yearly maintenance	$750	$513−995

[a]The full range of values used in the probabilistic model were determined by various distributions, which included beta, gamma, and triangular. The ranges listed here are 95% confidence level equivalents for clinical event probabilities and utilities and the actual range (minimum and maximum) for cost values.

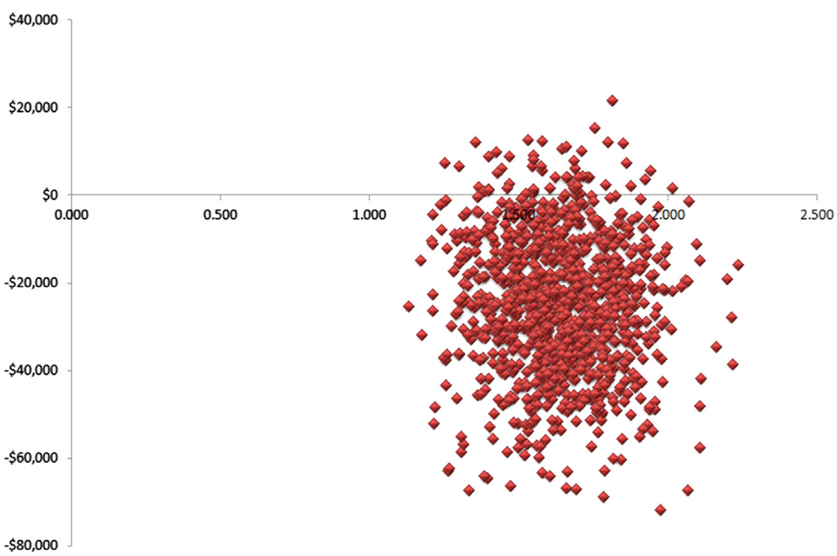

Fig. 1. Scatterplot of the differences in long-term total costs (*x*-axis) and median ambulatory years (*y*-axis) when comparing purely endovascular intervention (strategy 3) with wound care (strategy 1) in the base case scenario. Of the 1000 simulations, 915 (91.5%) demonstrated cost savings.

Table II. Estimated clinical outcomes, costs, and health benefits of various strategies for managing chronic foot wounds and chronic limb ischemia among patients with marginal baseline function

Strategy	Median 5-year limb salvage	Median total costs (2011 USD)	Median years of limb salvage	Median ambulatory years
Initial endovascular intervention; repeat intervention(s) as needed (*strategy 5*)	80.5	104,118	3.031	2.468
Initial endovascular intervention; surgical bypass +/− revision(s) as needed for failure (*strategy 6*)	80.3	108,794	3.015	2.459
Initial surgical bypass; endovascular revision(s) as needed (*strategy 4*)	79.8	110,910	2.941	2.410
Initial surgical bypass; surgical revision(s) as needed (*strategy 3*)	79.8	113,944	2.941	2.410
Wound care only; major amputation as needed (*strategy 1*)	27.9	129,651	1.473	0.834
Primary amputation (*strategy 2*)	0	185,955	0	1.585

median total 10-year costs estimated for the general population of patients with foot wounds and chronic limb ischemia. The health benefits after revascularization, measured in median number of years of limb preservation, were lower: approximately 3.0 years for the marginal patient population versus 4.2 years for the general patient population. Likewise, measured in median years of ambulatory function—the most patient-oriented outcome available for analysis—the absolute benefit was lower: approximately 2.5 years for the marginal patient population versus 4.6 years for the general population.[5]

In spite of these findings, revascularization still appears to be the most cost-effective alternative to wound care and primary amputation. As in the general population of patients with foot wounds and chronic limb ischemia,[5] primary major amputation produces fewer health benefits than revascularization or wound care and is much more expensive. Much of the increase in costs is due to the need for long-term nursing home care, which is more prevalent after amputation in marginal patients than in the general dysvascular population (D.T. Baril, personal communication, 2012).[10]

Although this study has shown that the outcomes of revascularization for limb preservation in marginal patients are worse than for non-marginal patients, the outcomes are worse still with primary amputation or wound care alone. In

Table III. Estimated clinical outcomes, costs, and health benefits of various strategies for managing chronic foot wounds and chronic limb ischemia among patients with marginal baseline function in a sensitivity analysis that assumed increased rates of limb loss after revascularization

Strategy	Median 5-year limb salvage	Median total costs (2011 USD)	Median years of limb salvage	Median ambulatory years
Initial endovascular intervention; repeat intervention(s) as needed (*strategy 5*)	70.2	124,125	2.676	2.372
Initial endovascular intervention; surgical bypass +/− revision(s) as needed for failure (*strategy 6*)	69.8	125,754	2.656	2.362
Initial surgical bypass; endovascular revision(s) as needed (*strategy 4*)	69.2	129,777	2.598	2.325
Initial surgical bypass; surgical revision(s) as needed (*strategy 3*)	69.2	132,413	2.598	2.325
Wound care only; major amputation as needed (*strategy 1*)	27.7	131,055	1.469	0.840
Primary amputation (*strategy 2*)	0	187.182	0	1.610

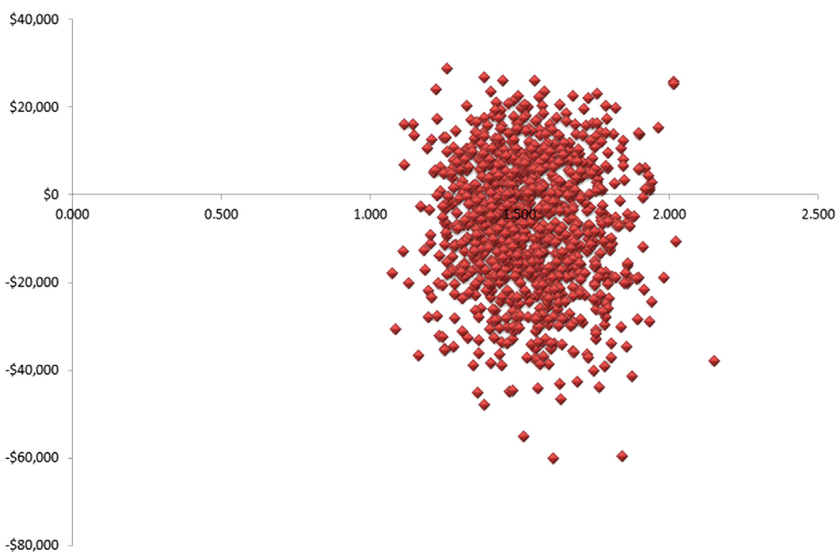

Fig. 2. Scatterplot of the differences in long-term total costs (*x*-axis) and median ambulatory years (*y*-axis) when comparing purely endovascular intervention (strategy 3) with wound care (strategy 1) in the scenario of 57% increase in post-revascularization limb loss over baseline. Of 1000 simulations, 644 (64.4%) demonstrated cost savings.

other words, the difference in outcomes between revascularization and either local wound care or primary amputation is much larger in this marginal patient population and is therefore more likely to produce cost savings (i.e., better relative outcomes at lower relative costs). The situation is akin to performing carotid endarterectomy early after a completed stroke—although the absolute risk of perioperative stroke is higher than when it is delayed for 6 weeks, the risk *reduction* of early carotid endarterectomy is significant compared with late carotid endarterectomy.[20]

The results of this cost-effectiveness analysis are consistent with other publications describing clinical outcomes of revascularization for octogenarians. Brosi and colleagues demonstrated that early revascularization of octogenarians presenting with critical limb ischemia results in better clinical improvement than initial management and selective delayed revascularization.[15] Two other groups have demonstrated better limb salvage and amputation-free survival rates with endovascular intervention than with surgical bypass.[12,14] Lejay and colleagues also clearly demonstrated that endovascular intervention is much more likely than surgical revascularization to maintain or improve mobility and independence among octogenarians.[13] Similar to findings from the Bypass or Angioplasty in Severe Ischemia of the Limb (BASIL) trial,[8] the results from these studies and ours may suggest that, although endovascular intervention may not be the most cost-effective option for the general population with foot wounds and chronic limb ischemia, it may be the most cost-effective management option for marginal patients, elderly patients, or others considered to have a limited lifespan. Surgical revascularization has a more durable outcome than endovascular intervention but has higher initial costs, so the higher annual mortality in this patient subset may absorb many of these initial costs for surgical revascularization but limit the realization of the long-term benefits.

As always, clinical decision-making must be tailored to each individual patient's clinical situation and preferences for health outcomes. Our intent in this study was to model the outcomes of patients with poor baseline functional status (e.g., previous major amputation of the contralateral limb) and advanced age or other comorbidities that would decrease the likelihood of long-term survival and increase the likelihood of perioperative mortality. Obviously not all ''marginal'' patients would be accurately modeled by this study; these results cannot be generalized to those with comorbidities that would limit lifespan even more still (e.g., unresectable primary brain cancer or pancreatic cancer). Nonetheless, we suggest that the best options for treating ischemia-associated limb-threatening wounds in such patients would be between revascularization (specifically endovascular when possible) or local wound care only. We also believe that major amputation be reserved for patients who develop life-threatening foot infections that cannot be controlled with foot drainage or minor amputations and subsequent palliative wound care. Primary amputation is more costly and less beneficial than wound care. The presence of severe systemic comorbidities need not be a contraindication to attempts at revascularization, as primary amputation is *not* safer than revascularization; in fact, after adjustment for baseline comorbidities, amputation appears to be associated with *higher* perioperative rates of morbidity and mortality than surgical revascularization.[18]

There are other limitations to this study. First, it is an analysis based on simulated data. Although it was based on a review that identified the highest quality parameter estimates available,[1] it should still be corroborated with subsequent reports of cost and health outcomes specific to this patient population. Second, we did not consider patients with end-stage renal disease in this model. Patients with end-stage renal disease frequently develop foot ulcers but are often considered to be poor candidates for revascularization because of low limb salvage rates—often seen even in spite of successful revascularization.[21,22] An analysis of the cost-effectiveness of revascularization and attempts at limb salvage in this patient population is worthwhile, but should be considered separately.

In conclusion, revascularization for attempts at limb preservation in marginal patients (those with poor baseline functional status, advanced age and/or severe systemic comorbidities) appears to provide more health benefits and have lower long-term costs than wound care alone or primary amputation. In spite of the poorer outcomes and higher costs relative to a nonmarginal patient population, revascularization strategies may provide cost savings in the management of limb-threatening foot wounds associated with chronic limb ischemia.

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