A cost-effectiveness analysis of infrainguinal bypass in the absence of great saphenous vein conduit

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Background: **Good-quality great saphenous vein (GSV) is the preferred conduit for infrainguinal surgical revascularizations, but it is not available in all patients. We sought to identify the alternative conduit that would maximize cost-effectiveness in the context of infrapopliteal bypass for critical limb ischemia and nonhealing foot wounds.**

Methods: **A Markov model was used to create a detailed simulation of 10-year outcomes in a hypothetical Edifoligide for the Prevention of Infrainguinal Vein Graft Failure (PREVENT) III-type patient cohort undergoing infrainguinal bypass for nonhealing foot wounds. The following management options were evaluated: (1) conservative therapy (local wound care, amputation as needed); (2) primary amputation; (3) bypass with autologous alternative vein (AAV), including arm or lesser saphenous vein; (4) bypass with GSV <3 mm in diameter; (5) bypass with polytetrafluoroethylene (PTFE); (6) cryopreserved venous allograft; and (7) cryopreserved arterial allograft. Estimates of 10-year total costs were incorporated into the model. Cost-effectiveness was measured in terms of incremental United States dollars per additional year of ambulation.**

Results: **Bypass with AAV had the highest effectiveness as measured in median years of ambulation. After primary amputation, bypass with PTFE had the lowest total costs. With incremental cost-effectiveness ratios of $5325 and $21,228, bypass with PTFE or AAV appeared to be cost-effective alternatives to conservative therapy for nonhealing ischemic wounds. Primary amputation, GSV <3 mm, and allograft options were dominated (ie, more costly and less effective). Primary amputation was weakly dominated.**

Conclusions: **Bypass with PTFE or AAV appears to be a cost-effective option for the management of critical limb ischemia and nonhealing foot wounds when good-quality GSV is not available. (J Vasc Surg 2013;57:1466-70.)**

Good-caliber single-segment great saphenous vein (GSV) stands as the best conduit for infrainguinal bypass grafting—regardless of bypass indication or level of distal target[1]—but is absent in ∼15% to 20% of patients.[2-4] In the absence of adequate GSV, vascular surgeons performing surgical revascularizations for nonhealing wounds use other conduits, including arm veins,[3,4] lesser saphenous veins,[5] prosthetic grafts (including Dacron [DuPont, Wilmington, Del] and polytetrafluoroethylene [PTFE], with or without distal vein patches or cuffs),[6,7] and cryopreserved venous[8] and arterial[9] allografts. Each of these conduit options has some distinct advantages and disadvantages in the setting of infrainguinal revascularizations. A wealth of literature exists to describe the patency rates and limb preservations rates associated with the various alternative conduit options, but none has emerged as an evidence-based alternative to adequate caliber, single-segment GSV.

Some doubts have been raised about the total costs and the cost-effectiveness of limb preservation efforts, even from those within the field of vascular surgery.[10-12] Our group published results of an analysis suggesting that surgical bypass can achieve high rates of limb preservation within acceptable levels of cost-effectiveness,[13] but the relatively longer operations, lower patency rates, and higher reintervention rates among patients who lack adequate GSV conduit raise further doubts about the merits of limb preservation efforts in this subgroup. It is not clear that intervening on patients lacking endovascular options for revascularization and also an adequate-caliber, single-segment GSV would be more cost-effective than primary amputation or even expectant management (local wound care alone).

Our goal in this study was to compare the cost-effectiveness ratios of several conduit options that serve as alternatives to adequate-caliber single-segment GSV. In particular, we sought to determine whether limb preservation efforts were within acceptable limits and if one particular conduit option appeared to be most cost-effective.

METHODS

Conduit options evaluated and overall study design. The focus of this study was to compare management options for patients with nonhealing foot wounds and chronic limb ischemia who had reconstructible infrainguinal arterial occlusive disease but lacked adequate caliber (ie, ≥3 mm) single-segment GSV and for whom an

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endovascular option of revascularization did not exist. We therefore examined the following management options:

1. Conservative management with local wound care and primary amputation as needed;
2. Primary major amputation;
3. Infrainguinal bypass using autologous alternative vein (AAV), comprising upper or lower extremity vein (but not single-segment GSV) that was single-segment or multiple-segments (ie, composite or spliced);
4. Infrainguinal bypass using GSV <3 mm in diameter;
5. Infrainguinal bypass using PTFE, with or without a vein patch;
6. Infrainguinal bypass using cryopreserved venous allograft; and
7. Infrainguinal bypass using cryopreserved arterial allograft.

We used the general framework of the Model to Optimize Value in Ischemic Extremities (MOVIE) study for the current work.[13] In brief, the MOVIE study was a cost-effectiveness analysis of contemporary strategies of managing chronic limb ischemia associated with nonhealing foot wounds in ambulatory, independently living patients. The patient demographics and baseline characteristics were modeled on an Edifoligide for the Prevention of Infrainguinal Vein Graft Failure (PREVENT) III-type cohort, which comprised a study population that was 64% diabetic, 64% male, 28% nonwhite, and was a median age of 69 years.[13]

Clinical parameter estimates and utility estimates were obtained from a thorough review of pre-existing literature and included a baseline annual mortality rate of ~11.4%.[14] The clinical parameter estimates specific to various conduit options were obtained from the best-quality literature available, preferentially from clinical trials, meta-analyses of observational studies, or from other observational studies. Most of the studies on which the outcome parameters were based were predominately studies of bypasses to infrapopliteal distal targets but did include some femoropopliteal bypasses.[15-17] Estimates of the costs associated with revascularization and major amputation were obtained using a transition cost accounting system to obtain patient-level activity-based estimates of the direct and indirect costs (Table I, online addendum).[13] The costs associated with other clinical states (eg, nonhealed wounds receiving local wound care) were obtained from a literature review. The goal was to include total costs (not charges) from the societal perspective whenever such cost estimates existed.[18]

A computer-simulated, probabilistic Markov model was used to compare the cost-effectiveness associated with various conduit choices. The simulations consisted of 1000 trials, each composed of cohorts of 1000 hypothetical patients simulated during a 10-year time horizon. All modeling and analysis was performed using Excel 2010 software with Visual Basic for Application (Microsoft Corp, Redmond, Wash). All cost-values are reported in 2011 United States dollars (USD) and represent a median value unless otherwise noted. The standard discounting rate of 3.5% was applied to utility and cost values.[19]

Table I. Median values for total (direct and indirect) costs of hospitalizations for various index procedures done for critical limb ischemia with nonhealing foot wounds in United States dollars (*USD*)[a]

Procedure	*Median cost of associated hospitalization (USD)*	*SE (USD)*
Endovascular intervention (initial)	26,509	2153
Bypass operation	44,635	6508
Major amputation	34,251	8305
Revision of surgical bypass	28,039	5075
Endovascular reintervention	13,138	2515

SE, Standard error.
[a]From Barshes et al.[13]

The primary end point was the incremental cost-effectiveness ratio (ICER) expressed as cost per year of preserving ambulatory ability in any form, including through successful limb salvage and preservation of ambulatory ability or through major amputation with ambulation using a limb prosthesis. All ICER ratios are presented as the comparison of one intervention vs the next lowest cost alternative.[20] These comparisons are described using terms that are standard for cost-effectiveness analyses, including "strongly dominated" (for an option that is both less effective *and* more costly than another alternative) and "weakly dominated" (for an option that is less effective and less costly than another alternative *but* has a higher ICER).[18] Secondary end points included cost per year of limb preservation, rate of limb preservation, and total costs.

Deterministic sensitivity analyses. Parameters with higher degrees of uncertainty about the estimates were subjected to deterministic sensitivity analyses. Two main parameters were the focus of these analyses: the cost of bypass using AAV and the cost of bypass using cryopreserved arterial allograft. The base-case scenario assumed that any additional costs associated with increased operative time or increased postoperative costs (prolonged index hospitalization, higher readmission rate, additional costs associated with complications of vein harvesting), or both, in the performance of a bypass using AAV was offset by the conduit not having any additional procurement costs. In addition, we assumed the additional direct costs associated with procurement of cryopreserved venous allograft and PTFE prosthetic graft was offset by the shorter operative time. A one-time additional initial direct cost of $5000 was used in the base-case scenario for cryopreserved arterial allograft; this was varied over the range of $0 to $5000 in the deterministic sensitivity analyses.

RESULTS

Comparison of clinical outcomes and cost-effectiveness. The median 5-year limb salvage rates seen over the 1000 consecutive simulations ranged from 60.6% for PTFE

Table II. Clinical outcomes estimated from 1000 consecutive simulations of the Markov model (median data)

Conduit option	Limb salvage rate at 5, % (range)	Incidence of major amputation after bypass: ≤1 year, % (range)	Incidence of major amputation after bypass: 2-10 years, % (range)	Annual incidence of revisions to restore or maintain patency, % (range)	Source for parameter estimates (first author)
Good-caliber, single-segment GSV[a]	80.7 (75.2-85.3)	10.6 (7.1-14.4)	2.6 (1.4-3.8)	22.7 (19.2-26.4)	Conte,[20] Berceli[21]
AAV	78.9 (72.1-83.9)	11.6 (7.5-14.4)	3.1 (1.7-4.6)	49.0 (29.1-65.6)	Albers,[22] Armstrong[23]
PTFE ± vein patch	60.6 (47.1-73.2)	22.3 (13.4-32.8)	6.2 (3.4-9.1)	24.8 (13.7-36.2)	Albers,[16] Neville[6]
Small-caliber GSV	77.1 (56.5-88.2)	14.1 (4.5-27.2)	2.6 (1.4-3.8)	40.6 (15.5-65.5)	Schanzer,[2] Slim[17]
Cryopreserved allograft					
Venous	62.4 (42.1-78.2)	22.0 (13.4-32.8)	4.8 (2.7-7.1)	52.6 (29.0-76.9)	Albers[17]
Arterial	79.6 (70.1-86.4)	19.0 (6.5-35.3)	3.4 (1.9-5.0)	52.6 (29.0-76.9)	Albers[17]

AAV, Autologous alternative vein; *GSV,* great saphenous vein; *PTFE,* polytetrafluoroethylene.
[a]Presented here for comparison purposes only; good-caliber single-segment saphenous vein was not included in the analysis.

to 79.6% for cryopreserved arterial allografts (Table II). The median 5-year limb salvage rate for conservative management was 26.7% (range, 14.7%-45.5%). The median incidence of major amputation during the first year after bypass ranged from 11.6% for AAV to 22.0% for cryopreserved venous allograft and to 22.3% for PTFE. During subsequent years, the incidence rates of major amputation were much more similar, ranging from 2.6% to 6.2%. The median 5-year patient survival rates for all management options were similar, ranging from 50.5% to 52.0% (minimum of 39.5% and maximum of 63.5% over the 1000 simulations).

The median 10-year total costs associated with each management option are presented in Table III. Conservative management had the lowest median 10-year cost, at $73,948. The costs of bypass with PTFE were only slightly higher than the costs of primary amputation ($87,463 vs $84,906, respectively). The median 10-year costs of bypass with AAV, cryopreserved venous allograft, and small-caliber GSV were also similar, ranging from $93,814 to $95,741. The median 10-year cost of bypass with cryopreserved arterial allograft was $100,575, the highest among all the options evaluated. Conservative management produced a median of 1.9 years of ambulation, the lowest health benefit among the options evaluated (Table III). Primary amputation resulted in a median of 2.9 years of ambulation, whereas bypass with various conduits resulted in 4.3 to 4.5 years of ambulation.

Compared with conservative management, bypass with PTFE had an ICER of $5325 per year of ambulation and was therefore the first cost-effective alternative to conservative therapy (Table III; Fig). Bypass with AAV had an ICER of $21,228 per additional year of ambulation vs bypass with PTFE ($7508 per year of ambulation over conservative therapy) and therefore also appeared to be a cost-effective alternative. Primary amputation was weakly dominated by bypass with PTFE (lower cost and lower effectiveness but higher ICER). Bypass with small-caliber GSV, bypass with cryopreserved venous allograft, and bypass with cryopreserved arterial allografts were strongly dominated by bypass with AAV (higher cost and lower effectiveness).

Results of deterministic sensitivity analyses. The base-case scenario assumed an additional $5000 of direct costs associated with the procurement of cryopreserved arterial allograft that was not offset by the decrease in operative time. To test whether the results or conclusions of the analysis changed based on this estimate, we performed a deterministic sensitivity analysis assuming no additional direct costs associated with this conduit. In this sensitivity analysis, the median total costs decreased to $94,708 (range, $69,034-$132,699), but this option remained dominated (ie, more costly but less effective) compared with bypass with PTFE and bypass with AAV.

In another deterministic sensitivity analysis, we included up to an additional $10,000 of additional costs associated with AAV. The median total costs for bypass with AAV increased up to $103,557 (range, $77,470-$162,614) in these analyses. In these sensitivity analyses, the ICER of bypass with AAV and bypass with small-caliber GSV became equivalent when the additional total costs associated with bypass with AAV exceeded ~$3000.

DISCUSSION

Single-segment GSV remains the preferred conduit for infrainguinal bypass but may be unavailable in 15% to 20% of patients in need of a bypass. This has led many groups to describe their experience with various alternative conduits. Using purely clinical end points, none has emerged as a clear second-best alternative. In this context and with increasing emphasis on costs and cost-effectiveness in health care, the current study was undertaken to evaluate alternative conduits from the perspective of cost-effectiveness.

Three main conclusions can be drawn from the current results. First, infrainguinal bypass with PTFE or AAV may be a reasonably cost-effective alternative to conservative management (local wound care and major amputation as

Table III. The costs, health benefits, and cost-effectiveness of various conduit options used for infrapopliteal bypass in the absence of adequate caliber, single-segment great saphenous vein (*GSV*)

Management option	*Cost in 2011 USD, median (range)*	*No. of ambulatory years, median (range)*	*Incremental cost per limb-year in 2011 USD*
Conservative management	73,948 (45,118-111,554)	1.912 (1.182-2.477)	…
Primary amputation	84,906 (42,540-139,226)	2.931 (2.142-3.757)	Weakly dominated
Bypass with			
PTFE ± vein patch	87,463 (62,533-119-658)	4.256 (3.414-5.236)	$5325
AAV	93,814 (68,061-126,033)	4.558 (3.673-5.400)	$21,228
Cryopreserved venous allograft	95,557 (68,604-128,076)	4.242 (3.414-5.236)	Dominated
Small-caliber GSV	95,741 (68,590-124-632)	4.537 (3.686-5.585)	Dominated
Cryopreserved arterial allograft	100,575 (73,092-131,244)	4.352 (3.490-5.329)	Dominated

AAV, Autologous alternative vein; *PTFE,* polytetrafluoroethylene; *USD,* United States dollars.

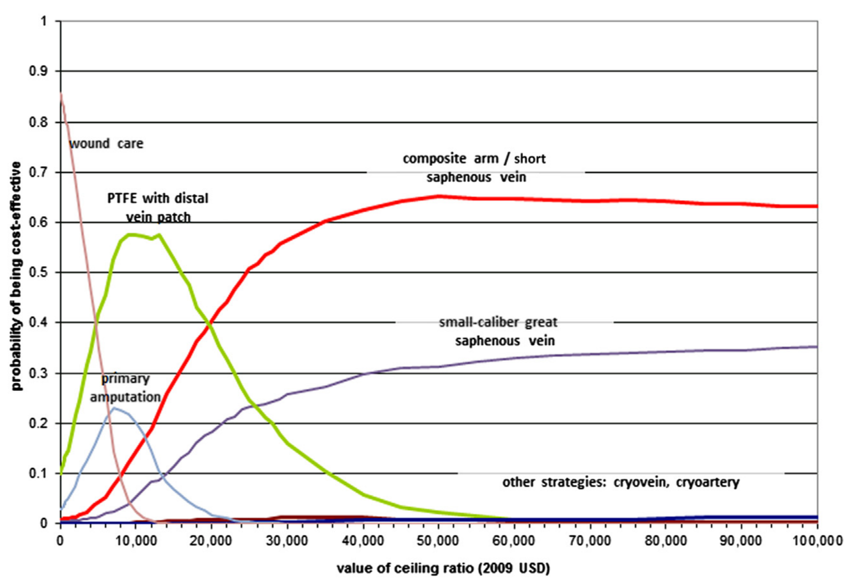

Fig. Cost-effectiveness acceptability curves demonstrate the probability of the conduit options evaluated (*vertical axis*) having an incremental cost-effectiveness ratio (2009 United States dollars [*USD*] per quality-adjusted life-year) at or below various ceiling ratios (*horizontal axis*). *PTFE,* Polytetrafluoroethylene.

needed) for patients with nonhealing foot wounds and chronic limb ischemia. Bypass with PTFE appears to have a lower total cost and good outcomes. Bypass with AAV appears to have better outcomes but at a higher total cost, although both options have ICERs that appear reasonable when compared with conservative management ($5305 and $7508, respectively, per additional year of ambulation over conservative management). Bypass with small-caliber GSV may also be a reasonable alternative if the additional costs associated with AAV exceed $3000 and the clinical outcomes of small-caliber GSV are similar to those reported in the few publications that exist on this topic.[2,21]

Some qualifications of these conclusions must be made. The results of this study are based on estimates of clinical outcome and health utility parameters derived from the literature and cost parameters drawn from a single-center study of costs.[13] We do believe that these parameters are representative of most U.S. nonfederal medical centers. As with clinical studies (including randomized trials), however, the generalizability of these findings to any particular practice setting depends on specific parameters—including baseline patient characteristics, clinical outcomes, and health care system cost structure—being at least comparable to the parameter estimates used in this study. Additional estimates of the long-term costs associated with bypass with various alternative conduits (especially small-caliber GSV, for which very few studies exist) are necessary and would help inform more precise ICER estimates.

The second key conclusion is that venous and arterial cryopreserved allografts do not appear to be good alternatives to conservative management compared with conservative management or bypass with PTFE or AAV. The option of bypass with either of these conduits was dominated in this cost-effectiveness analysis, meaning they were associated with higher costs and lower benefits than other options. This appears not to be due to increased costs associated with the graft material itself but rather a combination of higher reintervention rates and lower limb preservation rates. Indeed, venous and arterial allografts both remain dominated even when the costs of the grafts are assumed to be zero.

Finally, we found that primary amputation does not appear to be a cost-effective alternative to conservative management or bypass. Primary amputation was weakly dominated by bypass with PTFE, meaning that the ICER of primary amputation vs conservative management was higher than the ICER of bypass with PTFE (the next-cheapest alternative) vs primary amputation. Primary amputation remains a standard approach for patients with a nonsalvageable limb, patients who are nonambulatory at baseline, and for patients who are not interested in limb preservation efforts. The results of this analysis, however, suggest that primary amputation does not appear to be justified on the basis of cost-effectiveness in patients who otherwise appear to be candidates for limb preservation efforts, as some authors have suggested.[11,12]

We have previously reported the ICERs associated with managing nonhealing wounds in the ischemic lower limb in the form of costs per quality-adjusted life-year, and the ICER of infrainguinal bypass seems well within the ceiling values suggested for reimbursement in the United States.[13] The recent Patient Protection and Affordable Care Act, however, has discouraged the use of measures such as quality-adjusted life-years that "[discount] the value of a life because of an individual's disability,"[22] and this does pose some limitations for formal cost-utility analyses.[23] In this study we therefore instead focused on cost per year of ambulatory ability because it is the preservation of ambulatory ability—not simply the avoidance of major amputation or "anatomic" limb salvage—that is ultimately the goal of revascularization in the context of non-healing wounds on ischemic limbs.

CONCLUSIONS

Future studies in the field of limb preservation should continue to focus on functional, patient-centered outcomes and consider costs whenever possible. We hold that evaluation of cost per year of ambulation serves as a useful measure for future evaluations of the value of limb preservation efforts.

AUTHOR CONTRIBUTIONS

Conception and design: NB, MB
Analysis and interpretation: NB, MB
Data collection: NB
Writing the article: NB
Critical revision of the article: NB, MB, PK, CO
Final approval of the article: NB, MB, PK, CO
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