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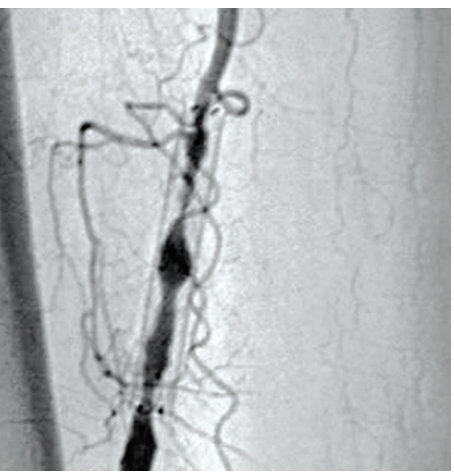
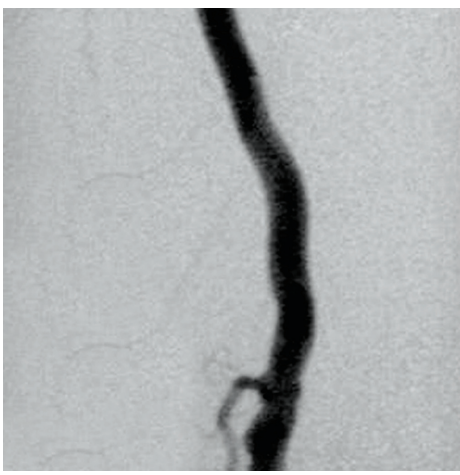
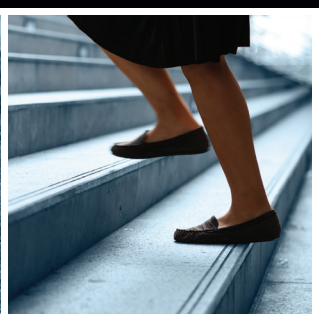
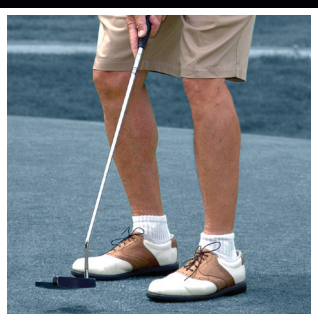


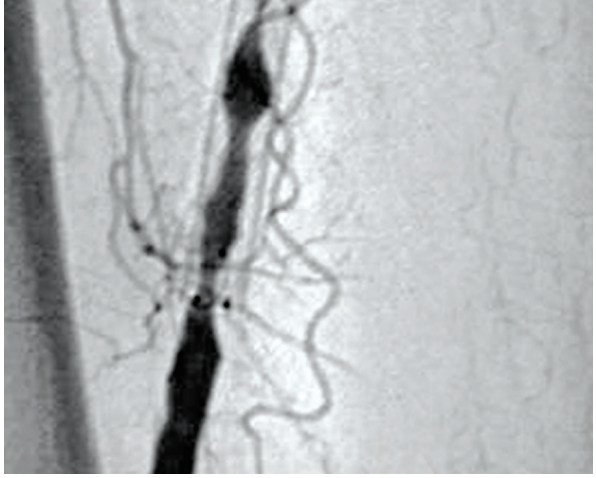


SURGICAL BYPASS SUMMIT

Individualizing Surgical Bypass
Changing the Paradigm







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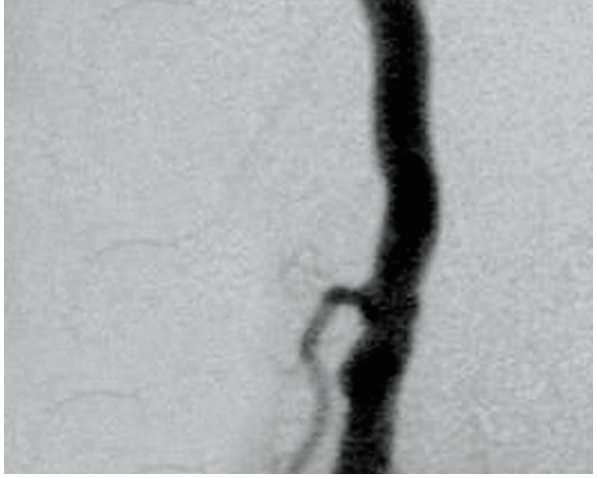

CONTENTS

Surgical Bypass Summit

BY RUSSELL H. SAMSON, MD, FACS, RVT

Over 3 days in early December 2014, Gore & Associates sponsored an educational summit of thought leaders focused on the management of infrainguinal vascular disease. The 15 vascular surgeons from around the world represented France, Germany, Mexico, Italy, and many regions of the United States. All had published extensively in the field of infrainguinal bypass, had significant clinical experience with both saphenous vein as well as nonautogenous grafts, and were proficient in endovascular techniques. The participants represented both academic and private practice, bringing "real-world" experience to the discussion.

Because of the increasing utilization of endovascular procedures, the summit was an attempt to reach consensus on the current state of infrainguinal bypass as a form of revascularization for patients with claudication or chronic limb ischemia. A dominant theme of the summit was to define the conditions most appropriately treated by infrainguinal bypass surgery, and if so treated, the most appropriate type of bypass, especially with regard to the type of conduit. It has been a well-accepted paradigm that autogenous vein is the conduit of choice and prosthetic bypasses should only be utilized when adequate vein is not available. However, autogenous saphenous vein may not be available; therefore, other conduits, such as arm vein, Dacron (polyethylene terephthalate), expanded polytetrafluoroethylene (ePTFE), and now heparin-bonded prosthetic grafts, may be utilized. Some surgeons may also use saphenous vein alternatives as a primary conduit under certain circumstances. The role of adjuvant medications and other techniques to maintain graft patency is also controversial.

In order to facilitate the consensus, each participant provided a lecture on a specific aspect of the overall topic. Discussions then focused on clinical scenarios, treatment algorithms, health care economic value of durable solutions, and breakthroughs that could improve performance and patient outcomes. Since Gore & Associates has adopted the CBAS® Heparin Surface technology for some of its ePTFE grafts, participants also discussed the advantages and disadvantages of heparin bonding to prosthetic grafts and what role, if any, heparin-bonded grafts have in the future. On the final day, participants voted on fundamental questions that arose as part of the discussions and presentations. The results of these questions can be found at www.surgicalbypass.com.

The summit did result in consensus—infrainguinal bypass remains a critical portion of current vascular practice and may be the most appropriate treatment in approximately 15% to 30% of patients in a standard practice dealing with limb preservation. Consensus was also reached with regard to quality saphenous vein, either ipsilateral or contralateral, as the ideal conduit for distal bypass. The group also considered heparin-bonded ePTFE to be an improvement over standard ePTFE, with the caveat that various forms of heparin bonding may have different long-term outcomes. A consistent theme was that although treatment algorithms could be determined, they should be applied on an individual basis. Readers are encouraged to review the summaries of the presentations and formulate their own opinions as to whether appropriate consensus was achieved. ■

Russell H. Samson, MD, FACS, RVT, is Clinical Professor of Surgery at Florida State University Medical School and is an attending surgeon with Sarasota Vascular Specialists in Sarasota, Florida. He has disclosed that he has received compensation from Gore for participating in the Summit and has received honoraria from Gore for writing this article. Dr. Samson may be reached at rsamson@veinsandarteries.com.

Session 1

Current state of bypass for lower extremity revascularization: What are the real results?

Role of Surgical Bypass in a Limb Preservation Program

Who needs a bypass and what is the best conduit?

BY RICHARD F. NEVILLE, MD

There are approximately seven million chronic wounds treated annually in the United States—the treatment of which costs the health care system $20 billion per year. A multidisciplinary, limb preservation program brings together a team of experts whose goal is to achieve healing and preserve functional limbs, and raise awareness about successful limb preservation. The major vascular and podiatric societies have recognized the benefits of such a collaborative program to patients and physicians.[1] Such programs are particularly useful for patients with the added complexities presented by diabetes mellitus and end-stage renal disease. While the purpose of a limb preservation center is to preserve the limb, experts acknowledge that amputation is an important option for the patient in certain cases, and rehabilitation and optimal prosthetics are an important part of the program. Due to the complex nature of this health problem, a patient with a limb threatened by peripheral artery disease may require multiple visits with different physicians and diagnostic tests to determine and carry out a treatment plan. This is not an insignificant issue in patients with limited mobility. Multidisciplinary programs can streamline this process via an integrated team approach that combines a multispecialty physician team with supportive staff. This care increases patient satisfaction and therapeutic success by more rapidly providing care in situations in which time is of the essence. It is important to appoint a program director to oversee operational details of the entire process, as well as a core group of physicians who have a passion for limb preservation.

A dedicated space is important to the identity and smooth performance of the program. A noninvasive vascular diagnostic vascular laboratory is critical to the program, ideally with diagnostic imaging capable of assessing tissue perfusion. Access to arterial and soft tissue imaging by computed tomography and/or magnetic resonance

	GSV	SPLICED VEIN	ARM VEIN	PROS	PROS + VP	COMPOSITE
OP time (hrs) **	4.4 (1.8)	6.1 (1.9)	5.1 (2.3)	3.7 (1.6)	4.4 (1.8)	4.7 (2.0)
Transfusion**	0.5 (1.1)	1.2 (1.7)	0.4 (0.8)	0.5 (1.2)	0.7 (1.1)	0.6 (1.2)
30-day graft failure **	300 (7.5%)	9 (5.6%)	4 (4.3%)	94 (10.5%)	11 (9.8%)	14 (15.4%)

Figure 1. A comparison of perioperative parameters for different bypass conduits; great saphenous vein (GSV), spliced vein, arm vein, prosthetic (PROS), prosthetic with an anastomotic vein patch (PROS+VP), prosthetic with a vein segment (COMPOSITE). Reprinted from J Vasc Surg, 59, Nguyen BN, Neville RF, Abugidieri M, et al, The effect of graft configuration on 30-day failure of infrapopliteal bypasses, 1003-1008, 2014, with permission from Elsevier.

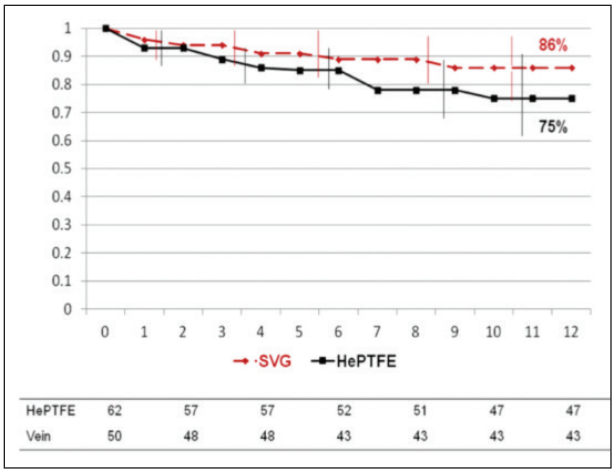

Figure 2. Primary patency at 1 year for tibial bypass using great saphenous vein (SVG) and heparin-bonded ePTFE with a distal vein patch (HePTFE). Reprinted from J Vasc Surg, 56, Neville RF, Capone A, Amdur R, et al, A comparison of tibial artery bypass performed with heparin-bonded expanded polytetrafluoroethylene and great saphenous vein to treat critical limb ischemia, 1008-1014, 2012, with permission from Elsevier.

imaging is required. However, there is still a major diagnostic and therapeutic role for catheter-based arteriography, especially for distal tibial occlusive disease. Thus, in addition to new imaging modalities, the program needs convenient access to a cath lab, hybrid operating room, and/or an on-site, office-based angiography suite.

The program must offer the entire range of therapeutic options, including wound care, hyperbaric oxygen therapy, and certainly a method of revascularization (both endovascular and surgical bypass). In our practice, approximately 70% of patients are best treated with an endovascular-first approach. The remaining 30% are bested treated with initial surgical bypass. This patient cohort includes those presenting with large-volume tissue loss or ulcerative disease (> 2 cm), good life expectancy, long segment occlusive arterial disease (TASC D), and/or previous unsuccessful endovascular intervention. In the group requiring bypass, 30% to 50% will not have a quality venous conduit, and bypass with a prosthetic graft may be required for revascularization. Data suggest that prosthetic graft performance can be enhanced with a venous adjunct at the distal anastomosis (distal vein patch [DVP])[2] and by heparin bonding on the inner surface of the graft. Heparin-bonded grafts have been used extensively in Europe, with excellent results.[3-5] The CBAS® Heparin Surface (Gore & Associates) technology and the heparin-bonded grafts have been a great addition to the armamentarium of the limb preservation center for patients who require prosthetic grafts. With these adjuncts (DVP and heparin bonding), a 50% patency can be achieved at 4 years.[6]

The current state of bypass in today's practice was reflected in an analysis of the National Surgical Quality Improvement Program database including only tibial bypasses, the majority (75%) of which used the greater saphenous vein (GSV).[7] Several factors were identified as contributing to decreased 1-year patency in the cohort; end-stage renal disease and nonhealing ulceration as the indication for revascularization. With regard to perioperative outcomes, the database revealed that spliced vein grafts had a longer operative time and a higher transfusion requirement. Arm vein bypasses also had a longer operative time. Standard prosthetic grafts and composite grafts had higher 30-day perioperative graft failure when compared to bypasses with GSV (Figure 1).

In 2012, we published our experience with the GORE® PROPATEN® Vascular Graft (Gore & Associates) with a DVP compared to quality saphenous vein.[8] The study was a retrospective analysis of prospectively collected data, and included suitable follow-up of patients by pulse examination, ankle-brachial index, and duplex graft surveillance. The bypass procedures included 62 heparin-bonded polytetrafluoroethylene (HePTFE) grafts and 50 GSV grafts. Most of the vein grafts (80%) were translocated veins. The main differences in patient demographics between the two groups were a slightly higher incidence of gangrene in the vein group and a higher incidence of previous bypass in the heparin-bonded group, hence the need for a prosthetic conduit. The amputation-free survival was similar between the two groups and the difference in primary patency was not statistically significant (Figure 2).

SUMMARY

Revascularization is an integral part of a limb preservation program and surgical bypass remains the optimal method of revascularization in 20% to 30% of patients in such a program. Prosthetic grafts will continue to play a role in limb preservation, and adjuncts can be used to improve prosthetic graft performance. Adjuncts include the distal vein patch technique and the heparin surface on the GORE® PROPATEN® Vascular Graft. ■

Richard F. Neville, MD, is from the George Washington University MFA in Washington, DC. He has disclosed that he is on the scientific advisory board for Gore & Associates, has received compensation from Gore for participating in the Summit, and has received honoraria from Gore for writing this article. Dr. Neville may be reached at rneville@mfa.gwu.edu.

1. Sumpio BE, Armstrong DG, Lavery LA, Andros G; SVS/APMA writing group. The role of interdisciplinary team approach in the management of the diabetic foot: a joint statement from the Society for Vascular Surgery and the American Podiatric Medical Association. J Vasc Surg. 2010;51:1504-1506.
2. Neville RF, Tempesta B, Sidway AN. Tibial bypass for limp salvage using polytetrafluoroethylene and a distal vein patch. J Vasc Surg. 2001;33:266-271.
3. Pulli R, Dorigo W, Castelli P, et al. Midterm results from a multicenter registry on the treatment of infrainguinal critical limb ischemia using a heparin-bonded ePTFE graft. J Vasc Surg. 2010;51:1167-1177 e1161.
4. Peeters P, Verbist J, Deloose K, et al. Results with heparin bonded polytetrafluoroethylene grafts for femorodistal bypasses. J Cardiovasc Surg (Torino). 2006;47:407-413.
5. Wallus check K. Heparin-bonded expanded polytetrafluoroethylene vascular graft for occlusive vascular disease of the lower extremity. Ital J Vasc Endovasc Surg. 2006;13:137-147.
6. Neville RF, Lidsky M, Capone A, et al. An expanded series of distal bypass using the distal vein patch technique to improve prosthetic graft performance in critical limb ischemia. Eur J Vasc Endovasc Surg. 2012;44:177-182.
7. Nguyen BN, Neville RF, Abugideiri M, et al. The effect of graft configuration on 30-day failure of infrapopliteal bypasses. J Vasc Surg. 2014;59:1003-1008.
8. Neville RF, Capone A, Amdur R, et al. A comparison of tibial artery bypass performed with heparin-bonded expanded polytetrafluoroethylene and great saphenous vein to treat critical limb ischemia. J Vasc Surg. 2012;56:1008-1014.

Alternative Conduits

Are arm vein and spliced vein conduits effective?

BY EFTHYMIOS D. AVGERINOS, MD, PHD

Ipsilateral, single-segment great saphenous vein (GSV) remains the ultimate conduit for below-the-knee bypass in critical limb ischemia. The choice of conduit becomes problematic, however, when GSV is unavailable or not usable. The results of alternative autologous veins (AAV) are variable and, despite a general consensus favoring them as a second choice conduit, their benefit has been controversial, particularly for the below-the-knee popliteal targets.[1-5]

Contemporary data from the University of Pittsburgh

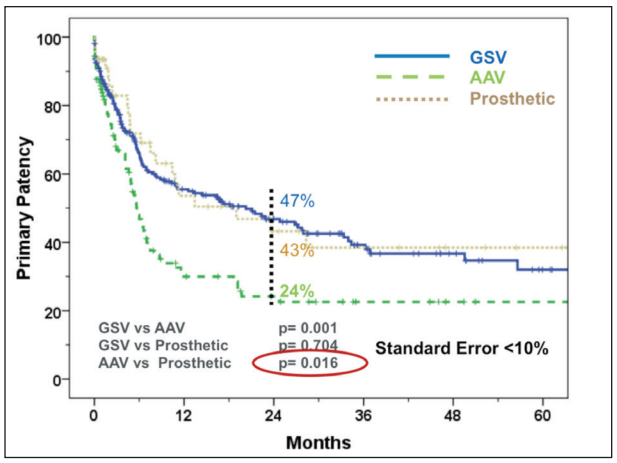

Figure 1. Primary patency curves by type of conduit. Dashed line cutting the curve at 24 months indicates that the number of grafts at risk thereafter is small. Reprinted from J Vasc Surg, Avgerinos ED, Sachdev U, Naddaf A, et al, Autologous alternative veins may not provide better outcomes than prosthetic conduits for below-knee bypass when great saphenous vein is available, 2015, with permission from Elsevier.

Medical Center (UPMC) add some insight in the controversy. In a retrospective review of consecutive below-the-knee bypasses for critical ischemia from 2007–2011, single-segment GSV, alternative autologous veins, and prosthetic grafts were compared.[6] This is the first study to feature this three-group comparison. Two hundred fifty-five patients received GSV, 106 patients received alternative vein conduits, and 46 patients received prosthetic grafts. Of the 106 patients who received AAVs, most received spliced veins (n = 74) and the rest received single-segment arm veins. The prosthetic group included primarily heparin-bonded grafts (n = 41) and approximately half had a distal anastomotic adjunct.

The postoperative outcomes for the entire cohort were a 12% major adverse limb event rate (reintervention or amputation), a 6.5% major adverse cardiac event rate (myocardial infarction, stroke, or death), a 16.5% wound complication rate, and a 2.5% mortality rate at 30 days. The prosthetic group had significantly fewer 30-day major adverse limb events (4.3%), whereas the AAV group had the most (16%) and the GSV group fell in between (11.8%). The remaining 30-day outcomes (major adverse cardiac events, wound complications) did not differ among the three groups. At 2 years, the AAV group had the worst primary patency (24%), whereas the GSV and prosthetic groups had a fairly similar patency (47% and 43%, respectively) (Figure 1). The AAVs tended to fail early and required reintervention. A multivariate analysis confirmed that the conduit was a predictor of patency, with prosthetic graft and GSV performing significantly better than AAV (Table 1). Not surprisingly, surgeons' level of experience affected patient outcomes and was a predictor of patency.

The AAV and prosthetic groups showed no statistically significant difference with regard to primary assisted patency: 53% for AAVs versus 45% for prosthetic grafts. This was further confirmed by multivariate analysis. The GSV performed significantly better when compared to the other two conduits. Similar results, also confirmed by multivariate analysis, were seen with secondary patency: the performance of AAVs was not significantly different than prosthetic grafts and both were inferior to GSV. Limb salvage at 2 years was 86% for GSV, 78% for alternative veins, and 72% for prosthetic grafts. Multivariate analysis showed no statistically significant difference between these groups.

In subgroup analysis dividing bypasses in popliteal and infrapopliteal targets, primary patency, primary assisted patency, and secondary patency rates at 2 years were better for the GSV compared to the other groups. AAVs showed worse primary patency but better primary assisted and secondary patency compared to prosthetic conduits, although these differences were not significant. Single-segment AAVs did not have different outcomes when compared with spliced AAVs.

As a retrospective study, these results may be confounded by several biases and limitations that should be taken into consideration when interpreting the findings.

SUMMARY

There is no clear mid-term advantage of AAV conduits over prosthetic grafts. AAVs have poor primary patency because of early failures and frequent reintervention and, despite "catching up" later on, primary assisted and secondary patencies remain comparable between AAVs and prosthetic grafts. Thus, candidates for AAV should be thoughtfully selected. We recommend that AAVs should

TABLE 1. INDEPENDENT RISK FACTORS ASSOCIATED WITH BYPASS PRIMARY PATENCY

	Cox Regression Analysis	
	Hazard Ratio	***P* Value**
Primary Patency		
Conduit (reference AAV)		< .001
Conduit GSV	0.55	< .001
Conduit prosthetic	0.37	< .001
Female gender	1.47	.028
Prior procedures	1.36	.035
Experience (reference 6–10/yr)		.000
0–5 procedures/yr	.97	.918
>10 procedures/yr	.52	< .001

Reprinted from J Vasc Surg, Avgerinos ED, Sachdev U, Naddaf A, et al, Autologous alternative veins may not provide better outcomes than prosthetic conduits for below-knee bypass when great saphenous vein is available, 2015, with permission from Elsevier.

be reserved for distal tibial or pedal bypasses, patients with good life expectancy (> 5 years) and low risk for perioperative complication, and in the setting of infection. For all other patients, heparin-bonded prosthetic grafts can be an equal—if not better—alternative in the absence of GSV. ■

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1. Calligaro KD, Syrek JR, Dougherty MJ, et al. Use of arm and lesser saphenous vein compared with prosthetic grafts for infrapopliteal arterial bypass: are they worth the effort? J Vasc Surg. 1997;26:919-924.
2. Faries PL, Arora S, Pomposelli FB Jr, et al. The use of arm vein in lower-extremity revascularization: results of 520 procedures performed in eight years. J Vasc Surg. 2000;31:50-59.
3. Kreienberg PB, Darling RC 3rd, Chang BB, et al. Early results of a prospective randomized trial of spliced vein versus polytetrafluoroethylene graft with a distal vein cuff for limb-threatening ischemia. J Vasc Surg. 2002;35:299-306.
4. McPhee JT, Barshes NR, Ozaki CK, et al. Optimal conduit choice in the absence of single-segment great saphenous vein for below-knee popliteal bypass. J Vasc Surg. 2012;55:1008-1014.
5. Neville RF, Capone A, Amdur R, et al. A comparison of tibial artery bypass performed with heparin-bonded expanded polytetrafluoroethylene and great saphenous vein to treat critical limb ischemia. J Vasc Surg. 2012;56:1008-1014.
6. Avgerinos ED, Sachdev U, Naddaf A, et al. Autologous alternative veins may not provide better outcomes than prosthetic conduits for below-knee bypass when great saphenous vein is unavailable. J Vasc Surg. 2015; May 2 [Epub ahead of print].

Vein Versus Heparin-Bonded ePTFE

What do the data really say?

BY PROF. RAFFAELE PULLI; WALTER DORIGO, MD; AND PROF. CARLO PRATESI, ON BEHALF OF THE ITALIAN REGISTRY GROUP*

The great saphenous vein (GSV) is superior to polytetrafluoroethylene (PTFE), and therefore should be preferentially used. Dr. Neville reviewed this topic[1] and described data indicating that the GORE® PROPATEN® Vascular Graft (Gore & Associates) performed better than standard PTFE in a European-run randomized trial.[2] Dr. Samson presented his single-center experience at Charing Cross in 2013, suggesting the GORE® PROPATEN® Vascular Graft performed better than standard GORE-TEX® Vascular Grafts (Gore & Associates) and ADVANTA PTFE Vascular Grafts (Atrium).[3] Over the past decade there have been several other reports published on the subject, most of which were from Italian surgeons. The extensive Italian experience warranted creation of an Italian registry encompassing seven institutions throughout Italy. While not a randomized controlled trial, the registry provides insight into the real world of surgery and reflects what surgeons face in their daily practice.

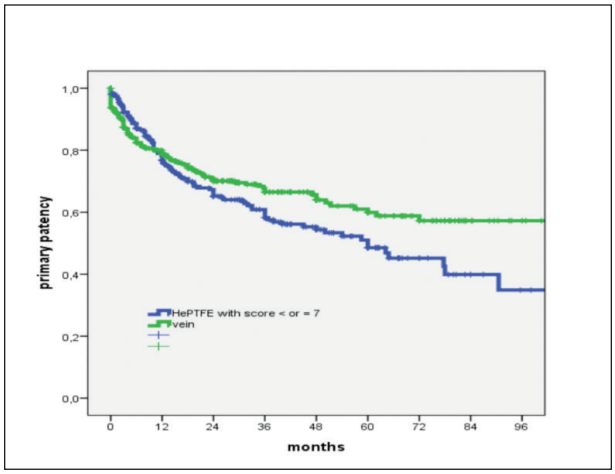

Figure 1. Kaplan-Meier curve of estimated primary patency in patients undergoing a GORE® PROPATEN® Vascular Graft bypass with a score ≤ 7 (blue line) compared with that obtained in patients undergoing a vein bypass (green line) (Log-rank 3.1; *P* = .08).

Patients in the Italian Registry who received a below-the-knee bypass using vein had better primary patency than patients who received a bypass with heparin-bonded expanded polytetrafluoroethylene (ePTFE). Based upon these results, a GORE® PROPATEN® Vascular Graft score was created to summarize the circumstances under which the GORE® PROPATEN® Vascular Graft might perform as well as vein. A univariate analysis revealed the factors that affected primary patency (Table 1), and these factors were assigned point values (Table 2). For example, male gender was assigned one point and female gender was assigned two points. A low total point score indicated that a particular patient was a good candidate for receiving a GORE® PROPATEN® Vascular Graft preferentially to vein because the risk of thrombosis was low. An ANOVA test for thrombosis during follow-up was applied to the patients in the registry, and 7.502 was determined to be the cutoff score value ($P < .001$; R = 0.09), below which the GORE® PROPATEN® Vascular Graft could be used preferentially due to low risk of thrombosis, and above which vein would be likely to perform better. To validate this analysis, primary patency results for patients with a GORE® PROPATEN® Vascular Graft score of ≤ 7 who received bypasses with this device were compared to the primary patency results for vein bypasses (Figure 1). Although there was a trend toward better patency with vein, in contrast to the overall cohort, the difference was not statistically significant.

By definition, registry results have no inclusion or exclusion criteria, and there was no request of homogeneous indication for the choice of grafts. Thus, the study was

TABLE 1. UNIVARIATE AND MULTIVARIATE ANALYSIS FOR FACTORS AFFECTING PRIMARY PATENCY IN PATIENTS RECEIVING A HEPARIN-BONDED GRAFT

	Univariate Analysis				Multivariate Analysis		
	Log-rank	*P* value	95% CI	OR	95% CI	OR	*P* value
Female gender	6.2	.002	1.1–2.2	1.6	1–1.9	1.5	.02
Chronic renal failure	0.1	.4	0.7–1.7	1.1			
Reintervention	19.7	.001	0.4–0.8	0.6	0.4–1	0.6	.003
Diabetes	0.1	.3	0.8–1.5	1.1			
Tibial anastomosis	4.6	.02	1–2	1.4	0.8–1.7	1.2	.2
Distal procedures	1.7	.08	0.9–1.7	1.2			
Runoff score < 2	6.4	.003	1.1–1.9	1.5	0.9–1.6	1.2	.2
Rutherford 5–6†	0.9	.1	0.9–1.6	1.2			

CI = confidence interval, OR = odds ratio.
†This factor affects limb salvage, but not primary patency.

TABLE 2. SCORES ASSIGNED BASED ON RESULTS OF UNIVARIATE ANALYSIS

Gender	Male = 1 point	Female = 2 points	—
Reintervention	No = 1 point	Yes = 2 points	—
Tibial anastomosis	No = 1 point	Yes = 2 points	—
Runoff score	2 vessels = 2 points	< 2 vessels = 3 points	—
Rutherford class	Class 4 = 1 point	Class 5 = 2 points	Class 6 = 3 points

limited by the fact that it was registry-based and not randomized, and therefore the two treatment groups differed in several ways that likely reflected different approaches and patient selection among participating surgeons. As such, the calculated scores are primarily hypothesis generating, and should be validated in prospective studies and in other series of patients.

SUMMARY

The GORE® PROPATEN® Vascular Graft offers satisfactory results in terms of patency and limb salvage rates. Moreover, venous adjuncts at the distal anastomosis seem to offer improved outcomes. Vein remains the best choice; however, in the case of unsuitable vein, a heparin-bonded PTFE graft is a good alternative with a comparable limb salvage rate. In some situations, on the basis of the above mentioned score, patients may benefit from the GORE® PROPATEN® Vascular Graft as a first choice. ■

**The results presented in this article are first-line results and the Italian registry group is looking to prospectively validate their scoring system in another region.*

Prof. Raffaele Pulli is from the University of Florence in Florence, Italy. He has disclosed that he has received compensation from Gore for participating in the Summit and has received honoraria from Gore for writing this article. Dr. Pulli may be reached at rpulli@unifi.it.

Walter Dorigo, MD, is from the University of Florence in Florence, Italy. He has stated that he has no financial interests related to this article.

Prof. Carlo Pratesi is from the University of Florence in Florence, Italy. He has disclosed that he has received compensation from Gore for participating in the Summit.

1. Neville RF. Role of surgical bypass in a limb preservation program. Endovascular Today. 2015;14(Suppl):5-6.
2. Lindholt JS, Gottschalksen B, Johannesen N, et al. The Scandinavian Propaten((R)) trial: 1-year patency of PTFE vascular prostheses with heparin-bonded luminal surfaces compared to ordinary pure PTFE vascular prostheses: a randomised clinical controlled multi-centre trial. Eur J Vasc Endovasc Surg. 2011;41(5):668-673.
3. Samson RH. Surgical bypass summit. Endovascular Today. 2015;14(Suppl):4.

Is Vein Still the First Choice When a Leg Bypass Is Needed?

Examining the evidence.

BY JOSEPH L. MILLS, SR, MD

The Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial is the only large, prospective, randomized trial published to date to compare surgical bypass and endovascular therapy as treatments for patients with severe limb ischemia.[1] It indicated that autogenous vein is superior to prosthetic conduits for patients undergoing bypass in this setting. Multiple studies have confirmed the overall superiority of vein conduits for leg bypass.[2,3]

When autogenous vein is truly lacking, there is general consensus that a short graft above the knee joint is the most favorable location for use of a prosthetic conduit. Below the knee, many of the published studies are confounded by the use of patches and cuffs; different surgeons employ a variety of distal anastomotic adjuncts. The challenge therefore lies in determining whether improved clinical outcomes are the result of the conduit or a result of the adjunct. Taylor vein patches likely improve prosthetic bypass outcomes below the knee.[4] Dr. Neville's distal vein patch is another important prosthetic bypass adjunctive technique.[5] Dr. Neville has published research suggesting that even at 1 year, a separation in outcomes between patients who receive heparin-bonded expanded polytetrafluoroethylene and patients who receive saphenous vein may begin to appear.[6]

The spectrum of peripheral artery disease (PAD) is broad, and therefore surgical outcomes will be markedly different depending upon which patient is selected for which intervention. Critical limb ischemia was defined in 1982 in a one-page consensus document[7] written by vascular surgeons. There are major problems with this definition, in particular its lack of applicability to patients with diabetes. The Society for Vascular Surgery (SVS) Wound, Ischemia, and foot Infection (WIfI) limb classification system may be a useful tool for controlling study outcomes and determining which therapeutic option is best for a particular patient.

The classification is based on three major factors that influence amputation risk and clinical management.[8] When the WIfI scores are combined, patients can be classified into four clinical stages of disease. Two recent studies have already validated the concept of the SVS WIfI classification and confirm its utility in predicting amputation risk.[9,10]

SUMMARY

A uniform classification system is required in order to accurately assess outcomes and relative efficacy of interventions intended to prevent limb amputation in patients with PAD and diabetes. The WIfI index includes critical factors that must be considered and graded for patient evaluation. In many ways, the WIfI index is similar to the TNM (tumor, nodes, metastasis) classification of malignant tumors because it is intended to allow assessment, comparison, and improvement of outcomes. It is acknowledged that therapies will change over time, so therefore WIfI is not intended to dictate therapy. The WIfI index would also benefit from an updated practical arterial anatomic classification system. ■

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1. Adam DJ, Beard JD, Cleveland T, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet. 2005;366:1925-1934.
2. Mills JL. Infrainguinal bypass. In: Cronenwett JC, Johnston W, editors. Rutherford's Textbook of Vascular Surgery. 8th edition. Philadelphia: Elsevier Saunders; 2014:1758-1781.
3. Mills JL. Open bypass and endoluminal therapy: complementary techniques for revascularization in diabetic patients with critical limb ischemia. Diabetes Metab Res Rev. 2008;24(Suppl 1):S34-39.
4. Yeung KK, Mills JL, Hughes JD, et al. Improved patency of infrainguinal PTFE bypass with distal Taylor vein patch. Am J Surg. 2001;182:578-83.
5. Neville RF, Tempesta B, Sidway AN. Tibial bypass for limb salvage using polytetrafluoroethylene and a distal vein patch. J Vasc Surg. 2001;33:266-271; discussion 271-262.
6. Neville RF, Capone A, Amdur R, et al. A comparison of tibial artery bypass performed with heparin-bonded expanded polytetrafluoroethylene and great saphenous vein to treat critical limb ischemia. J Vasc Surg. 2012;56:1008-1014.
7. Bell PRF, Charlesworth D, DePalma RG, et al. The definition of critical ischemia of a limb. Working Party of the International Vascular Symposium. Br J Surg. 1982;69(Suppl):S2.
8. Mills JL Sr, Conte MS, Armstrong DG, et al. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification based on wound, ischemia, and foot infection (WIfI). J Vasc Surg. 2014;59:220-234, e221-222.
9. Cull DL, Manos G, Hartley M, et al. Prospective analysis of wound characteristics and degree of ischemia on time to wound healing and limb salvage: an early validation of the Society for Vascular Surgery Lower Extremity Threatened Limb Classification System. J Vasc Surg. 2014;59:28s.
10. Zhan LX, Branco BC, Armstrong DG, Mills JL. The Society for Vascular Surgery (SVS) lower extremity threatened limb classification system based on Wound, Ischemia, and foot Infection (WIfI) correlates with risk of major amputation and time to wound healing. J Vasc Surg. 2015;61:939-944.

TAKE HOME POINTS

RICHARD F. NEVILLE, MD

A multidisciplinary limb preservation program assembles experts dedicated to healing and limb preservation in a challenging group of patients. Such a program requires an aggressive approach to lower extremity revascularization that will involve surgical bypass in 25% to 30%. Of those patients best treated with surgical bypass, as many as one half will not have quality autogenous conduit and will require a prosthetic graft for bypass. The performance of prosthetic conduit for distal bypass has been improved through venous adjuncts at the distal anastomosis and heparin bonding to the graft. Although quality large saphenous vein remains the ideal conduit for distal bypass, these improvements in prosthetic graft performance through anastomotic adjuncts and heparin bonding on the surface of the graft (as per the GORE® PROPATEN® Vascular Graft [Gore & Associates]) have made this technique a critically important alternative for those patients needing bypass for limb preservation.

EFTHYMIOS D. AVGERINOS, MD, PhD

There is no clear mid-term advantage of AAV conduits over prosthetic grafts. AAVs have poor primary patency because of early failures and frequent reintervention and, despite "catching up" later on, primary assisted and secondary patency rates remain comparable between AAVs and prosthetic grafts. Thus, candidates for AAVs should be thoughtfully selected. We recommend that AAVs should be reserved for distal tibial or pedal bypasses, patients with good life expectancy (> 5 years) and low risk for perioperative complication, and in the setting of infection. For all other patients, heparin-bonded prosthetic grafts can be an equal—if not better—alternative in the absence of GSV.

PROF. RAFFAELE PULLI

An autologous saphenous vein of small diameter, of poor quality, or previously used, is no longer a contraindication to below-the-knee femoropopliteal bypass in patients with CLI. Heparin-bonded ePTFE bypass grafts have been shown, in large multicenter studies with a robust number of patients, to provide equivalent long-term secondary patency and limb salvage rates with respect to autologous vein. However, autologous vein maintains its superiority in terms of primary patency. Moreover, an accurate subgroup analysis seems to indicate that in the presence of an adequate autologous vein, heparin-bonded ePTFE can be used primarily in highly selected patients (ie, male patients undergoing primary intervention rather than reintervention, with more than one patent tibial vessel and with rest pain rather than ulcers). In fact, in such patients, prosthetic graft provides similar results to autologous vein in terms of primary patency, allowing to preserve the vein for further revascularizations or for different therapeutic uses.

JOSEPH L. MILLS, Sr, MD

Endovascular therapy and open surgical bypass both have major roles to play in lower extremity revascularization. Appropriate patient selection is a key determinant of successful outcomes. A limb risk stratification system, such as SVS WIfI classification predicts baseline limb amputation risk and will likely be useful in selecting intervention type and allowing the comparison of outcomes using different, alternative approaches. Autogenous vein remains the most durable conduit for leg bypass. Prosthetic conduits, most likely with adjuncts such as cuffs, patches, and heparin bonding, seem to improve intermediate outcomes in patients requiring leg bypass in the absence of suitable vein conduit.

Session 2

Bypass in the world of "endovascular first": How does it fit in today's treatment algorithm?

There Are Negative Consequences That Persist After Failed Endovascular Treatment of CLI

BY ROSS MILNER, MD

Patients often prefer endovascular therapy because the treatment can be performed in angiography suites and does not require hospitalization. Endovascular therapy may also be preferred because surgeons may be reluctant to perform bypass due to a previous failed ipsilateral percutaneous endovascular intervention, which is an established negative predictor for future lower-extremity bypass success.[1] We investigated these assumptions at our institution.[2]

We performed a retrospective review of patients with failed endovascular therapy at both a university medical center as well as a US Department of Veterans Affairs (VA) hospital. Approximately one-third of patients were claudicants, whereas approximately 45% had tissue loss and approximately 17% had ischemic rest pain. Primary patency overall was 24% at 1 year and secondary patency was 51%. Patients in the TASC A group had the best primary patency results (Figure 1). Although TASC C patients had better outcomes than TASC B patients, the study numbers were so small in every group that the difference did not reach statistical significance. With regard to primary assisted and secondary patency, patients in TASC A and B groups had better outcomes than patients in TASC C and D groups. While it was difficult to reach firm conclusions, smoking was shown to have a negative effect on treatment success. Of the failed interventions, 76% were current smokers. The results suggest that it may be a mistake to perform endovascular therapy on smokers. A review of the failed interventions, and the consequences for patients who failed treatment, revealed that 70% of those patients developed claudication or recurrent claudication, while the rest of the patients developed ischemic rest pain.

SUMMARY

Stenting for TASC C and TASC D lesions is more likely to fail than stenting for TASC A and TASC B lesions. The failure in TASC C and TASC D lesions is also more likely to lead to either bypass or amputations than failures in TASC A and TASC B lesions. Moreover, when endovascular therapy is performed on a TASC C or TASC D lesion, there can be negative effects on limb salvage. In addition, a patent peroneal artery does not increase the likelihood of patency from endovascular intervention on the femoropopliteal segment.

Patients with TASC A and TASC B lesions can be safely treated with endovascular therapy. In contrast, while it is technically feasible to treat TASC C and TASC D lesions, it may not be optimal for the patient because the failure of a TASC C or TASC D intervention can potentially compromise future

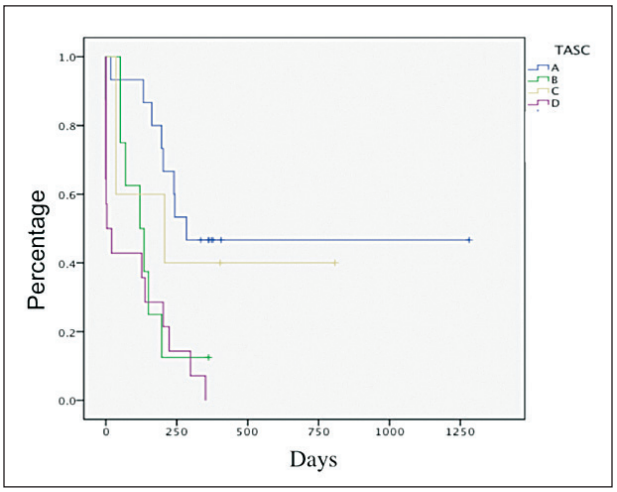

Figure 1. Primary patency by TASC classification. Reprinted from J Vasc Surg, 56, Al-Nouri O, Krezalek M, Hershberger R, et al, Failed superficial femoral artery intervention for advanced infrainguinal occlusive disease has a significant negative impact on limb salvage, 106-110, 2012, with permission from Elsevier.

bypass success. In addition, repeat interventions can be expensive. ■

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1. Nolan BW, De Martino RR, Stone DH, et al. Prior failed ipsilateral percutaneous endovascular intervention in patients with critical limb ischemia predicts poor outcome after lower extremity bypass. J Vasc Surg. 2011;54:730-735; discussion 735-736.
2. Cheng SW, Ting AC, Ho P. Angioplasty and primary stenting of high-grade, long-segment superficial femoral artery disease: is it worthwhile? Ann Vasc Surg. 2003;17:430-437.

Gender Differences in PAD Treatment

Is an endovascular-first strategy worse for women?

BY VENITA CHANDRA, MD

Although traditionally underrepresented in the literature and underdiagnosed, after age adjustment, women in fact have a higher prevalence of peripheral artery disease (PAD) as compared to men. Despite these findings, women have traditionally undergone revascularization, in particular open revascularization, at lower rates than men.[1] With the increasing trend toward endovascular strategies, the question remains whether such disparities continue to exist with this modality.

Several studies have evaluated the role of gender in outcomes from endovascular procedures. A study of a little under 400 men and women examined outcomes from endovascular infrainguinal revascularization that took place from 2001 to 2006.[2] The investigators found a similar patency rate between men and women; however, they also noted that women were older, had higher reintervention rates (17% vs 12.3%), and usually presented with limb threat. Another study by Pulli and colleagues[3] examined revascularizations that occurred from 2000 to 2010 at their institution,[4] and once again found that women tended to be older and have more advanced disease, but no significant difference in lesion location or intervention was found. However, a trend demonstrated poorer results in women.

Gender differences after open surgical bypass have also been demonstrated in a number of studies with variable results. Lancaster et al[5] evaluated the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) data from 2005 to 2008 to assess predictors of early surgical bypass graft failure. This large study found that being female was an independent risk factor for early graft failure; however, other large studies did not find any difference in terms of primary patency or limb salvage between genders.[6]

Review of the 2012 NSQIP data (author's unpublished data analysis) focusing on PAD in men and women revealed that, of the more than 12,000 patients who underwent open (approximately 60%) and endovascular (approximately 40%) revascularizations that year, approximately 60% of the procedures were performed in men and approximately 40% were performed in women. Women had a higher complication rate after endovascular procedures (12% vs 9.9%; $P = .017$), but no significant difference in 30-day mortality was found. After open procedures, however, women were found to have both higher complication rates (38.9% vs 28.9%; $P < .001$) and higher 30-day mortality rates (2.8% vs 1.9%; $P = .01$). The reason for these differences between men and women is unclear; vessel sizing and anatomic distribution in women may be contributing factors.

SUMMARY

Differences in outcomes for PAD treatment between women and men exist for both endovascular and open strategies. The issue of gender disparity in PAD treatment outcomes cannot be resolved until there are more studies that specifically address the subject. Therefore, further investigation with specific emphasis on tools and techniques targeted for women is warranted. Until then, consideration must be given to the fact that women have high complication and mortality rates, and consequently current vascular approaches may not be ideal for the female anatomy or common female comorbidities. ■

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1. Feinglass J, McDermott MM, Foroohar M, et al. Gender differences in interventional management of peripheral vascular disease: evidence from a blood flow laboratory population. Ann Vasc Surg. 1994;8:343-349.
2. DeRubertis BG, Vouyouka A, Rhee SJ, et al. Percutaneous intervention for infrainguinal occlusive disease in women: equivalent outcomes despite increased severity of disease compared with men. J Vasc Surg. 2008;48:150-157; discussion 157-158.
3. Pulli R. Vein versus heparin bonded ePTFE: what do the data really say? Endovascular Today. 2015;14(Suppl):8-9.
4. Pulli R, Dorigo W, Pratesi G, et al. Gender-related outcomes in the endovascular treatment of infrainguinal arterial obstructive disease. J Vasc Surg. 2012;55:105-112.
5. Lancaster RT, Conrad MF, Patel VI, et al. Predictors of early graft failure after infrainguinal bypass surgery: a risk-adjusted analysis from the NSQIP. Eur J Vasc Endovasc Surg. 2012;43:549-555.
6. Ballotta E, Gruppo M, Lorenzetti R, et al. The impact of gender on outcome after infrainguinal arterial reconstructions for peripheral occlusive disease. J Vasc Surg. 2012;56:343-352.

The BEST-CLI Trial: Will It Conclusively Direct Treatment?

BY MICHAEL S. CONTE, MD

In an effort to address the lack of data surrounding optimal treatment for patients with critical limb ischemia (CLI), the National Institutes of Health (NIH) has invested $25 million in the Best Endovascular vs. Best Surgical Therapy in Patients with Critical Limb Ischemia (BEST-CLI) trial. The NIH felt strongly that BEST-CLI must include all of the key stakeholders who currently treat CLI: vascular surgeons, interventional cardiologists, interventional radiologists, and vascular medicine specialists. The main differences between BEST-CLI trial and the Bypass vs. Angioplasty in Severe Ischemia of the Limb (BASIL) trial[1] are that BEST-CLI is a a pragmatic trial fully incorporating current therapies, is meaningfully stratified by clinical and anatomic severity, and uses a primary endpoint (major adverse limb event-free survival) that is more sensitive to clinical failure.

The BEST-CLI trial also differs from the BASIL trial in design. The BEST-CLI trial is based on the premise that event rates are different for patients who have an expected bypass with a good-quality saphenous vein when compared with those who do not. It includes two independently powered, parallel trials comparing bypass and endovascular intervention in patients with adequate saphenous vein (N = 1,620) and those lacking adequate saphenous vein (N = 480), as determined by preoperative vein mapping. The design of the BEST-CLI trial is complex because it will include all types of interventions (eg, angioplasty, stenting, and atherectomy). Minimum follow-up is 2 years.

Currently, 112 sites have been selected for the BEST-CLI trial (Figure 1). Although the sites are dominated by vascular surgery investigators (n = 492), other specialties are also represented, including cardiologists (n = 155), radiologists (n = 113), and vascular medicine specialists (n = 2). Each site has a CLI team that includes all individuals who treat CLI at that particular site. The BEST-CLI trial defines specific criteria for both open reconstruction and below-the-knee intervention, which are required in order for the patient to be approached for inclusion in the study. Two physicians on each team must evaluate the patient's case and confirm that the patient meets inclusion criteria and is therefore eligible for randomization. Two individual physicians on the team must also agree on the need for and the type of reintervention. The study was designed in this way as an acknowledgment that the type and timing of reintervention are both critical drivers of the trial endpoint. The trial also includes multiple measures of functional outcome and cost-effectiveness.

Not surprisingly, the BEST-CLI trial also has limitations, largely arising from the heterogeneity of patients and procedures that characterize current CLI practice. Despite its limitations, BEST-CLI represents a critical opportunity to collect high-quality, multicenter data from a randomized trial. Ultimately, more than one

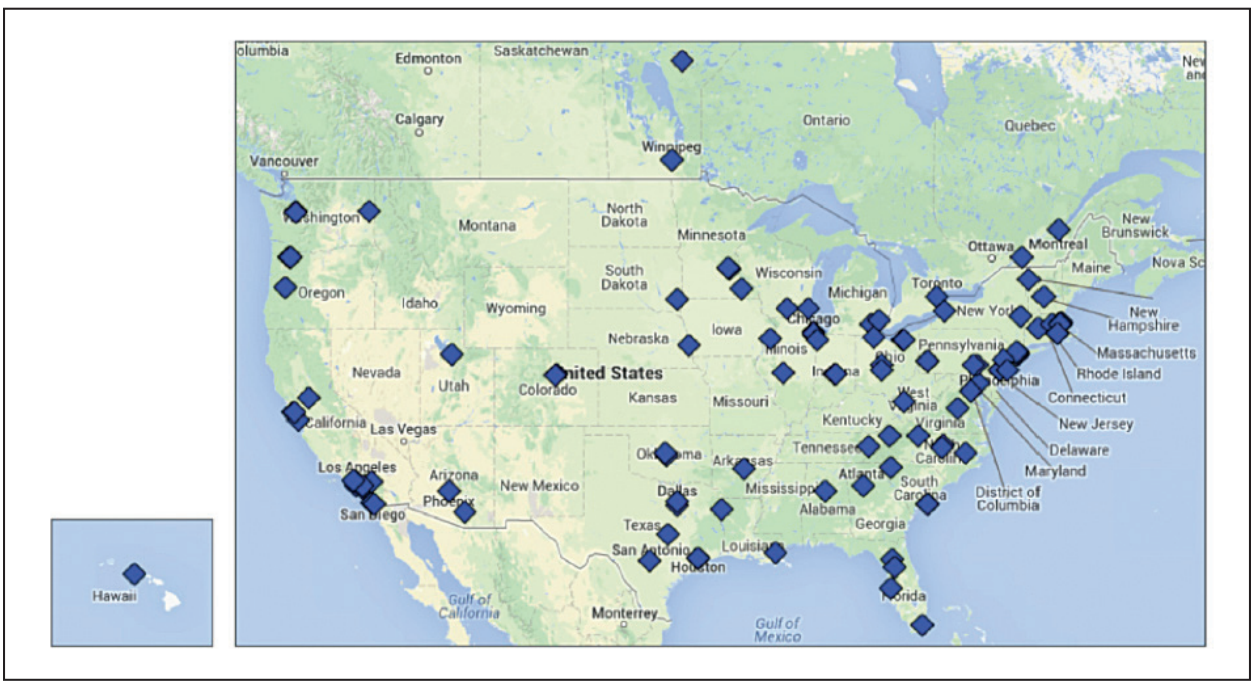

Figure 1. Site summary for the BEST-CLI trial. At the time of this writing, 92 of the selected sites have been activated. Figure and personal communication courtesy of Alik Farber, MD.

trial will be required to build a comprehensive evidence base in CLI.

SUMMARY

The field of CLI treatment needs high-quality, randomized controlled trials and other comparative effectiveness studies. The BEST-CLI trial was designed to address many of the key limitations of the BASIL trial. BEST-CLI is a landmark trial that will define the current state of outcomes for interventions in CLI. In particular, quality of life and cost-effectiveness outcomes from BEST-CLI will be carefully scrutinized by managed care organizations. That said, no single trial can address all of the evidence gaps in the treatment of CLI. BEST-CLI must be followed by additional comparative studies. ■

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1. Adam DJ, Beard JD, Cleveland T, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet. 2005;366:1925-1934.

TAKE HOME POINTS

ROSS MILNER, MD

The debate over surgical bypass or endovascular therapy for CLI has clearly tilted toward endovascular approaches. The expanding availability of less invasive technology (drug-eluting balloons/drug-coated balloons, drug-coated stents, atherectomy) has assumed the forefront of the podiums and journals. There is a large investment by industry in these technologies, and a desire from our patients to have less invasive repairs with shorter hospital stays. But, surgical bypass still has a significant role in the management of lower extremity arterial disease. There is only a small literature on the failure modes of endovascular interventions and risk of major amputation. TASC C and D lesions, despite initial effective treatment, can lead to a higher risk of a failed bypass when needed, as well as a higher risk of amputation.

VENITA CHANDRA, MD

While traditionally underrepresented in the literature and underdiagnosed, women actually have a higher prevalence of PAD as compared to men. In addition, they more often present at an older age, with more advanced disease, and with more significant mobility impairment. Despite these findings, women undergo revascularization, in particular open revascularization, at lower rates than men. The reason for this is unclear. Female vessel sizing and anatomic distribution may be different than in men. In addition, women have higher complication rates and, in some instances, higher mortality rates than men after revascularization for PAD; however, patency and limb salvage rates appear to be similar. These findings suggest that current vascular approaches/tools and techniques may not be ideally suited for female anatomy/comorbidities. Further study on this topic, with a focus on the development of tools and techniques targeted for women with PAD, is warranted.

MICHAEL S. CONTE, MD

Results from the BEST-CLI trial will help vascular specialists select treatment for patients with CLI. Although the BEST-CLI trial is unlikely to provide a singular answer accepted by all, it will provide contemporary, high-quality evidence to guide clinical decisions. Until the results from the BEST-CLI trial are in, most patients with advanced limb ischemia should be offered revascularization based on stratification by patient risk, limb severity, and anatomic pattern of disease.

Session 3

What are the advantages of a prosthetic conduit?

Should Complications and Modes of Failure Affect Our Choice?

BY R. CLEMENT DARLING, III, MD

Patients with rest pain and shallow ulcers likely require a different treatment than patients presenting with profound tissue ischemia. Patients who present with more profound ischemia are best served by more direct blood flow to the affected area, yet surgeons are not often fully aware of the lack of blood flow in these patients.[1] While endovascular therapy may appear to increase blood flow, the volume of direct blood flow may be less than what can be achieved with open bypass therapy, and may also be insufficient to meet a patient's needs. This is reflected in the observation that approximately 60% of patients who receive a distal bypass had previous endovascular interventions. This percentage is continuing to increase because many patients who receive endovascular therapy experience recurrent complications that require surgical intervention. In addition, patients who experience failures from endovascular therapy cross over to open therapy much more aggressively than patients who experience failures from open therapy.[2]

No single treatment modality will cure all patients.[3] As surgeons, we seek a therapy that is effective with low morbidity, low mortality, and high limb salvage rate. On one hand, poor patient selection for surgery can lead to increased morbidity. On the other hand, endovascular therapy can lead to increased limb loss via inadequate increase in perfusion. In an ideal world, patients will have the option of multiple therapies, and surgeons will acknowledge that not all patients with chronic limb ischemia are equal. Patient factors such as diabetes, renal failure, cardiac disease, obesity, and age should affect the choice of therapy.[3] Using these factors, patients can be stratified such that approximately 34% are classified as "high risk" and 45% are classified as "low risk."[4]

SUMMARY

There should be a better, more concise algorithm for predicting complications from endovascular interventions. Such an algorithm will improve the ability of surgeons to inform patients about their alternatives, as well as the risks and benefits of the alternatives. Patients should also be followed closely for objective endpoints, and these outcomes should be constantly evaluated.[3,4] In order to achieve these goals, surgeons must perform an objective evaluation that includes an analysis of failures in order to determine changes that can lead to an improvement in patient outcomes. Surgeons must also have the training and comfort level to execute multiple therapeutic options. To achieve this, endovascular interventions may need to be implemented via a team approach that removes economic imperative as a factor in treatment selection. If surgeons do not lead the effort in making these changes, market forces may dictate better treatment selection, and third-party payers may mandate better treatment algorithms. ■

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1. Adam DJ, Beard JD, Cleveland T, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet. 2005;366:1925-1934.
2. Bradbury AW, Adam DJ, Bell J, et al. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: a survival prediction model to facilitate clinical decision making. J Vasc Surg. 2010;51(5 Suppl):52S-68S.
3. Rogers JH, Laird JR. Overview of new technologies for lower extremity revascularization. Circulation. 2007;116:2072-2085.
4. Schanzer A, Goodney PP, Li Y, et al. Validation of the PIII CLI risk score for the prediction of amputation-free survival in patients undergoing infrainguinal autogenous vein bypass for critical limb ischemia. J Vasc Surg. 2009;50:769-775; discussion 775.

CBAS® Heparin Surface

Performance in a technology context.

BY RUSSELL H. SAMSON, MD, FACS, RVT

Heparin has now been incorporated into multiple prosthetic vascular grafts, including Dacron (polyethylene terephthalate) grafts and the GORE® PROPATEN® Vascular Graft (Gore & Associates). A key aspect of heparin-bonding technology is the chemical means by which the heparin is bonded to the device lumen. The functionality of the bonded surface depends not just on the amount of heparin that is bound to the graft, but also the activity of the bonded heparin itself and whether it is able to interact freely with the blood. These three factors—the presence, availability, and activity of heparin dictate the efficacy of the bonded surface as a thromboresistant coating and differ based on which heparin-bonding method is employed.

One way of demonstrating the difference in the functionality of heparin applied to a surface using alternative bonding methods is an in vitro recirculating human blood model. In this model, flexible medical tubing is coated with heparin and exposed to freshly collected, nonanticoagulated whole blood. After 1 hour of blood contact, adsorbed plasma proteins are eluted from the tubing surface and separated by gel electrophoresis. The identities of the proteins are then determined by a Western blot. A tube that is coated with functional, available heparin should have more elutable antithrombin than a tube coated with heparin that is either nonfunctional (having had its active site removed) or not available. The Western blot technique revealed a great deal of antithrombin bound to a tubing surface that was coated using the CBAS® Heparin Surface technique, suggesting that the heparin on the surface is active and available (Figure 1). The presence of active, available heparin should result in very little platelet activation. Indeed, the Western blot revealed minimal platelet activation, as demonstrated by very little platelet factor 4 eluted from the surface. Thus, in an in vitro assay, heparin bonding (using the CBAS® Heparin Surface technique) resulted in a great deal of bound antithrombin and minimal platelet activation. In contrast, under the same assay conditions, a randomly bonded heparin surface activated platelets as much as a nonfunctional heparin surface and did not bind as much antithrombin as the CBAS® Heparin Surface. These results would suggest that the randomly bonded heparin technique does not perform as well as CBAS® Heparin Surface technology in vitro.

While both in vitro and in vivo studies have demonstrated that heparin bonding is effective in the short term,

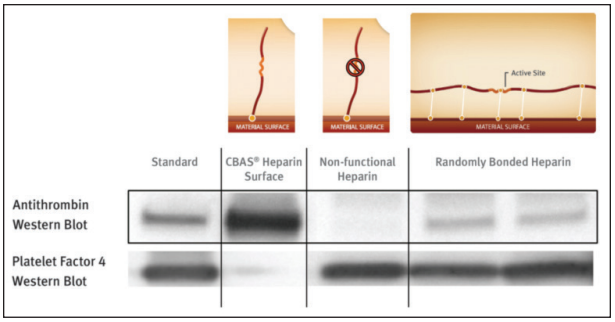

Figure 1. Three different covalently immobilized heparin surfaces were applied to separate loops of flexible medical tubing and exposed to freshly collected, nonanticoagulated whole blood. After 1 hour of blood contact, adsorbed plasma proteins were eluted from the tubing surface, separated by gel electrophoresis, and the identity of the proteins analyzed by Western blot. Note: Data presented are derived from an in vitro recirculating human blood model (modified Chandler loop).

researchers are beginning to investigate whether heparin bonding works in the long term.[1,2] An evaluation of an 8-year-old GORE® PROPATEN® Vascular Graft explant suggested that the heparin technology continued to be effective as measured by an assay for heparin activity (antithrombin binding). Results from one nonrandomized study comparing 3-year experience with standard expanded polytetrafluoroethylene (ePTFE) to the CBAS® Heparin Surface on the GORE® PROPATEN® Vascular Graft suggest that the latter technology affords better long-term outcomes for femoropopliteal grafts.

Currently there are no long-term data on alternative heparin-bonded grafts. In the absence of such data, surgeons cannot assume that all heparin-bonding technologies will be equally effective.

SUMMARY

CBAS® Heparin Surface bonding is likely providing long-term antithrombotic protection to the ePTFE surface. It is possible, however, that other methods of "attaching" heparin to ePTFE may not have such long-term protective effects. Vascular surgeons need to be aware of the construct of newer grafts in order to make valid determinations regarding the potential benefits of trying new, nonautogenous materials. ■

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1. Lösel-Sadée H, Alefelder C. Heparin-bonded expanded polytetrafluoroethylene graft for infragenicular bypass: five-year results. J Cardiovasc Surg. 2009;50:339-343.
2. Pulli R, Dorigo W, Piffaretti G, et al. A decade of arterial bypass results with the Gore Propaten Vascular Graft: long term clinical results from more than 1,000 cases in the multicenter Italian Registry. Ital J Vasc Endovasc Surg. 2014;21:101-107.

When to Use Graft Versus Multisegment Spliced Vein

BY PROF. THOMAS SCHMITZ-RIXEN

Despite advances in endovascular techniques, surgeons acknowledge that there is still a role for infrapopliteal bypasses for limb salvage. This is especially the case for patients with critical limb issues, when surgeons must get pulsatile blood flow down to the foot—regardless of which artery is available. Although the greater saphenous vein is the best replacement material, arm vein is considered the last autogenous option for infrainguinal bypass surgery, and several studies have evaluated the efficacy of long arm veins as an alternative conduit for treating critical limb ischemia (CLI).[1,2] While the results have varied, bypass surgeries performed using arm vein are generally safe and result in favorable patency and high rates of limb salvage.[3] Moreover, a direct comparison of arm vein versus prosthetic graft for infrapopliteal bypasses for CLI found that, even when spliced, arm vein conduits are superior to prosthetic grafts in terms of midterm-assisted primary patency, secondary patency, and leg salvage.[4] Despite the documented superiority of arm veins to prosthetic grafts, there appears to be a role for the GORE® PROPATEN® Vascular Graft (Gore & Associates) for the treatment of claudication and noninfected CLI, particularly when the patient does not have an available vein.

Our group performed a retrospective analysis of patients who received surgical bypass as a treatment for peripheral artery disease (PAD) between January 2011 and July 2014. The GORE® PROPATEN® Vascular Graft was used for two different indications: claudication (n = 8) and noninfected CLI (n = 67). Overall, 1-year patency was 69% and 2-year patency was 65%. Thus, most failures occurred in the first year. Patients who received alternative veins had an 81% patency rate in the first year and a 75% patency rate in the second year. Complication rates were low for both groups. There were no differences in wound-healing complications and cardiac complications between patients who received the GORE® PROPATEN® Vascular Graft and those who received spliced vein. However, there was one death in the GORE® PROPATEN® Vascular Graft group from an acute, infected graft. During the study period, there were 25 failed grafts in the below-knee popliteal artery and femorocrural groups, including three infected grafts that required explant. There were no problems with the other grafts. Graft failures resulted in 10 major amputations.

SUMMARY

The treatment approach used at our facility appears to have delivered results that fall within the expected range. The next step is to extend the analysis of PAD treatment policy to a nationwide registry. ■

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1. Brochado Neto F, Sandri GA, Kalaf MJ, et al. Arm vein as an alternative autogenous conduit for infragenicular bypass in the treatment of critical limb ischaemia: a 15 year experience. Eur J Vasc Endovasc Surg. 2014;47:609-614.
2. Nguyen BN, Neville RF, Abugideiri M, et al. The effect of graft configuration on 30-day failure of infrapopliteal bypasses. J Vasc Surg. 2014;59:1003–1008.
3. Robinson DR, Varcoe RL, Chee W, et al. Long-term follow-up of last autogenous option arm vein bypass. ANZ J Surg. 2013;83:769-773.
4. Arvela E, Soderstrom M, Alback A, et al. Arm vein conduit vs prosthetic graft in infrainguinal revascularization for critical leg ischemia. J Vasc Surg. 2010;52:616-623.

TAKE HOME POINTS

R. CLEMENT DARLING, III, MD

To optimize limb preservation, one must use a balanced approach of endovascular and open reconstruction. Groups must have expertise in both endovascular and open infrainguinal reconstructions. Each patient's procedure must be selected based on their indications, anatomy, and availability of conduit.

RUSSELL H. SAMSON, MD, FACS, RVT

In order for heparin bonding to be efficacious, it has to be present, available, and active. Because there are various methods of bonding heparin to PTFE, it is possible that not all methods will be equally beneficial. In vitro and in vivo studies have shown that the CBAS® technology incorporated into the GORE® PROPATEN® graft is effective in binding antithrombin and reducing platelet deposition. These effects are well demonstrated in short-term tests. Data suggest that heparin may still be active years after implantation. Vascular surgeons need to be aware of the construct of newer grafts that incorporate heparin in order to make valid determinations regarding the potential benefits of trying new, nonautogenous materials.

PROF. THOMAS SCHMITZ-RIXEN

At the University of Frankfurt in Germany, our goal is to facilitate personalized medicine for patients with PAD. Patients with claudication who do not have infection are treated with endovascular therapy whenever possible. Long occlusions and ultimately failed endovascular therapy are treated with bypass surgery. Patients with CLI who have an infection are treated first with endovascular therapy and then with surgical intervention. The treatment approach used at our facility appears to deliver results that are consistent with published data.

Session 4

Future improvements in graft performance

The Impact of Drug Therapy on Surgical Bypass

BY RUSSELL H. SAMSON, MD, FACS, RVT

Infrainguinal arterial bypass grafts are prone to early and late failure. This is irrespective of whether they are constructed from autologous vein or prosthetic, nonautogenous material such as expanded polytetrafluoroethylene (ePTFE). Early graft failures (< 30 days) are typically technical failures, so most adjuvant medications will not be effective during the first 30 days. Failures after 30 days are likely due to a confluence of factors that may differ depending upon the conduit used. These factors include intimal hyperplasia, spontaneous graft thrombosis, and the development of proximal or distal atherosclerosis. Further, atherosclerotic disease can also occur within vein grafts. These factors are all interrelated and reflect ongoing disease processes. Although graft thrombosis is often idiopathic, it can also be associated with hypercoagulable states or external compression.

Adjuvant agents prescribed to help prevent graft failure may target intimal hyperplasia, graft thrombosis, atherosclerosis, or all factors concurrently. For the most part, current adjuvant medications include antiplatelet agents, antithrombotics, and statins. Beta-blockers, cilostazol, and the transcription factor decoy edifoligide have also been explored as adjuvants. Currently, there is no ongoing trial to compare the efficacy of these drugs in preventing graft failure. The largest study to evaluate any of these adjuvant agents was the PREVENT III trial of edifoligide.[1] Edifoligide targets E2F, which is a transcription factor that plays a critical role in coordinating the expression of several genes that regulate cell-cycle progression, thus potentially preventing the development of hyperplastic intimal thickening. However, ex vivo treatment of lower extremity vein grafts with edifoligide was unable to protect graft failure.[1]

ANTIPLATELET AGENTS

Antiplatelet agents are typically prescribed to help prevent platelet aggregation that leads to hyperplastic intimal thickening. They may also prevent platelet agglutination and subsequent spontaneous thrombosis. Activated platelets aggregate on injured endothelial cells in denuded areas and fibrin is deposited. The deposited fibrin acts with platelets to form an adhesive surface that binds circulating leukocytes. The leukocytes then become the central modulators in the development of hyperplastic intimal thickening.

There are multiple antiplatelet agents including ASPIRIN® (acetylsalicylic acid) (ASA), clopidogrel bisulfate, and ticagrelor. The field becomes even more complex with the addition of a new drug (eg, vorapaxar). Vorapaxar is unique in that it is the first antiplatelet agent approved by the US Food and Drug Administration (FDA) specifically for the treatment of peripheral artery disease. However, there are no current data to support its use in preventing graft failure.

In 1994, the Antiplatelet Trialists' Collaboration studied approximately 3,000 patients who underwent peripheral artery procedures.[2] The procedures included vein grafts and nonautologous grafts. The study found that antiplatelet therapy (primarily ASA) resulted in 38% fewer graft occlusions when compared with placebo. This study was seminal in the consideration of adjuvant therapy for improving vascular graft failure rates.

In 1999, Tangelder et al[3] reviewed trials comparing ASA versus anticoagulation versus placebo. The investigators found a 22% relative reduction (RR) with ASA, a 44% RR with warfarin, and a 62% RR with combined ASA and warfarin. However, patients who received ASA combined with warfarin had a higher incidence of bleeding.

A subgroup analysis of the CASPAR trial suggested a benefit for dual-antiplatelet agents (eg, ASA, clopidogrel) in prosthetic grafts (not vein grafts) without an increase in bleeding risk.[4] However, as a post hoc analysis this result may be suspect. Furthermore, the CASCADE trial failed to show any benefit for clopidogrel over ASA in the prevention of coronary artery graft intimal hyperplasia.[5,6]

ANTICOAGULANTS

Although there are many new novel anticoagulants, the only anticoagulants currently studied to prevent graft thrombosis have been heparin, low-molecular-weight heparin, and warfarin.

The Cochrane Review examined the effectiveness of low-molecular-weight heparin compared to unfractionated heparin and found no difference in graft patency between the two therapies.[7]

In 1998, Sarac et al examined the effects of warfarin and other vitamin K antagonists in a randomized trial.[8] The investigators reported a patency of 74% at 3 years in the high-risk group randomized to warfarin and ASA. Patency was significantly higher in the patients who received warfarin and ASA when compared to the patients who received only ASA. However, bleeding was more common in the group receiving warfarin.

The Dutch Bypass Oral Anticoagulants or ASPIRIN study compared oral anticoagulants to ASA in a large randomized trial that included vein grafts and prosthetic grafts.[9] The investigators found that ASA at a dose of 80 mg significantly reduced occlusion in prosthetic grafts when compared with warfarin. Patients who received ASA also experienced fewer bleeding episodes. This study from 2000 likely has had the largest influence on subsequent guidelines.

The Veteran Affairs Cooperative trial in 2002 included 665 patients undergoing femoropopliteal bypass.[10] Patients were randomized to 325 mg ASA and warfarin, or ASA alone. The investigators found no significant difference in patency rates between the treatment groups in the 8-mm bypass subgroup; however, they did find a difference in the 6-mm bypass subgroups (71.4% in the warfarin-plus-ASA group vs 57.9% in the ASA-only group; $P = .02$). However, again, warfarin nearly doubled the risk of major bleeding episodes when compared to patients who received ASA alone.

Guidelines published in 2004 recommend ASA for all patients undergoing prosthetic infrainguinal bypass.[11] Warfarin was not recommended due to an increased risk of bleeding. The guidelines suggest that patients who are at a high risk for occlusion should receive combination therapy with warfarin and ASA. However, these guidelines changed in 2008 with only ASA being recommended for all grafts (unless a patient has the rare ASA allergy).

Despite these published findings, the Vascular Study Group of New England reported that patients receiving prosthetic conduit were more likely to be treated with warfarin than those receiving a saphenous vein conduit (57% vs 24%; $P < .001$).[12]

STATINS

Although statins are primarily prescribed to prevent atherosclerotic disease, they are also effective in reducing inflammation.

In vitro studies have demonstrated that statins increase endothelial progenitor cells and promote smooth muscle apoptosis.[13] This suggests that statins may be helpful in bypass surgery through a mechanism of action that is distinct from lowering low-density lipoprotein (LDL) cholesterol.[14] A 2004 study found that the risk of graft failure was 3.2-fold higher in a control group when compared to patients who received statins.[15] The investigators reported that the levels of cholesterol were not statistically different between the two groups, suggesting that the mechanism behind the protective effect was distinct from the LDL-lowering effect of the statins. Statin therapy in the CASCADE trial[16] achieved an LDL level < 100 mg, which was associated with improved graft patency. On the other hand, PREVENT III[1] found that statins had no effect on patency at 1 year and no effect on perioperative mortality. However, patients who received statins did have decreased mortality at 1 year. Similarly, the Vascular Study Group of New England found that statin therapy was not associated with 1-year rates of major amputation or graft occlusion.[17]

SUMMARY

Current treatment guidelines are controversial. The American College of Chest Physicians recommends only ASA for prosthetic and vein grafts.[18] In 2011, the Cochrane Review suggested that all patients receiving a prosthetic graft benefit would benefit from platelet inhibitors, whereas vein grafts would more likely benefit from a vitamin K antagonist.[7] The consensus is that statins should be prescribed because even if they do not improve patency, they do appear to prolong life. Patients who receive high-risk prosthetic grafts may benefit from a vitamin K antagonist or dual-antiplatelet agents. ■

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1. Conte MS, Bandyk DF, Clowes AW, et al. Results of PREVENT III: a multicenter, randomized trial of edifoligide for the prevention of vein graft failure in lower extremity bypass surgery. J Vasc Surg. 2006;43:742-751; discussion 751.
2. Collaborative overview of randomised trials of antiplatelet therapy--II: maintenance of vascular graft or arterial patency by antiplatelet therapy. Antiplatelet Trialists' Collaboration. Br Med J. 1994;308:159-168.
3. Tangelder MJ, Lawson JA, Algra A, et al. Systematic review of randomized controlled trials of ASPIRIN and oral anticoagulants in the prevention of graft occlusion and ischemic events after infrainguinal bypass surgery. J Vasc Surg. 1999;30:701-709.
4. Belch JJ, Dormandy J, Committee CW, et al. Results of the randomized, placebo-controlled clopidogrel and acetylsalicylic acid in bypass surgery for peripheral arterial disease (CASPAR) trial. J Vasc Surg. 2010;52:825-833, e821-822.
5. Kulik A, Le May MR, Voisine P, et al. ASPIRIN plus clopidogrel versus ASPIRIN alone after coronary artery bypass grafting: the clopidogrel after surgery for coronary artery disease (CASCADE) Trial. Circulation. 2010;122:2680-2687.
6. Une D, Kulik A, Voisine P, et al. Correlates of saphenous vein graft hyperplasia and occlusion 1 year after coronary artery bypass grafting: analysis from the CASCADE randomized trial. Circulation. 2013;128(Suppl 1):S213-218.

7. Geraghty AJ, Welch K. Antithrombotic agents for preventing thrombosis after infrainguinal arterial bypass surgery. Cochrane Database Syst Rev. 2011(6):CD000536.
8. Sarac TP, Huber TS, Back MR, et al. Warfarin improves the outcome of infrainguinal vein bypass grafting at high risk for failure. J Vasc Surg. 1998;28:446-457.
9. Tangelder MJ, Algra A, Lawson JA, et al. Risk factors for occlusion of infrainguinal bypass grafts. Eur J Vasc Endovasc Surg. 2000;20:118-124.
10. Johnson WC, Williford WO. Benefits, morbidity, and mortality associated with long-term administration of oral anticoagulant therapy to patients with peripheral arterial bypass procedures: a prospective randomized study. J Vasc Surg. 2002;35:413-421.
11. Clagett GP, Sobel M, Jackson MR, et al. Antithrombotic therapy in peripheral arterial occlusive disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004;126(3 Suppl):609S-626S.
12. Suckow BD, Kraiss LW, Stone DH, et al. Comparison of graft patency, limb salvage, and antithrombotic therapy between prosthetic and autogenous below-knee bypass for critical limb ischemia. Ann Vasc Surg. 2013;27:1134-1145.
13. Erl W, Hristov M, Neureuter M, et al. HMG-CoA reductase inhibitors induce apoptosis in neointima-derived vascular smooth muscle cells. Atherosclerosis. 2003;169:251-258.
14. LaMuraglia GM, Stoner MC, Brewster DC, et al. Determinants of carotid endarterectomy anatomic durability: effects of serum lipids and lipid-lowering drugs. J Vasc Surg. 2005;41:762-768.
15. Kulik A, Voisine P, Mathieu P, et al. Statin therapy and saphenous vein graft disease after coronary bypass surgery: analysis from the CASCADE randomized trial. Ann Thorac Surg. 2011;92:1284-1290; discussion 1290-1281.
16. Abbruzzese TA, Havens J, Belkin M, et al. Statin therapy is associated with improved patency of autogenous infrainguinal bypass grafts. J Vasc Surg. 2004;39:1178-1185.
17. Suckow BD, Kraiss LW, Schanzer A, et al. Statin therapy after infrainguinal bypass surgery for critical limb ischemia is associated with improved 5-year survival. J Vasc Surg. 2015;61:126-133 e121.
18. Sobel M, Verhaeghe R, American College of Chest P, et al. Antithrombotic therapy for peripheral artery occlusive disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008;133(6 Suppl):815S-843S.

Sequential Bypass

An option for the tibials.

BY JEAN BISMUTH, MD

The first randomized trial to compare the GORE® PROPATEN® Vascular Graft (Gore & Associates) to expanded polytetrafluoroethylene (ePTFE) found that the GORE® PROPATEN® Vascular Graft significantly decreased the relative risk of losing primary and secondary patency by 36% and 40%, respectively.[1] The study joins a number of trials that have demonstrated the efficacy of prosthetic grafts.[2-5] A comparison of tibial bypass with saphenous vein graft to tibial bypass with heparin-bonded PTFE performed with autologous vein patch found comparable 1-year primary patency between the two groups: 86% for saphenous vein graft and 75.4% for heparin-bonded PTFE.[2] A prospective randomized trial evaluated spliced vein versus PTFE plus patch; the investigators concluded that both spliced vein bypass grafting and PTFE bypass grafting with a distal vein cuff produced acceptable limb salvage rates.[3] The Vascular Study Group of New England evaluated their experience with 1,227 patients from 2003 to 2009[5] who received a prosthetic graft to a below-the-knee target (70%) or more distal target (30%), and concluded that patients who receive below-the-knee prosthetic bypass grafting can have similar 1-year outcomes as patients who receive greater saphenous vein conduit.[5]

Sequential bypass is indicated for patients with multiple failed bypasses, critical ischemia, and adequate inflow, who are fit enough to undergo a lengthy procedure. Two different techniques are frequently used for sequential bypass configurations: composite sequencing and modified configuration of the prosthetic-vein anastomosis for composite sequential bypass.[6] Patients may receive sequential bypasses with PTFE and autologous vein if they do not have the required length of autologous vein. A series of six such procedures were performed at Houston Methodist Hospital over 18 months; of the six cases, four remained patent for 1 to 3 years with no intervention. The small series is consistent with results from published studies of sequential bypass. An analysis of patency rates of sequential bypass revealed 1-year patency rates of 91% with composite sequential, 73% with distal arteriovenous fistulae, and 52% with a disadvantaged vein.[7] A separate trial found a small benefit from sequential bypass for patients who have a single vein.[8]

Although trials typically measure patency rates and limb salvage rates, surgical outcomes can also be evaluated via visualization of muscle perfusion of the leg and foot using magnetic resonance imaging (MRI) with gadolinium contrast. We used the technique to image a series of patients who received open surgery and endovascular therapy. MRI was performed both before the intervention and at 6 months after revascularization. MRI revealed that patients who were healthy had well-defined muscle. As patients began to show symptoms, such as a decrease in ankle-brachial index, the muscles changed and collagen fibers replaced muscle. Collagen fibers continued to become more pronounced as ischemia increased. MRI also revealed a correlation between worsening scar tissue and worsening outcomes. A closer analysis by muscle group, as well as symptomatic and asymptomatic leg, should allow for further visualization of the changes effected by revascularization.

SUMMARY

Patients who do not have adequate saphenous vein can successfully receive a GORE® PROPATEN® Vascular Graft with a distal vein patch. An analysis of muscle perfusions suggests the perfusion effect is greater when several vessels are targeted for revascularization compared to a single vessel. We have attempted to harness this effect in a small series of sequential bypass, but this technique is best reserved as a potential last resort effort in patients fit enough to undergo a lengthy procedure. ■

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that he has received compensation from Gore for participating in the Summit and has received honoraria from Gore for writing this article. Dr. Bismuth may be reached at jbismuth@tmhs.org.

1. Lindholt JS, Gottschalksen B, Johannesen N, et al. The Scandinavian Propaten(R) trial--1-year patency of PTFE vascular prostheses with heparin-bonded luminal surfaces compared to ordinary pure PTFE vascular prostheses: a randomised clinical controlled multi-centre trial. Eur J Vasc Endovasc Surg. 2011;41:668-673.
2. Neville RF, Capone A, Amdur R, et al. A comparison of tibial artery bypass performed with heparin-bonded expanded polytetrafluoroethylene and great saphenous vein to treat critical limb ischemia. J Vasc Surg. 2012;56:1008-1014.
3. Kreienberg PB, Darling RC 3rd, Chang BB, et al. Early results of a prospective randomized trial of spliced vein versus polytetrafluoroethylene graft with a distal vein cuff for limb-threatening ischemia. J Vasc Surg. 2002;35:299-306.
4. Calligaro KD, Syrek JR, Dougherty MJ, et al. Use of arm and lesser saphenous vein compared with prosthetic grafts for infrapopliteal arterial bypass: are they worth the effort? J Vasc Surg. 1997;26:919-924; discussion 925-917.
5. Suckow BD, Kraiss LW, Stone DH, et al. Comparison of graft patency, limb salvage, and antithrombotic therapy between prosthetic and autogenous below-knee bypass for critical limb ischemia. Ann Vasc Surg. 2013;27:1134-1145.
6. Gargiulo NJ 3rd, Veith FJ, O'Connor DJ, et al. Experience with a modified composite sequential bypass technique for limb-threatening ischemia. Ann Vasc Surg. 2010;24:1000-1004.
7. Roddy SP, Darling RC 3rd, Ozsvath KJ, et al. Composite sequential arterial reconstruction for limb salvage. J Vasc Surg. 2002;36:325-329.
8. Mahmood A, Garnham A, Sintler M, et al. Composite sequential grafts for femorocrural bypass reconstruction: experience with a modified technique. J Vasc Surg. 2002;36:772-778.

TAKE HOME POINTS

RUSSELL H. SAMSON, MD, FACS, RVT

Original studies on drug therapy were performed in the era of ASA, at a time when clopidogrel was only beginning to be investigated. Data from more recent trials suggest that patients who receive ePTFE grafts should receive an antiplatelet agent. However, there are no current data to support clopidogrel over ASA, and dual-antiplatelet agents are not recommended for uncomplicated ePTFE bypasses. Patients who receive an ePTFE graft and appear to be at high risk for thrombosis may require dual-antiplatelet agents or warfarin. Patients who receive vein grafts may benefit from warfarin. Although statins have not been shown to prevent graft failure, they are important adjuvants to prevent cardiovascular mortality.

JEAN BISMUTH, MD

Evidence clearly supports the GORE® PROPATEN® Vascular Graft as the preferred conduit for below-the-knee bypasses in the absence of a suitable autologous vein graft. To further qualify this, it would seem that support for a suitable vein conduit is really only significantly better in single segment veins. Spliced veins have been shown to have only marginally better outcomes, with the consequence of increased operative times, blood loss, and mortality. Like many groups, when using PTFE below the knee, we also advocate for adjuncts such as a patch angioplasty or, in patients with multiple failed bypasses, a sequential bypass procedure. We have limited experience with sequential bypasses as a last resort for limb salvage and, in our experience, the procedures are generally time consuming and result in a greater burden to patients. Patients also have to be selected carefully, but the procedure is a valuable tool in the spectrum of limb salvage surgery and has acceptable outcomes.

Session 5

How will financial considerations affect future decisions?

Open Surgery Versus Endovascular Revascularization

Will cost play a role in the decision?

BY MICHAEL STONER, MD

Vascular care in the United States is largely supply-driven care that is not supported by robust science. This is because most randomized controlled trials fail to have external validity and are therefore not useful for science-based decision making. Thus, in the absence of quality science, advances in vascular care are driven by technological improvements and the lateral diffusion of technology. Patients, however, expect their surgeon to guide them to the safest and most effective procedure possible. Most patients do not care about the cost of the procedure because they are typically not the ones paying for it, so therefore their decision making is not driven by cost.

At first glance, an endovascular-first strategy appears to be a cost-saving approach to the treatment of peripheral artery disease (PAD). Moreover, many surgeons who use an endovascular-first strategy do so based upon the belief that a failed endovascular approach can be easily followed with surgical bypass. In actuality, a subset of patients who experience early failure with endovascular therapy develop more complex lesions (Figure 1). The patients then have a higher TASC grade and more distal targets. There are conflicting data about the outcomes for such patients, a group that is composed of more complex cases after failed endovascular therapy. Studies have attempted to determine if the more complicated cases reflect disease progression or are directly caused by endovascular therapy. A comparison of the subset of patients who received primary surgical revascularization versus those who received secondary surgical revascularization revealed that with regard to primary assisted patency, patients who underwent primary surgical revascularization had 75% primary assisted patency, whereas patients who underwent secondary surgery had 53% primary assisted patency. Limb salvage and tissue loss were also inferior in patients with critical limb ischemia who had a failed endovascular procedure and then went on to receive a surgical bypass.

The economic burden of reintervention may also provide a context for the creation of an endovascular treatment paradigm that reimburses based on patient value. An ideal organization for delivering such cost-efficient treatment would emphasize tighter collaboration between hospitals and providers and would create constant performance reporting and payment realignment for value. This has been proposed for the Centers for Medicare & Medicaid Services percutaneous coronary intervention pilot sites.

SUMMARY

Patients' lack of financial stake in the therapy is a weakness in current health care reform. Patients who have a financial stake in their therapy will place an increased value on durability, patency, and quality of life. Until the system has changed to incorporate patients as payors, surgeons must make pragmatic choices to use medication and technology, and to select patients for the appropriate therapy. ■

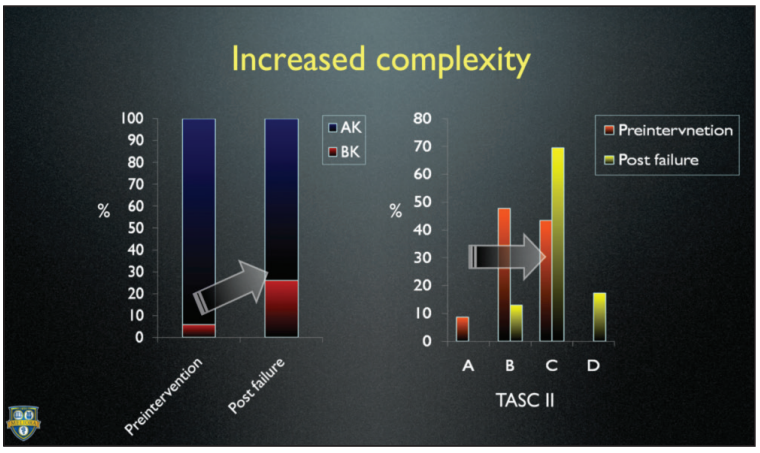

Figure 1. Increased incidence of below-knee target and more severe TASC grade lesions in patients undergoing bypass after failed endovascular therapy.

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Prevalence of Amputation

Can we make an impact?

BY ALEJANDRO FABIANI, MD

Peripheral arterial disease (PAD) affects more than 200 million people (2.85% of the population) around the world.[1] It is the pandemic of the 21st century, affecting more people than cholera in the 19th century and AIDS in the 20th century. Unfortunately in Mexico, PAD is primarily treated by amputation.

From 1970 to 1975, the average male life expectancy in Mexico was 62.57 years. From 1990 to 1995, the average male life expectancy had increased to 71.81 years; and from 2010 to 2015, it increased further to 76.26 years.[2] Despite the increases in life expectancy, Mexico has one of the highest per capita consumptions of cigarettes, as well as a high rate of hypertension and diabetes (Figure 1). Mexico leads the world in childhood obesity and is second in the world for adult obesity. Consequently, there are almost three million people in Mexico who have had amputations (estimation based on newspapers publications and expert opinion). The cost of a prosthetic is approximately $10,000, which only 10% of patients in Mexico can afford. Of these patients, only 30% will be able to use a prosthetic. Thus, if 100 patients are sent for primary amputation, only three of them (at most) will walk again. Statistics like these provide a great deal of room for improvement; therefore, most people in the vascular industry consider Mexico to be a "sleeping giant" for the potential of endovascular surgery to change the lives of its citizens.

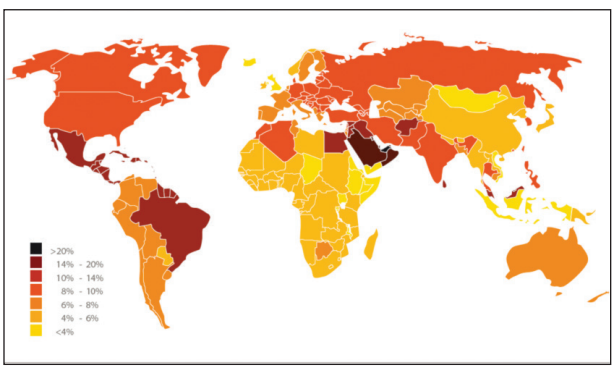

Figure 1. Mexico leads the United States in expected prevalence of diabetes for 2025. Reprinted with permission from International Diabetes Federation. IDF Diabetes Atlas, 6th edn. Brussels, Belgium: International Diabetes Federation, 2013. http://www.idf.org/diabetesatlas.

In the early 1990s, the requirements for saving an ischemic limb were threefold: a viable limb, a runoff vessel, and a conduit. Angiography was used to identify the presence of a runoff vessel and was thus an important first step in patient treatment. Today, the only real requirement for saving an ischemic limb is the presence of a viable limb. This change needs to be communicated to primary care physicians, vascular specialists, and patients. Only then will patients have improved access to therapeutic options other than amputation.

The School of Medicine at the Monterrey Institute of Technology (Instituto Tecnológico de Monterrey) is making an effort to change the amputation-first attitude that persists in Mexico. The main message for all stakeholders is that a diabetic foot does not necessarily have to be treated with amputation. Education grants for physicians have included courses for different specialties, education about abdominal aortic aneurysms and thoracic aortic aneurysms, carotid artery disease, PAD, and pelvic venous congestion. This education should help physicians diagnose PAD and encourage them to consider therapeutic options beyond amputation.

SUMMARY

While surgical bypass and new devices can save limbs and improve quality of life for patients, the most important factor for decreasing the amputation rate in Mexico is education. As physicians and patients become more educated about alternatives to amputation, an increasing number of patients will receive successful bypasses. Each of these patients will then inspire other patients and physicians to consider treatment alternatives to amputation. ■

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1. Fowkes FG, Rudan D, Rudan I, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. Lancet. 2013;382:1329-1340.
2. Global health observatory. http://www.who.int/gho/mortality_burden_disease/life_tables/situation_trends/en. Accessed October 20, 2014.

TAKE HOME POINTS

MICHAEL STONER, MD

US health care expenditure has continued to grow over the past three decades, despite the promise that improved resource allocation, biomedical research, and technology would improve both efficiency and outcomes. Current estimates from the US Congressional Budget Office estimate that 4% of the 2007 Gross Domestic Product was allocated to Medicare and Medicaid. This amount is estimated to increase to 20% of the federal budget by 2050 if current projections remain true. Thus, health care expenditure is quickly becoming the most significant factor in the already strained US federal budget. Payment for the treatment of PAD represents a significant amount of health care resource allocation. In 2007, the United States spent $151 billion in direct and indirect costs for the treatment of 12 million beneficiaries with PAD.

It is clear that these current trends are untenable within the constraints of the economic system. Vascular care is likely to become increasingly important as the overall population ages. It will become paramount to evaluate the appropriate treatment of each patient with vascular disease within the overall context of the national health care system.

Comparative effectiveness research must provide the scientific basis for this process. Simply put, comparative effectiveness is the study of two or more treatment options to address a given medical condition. Within the domain of vascular disease, there is an ever-increasing array of options and modalities to address our patients' disease processes. Many of these new modalities compete with either nonoperative management or traditional operative techniques, and have not been fully evaluated with respect to efficacy and health care economics. The implementation of comparative effectiveness research may be ideally suited for mechanisms such as Accountable Care Organizations. Within this construct, patients and providers use evidence-based medicine to decide on clinically and financially treatment courses, and both benefit from maximizing these factors. Within the limb salvage disease space, this is accomplished by choosing the safest, most efficacious, and durable procedure. These factors have begun to translate into the federal regulatory process, as the Food and Drug Administration is now considering patient-centric outcomes for new device approvals.

ALEJANDRO FABIANI, MD

PAD is a critical 21st century pandemic affecting 3% of the world population. In low or middle-income countries, the incidence of PAD has increased 30% between 2000 and 2010. The amputation rate seems to be 10 times higher in poor diabetic patients than wealthy diabetic patients.

In Mexico, primary amputation is the most frequent approach to patients with diabetic foot. As a consequence, there are more than 3 million amputees. Just 10% of these amputees can afford the cost of a prosthesis and, of those patients, only 30% are able to walk. Therefore, just 3% of the patients with major amputation will walk again.

In the early 1990s, my team in Argentina attempted revascularization in all patients with critical limb ischemia. We only needed a viable limb, an autologous conduit, and a runoff vessel. The 3-year limb salvage rate was up to 70%, whether or not the patient was diabetic.

Nowadays, the only requirement is to have a viable limb. In most cases, a runoff vessel can be endovascularly built and the conduit can be done in the same way, or a heparin-bonded graft can be used with long-term results comparable to those obtained with autologous veins.

A limitation in Mexico seems to be patient referral. Most physicians believe that there is no better option for diabetic patients with PAD than major amputation. The goal is to improve education on this field through efforts directed at general physicians, patients, and the community.

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