

Ten Years of Experience with the Heparin-Bonded ePTFE Graft — The Newest Advancement in Vascular Surgery

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University of California, San Diego Health Sciences
San Diego, California

Introduction: Ten Years of Experience with the Heparin-Bonded ePTFE Graft

Richard Neville, MD

Heparin-bonded expanded polytetrafluoroethylene (Gore Propaten Vascular Graft, W.L. Gore & Associates, Flagstaff, Arizona) has now been clinically used for nearly 10 years, with the first human implant in 2000. More than 80,000 of these prostheses have been implanted and a 2010 Cochrane review noted that they are “widely utilized in contemporary practice.”¹

During this time, clinical trials have generated data regarding graft performance in lower-extremity bypasses for patients with significant peripheral arterial disease (see Table 1 on p. 4).²⁻⁷ Over this period, use of the Propaten graft has generated an experience that includes approximately 1,100 bypasses. In 66% of these cases, the distal anastomosis was below the knee (BK) with a composite 1-year primary patency of 77%.

The largest series is the retrospective Italian registry of 425 patients, which reported a 3-year primary patency rate of 61% for below-knee bypass.³ Prospective data have been collected with 3-year primary patency rates of 75% for the below-knee popliteal and 60% for tibial bypasses.³ The series with the longest follow-up reported 4- and 5-year primary patency rates of 50% to 71%.⁶ These results are in comparison to the historical results reported with standard synthetic grafts with a meta-analysis of 43 studies that demonstrated inferior below-knee patency of 31%.⁸

This supplement includes several articles that review in more detail the experience of several clinicians with the Propaten heparin-bonded graft. It begins with an explanation of the science and technology behind the graft. This is followed by additional observations as reported from the Italian registry by Drs. Pratesi and Pulli, as well as Dr. Walluscheck expanding on his and other previous reports that included animal and clinical studies.⁹ Several authors share their individual experiences with patients for whom the Propaten graft serves as an alternative to autologous conduit. Finally, a hemodynamic analysis, which examines several different anastomotic geometries used with PTFE conduits, has been included.¹⁰

The clinical experience to date with the heparin-bonded Propaten graft supports the concept that this prosthetic graft may have an important role in the management of lower extremity occlusive disease. This role would be best defined by the results of randomized, controlled trials, and we await the findings of future investigations and additional years of experience which will hopefully provide clinicians with information essential for choosing the optimal treatment for each patient.

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From: From Georgetown University Hospital, Washington, D.C.

Address correspondence to Richard F. Neville, MD, Division of Vascular Surgery, Georgetown University Hospital, 3800 Reservoir Road, 4 PHC, Washington, DC 20007; e-mail: neviller@gunet.georgetown.edu.

Table 1. Clinical Studies of the Gore Propaten Vascular Graft for Lower-Extremity Bypasses

Study Characteristics	Study Reference					
	Walluscheck, et al. ²	Peeters, et al. ³	Hugl, et al. ⁴	Daenens, et al. ⁵	Lösel-Sadée, et al. ⁶	Pulli, et al. ⁷
No of patients/bypasses with Propaten	40/43	138/153	142/139	240	75	425
Patients' mean or median age (years)	71	73	69.8	70.4	73	73.5
Patients' sex (M/F)	24/16	97/41	96/46	161/79	39/36	338/87
No. of AK bypasses	12	75	87	86	0	101
No. of BK bypasses (FP/FC)	31 (17/14)	78 (41/37)	52 (37/15)	154 (57/97)	75 (30/45)	324 (238/86)
Mean follow-up duration (months)	17	36	12	25 (AK)/25 (BK-FP)/19 (BK-FC)	23	26
Overall 1-year primary patency (%)	NR	80	80	NR	NR	75
Overall 2-year primary patency (%)	NR	74	NI	NR	NR	66
Overall 3-year primary patency (%)	NI	72	NI	NR	NR	61
AK bypasses: 1-year primary patency rate (%)	91	81	83	92	NI	80
BK bypasses: 1-year primary patency rate (%)	92	86 (FP)/71 (FC)	74 (FP) / 79 (FC)	92 (FP)/79 (FC)	77 (FP)/64 (FC)	75 (FP)/66 (FC)
AK bypasses: 2-year primary patency rate (%)	68	78	NI	83	NI	72
BK bypasses: 2-year primary patency rate (%)	81	79 (FP)/60 (FC)	NI	83 (FP)/69 (FC)	71(FP)/57 (FC)	67 (FP)/57 (FC)
AK bypasses: 3-year primary patency rate (%)	NI	75	NI	NI	NI	72
BK bypasses: 3-year primary patency rate (%)	NI	75 (FP)/60 (FC)	NI	NI	71 (FP)/50 (FC)	61 (FP)/52 (FC)

FP = femoro-popliteal; FC = femoro-crural; NI = not investigated; NR = not reported

The Gore Propaten Vascular Graft: The Combination that Lasts

Jennifer B. Recknor, PhD

Introduction

Autologous saphenous vein is widely regarded as the bypass conduit of choice for small-diameter arteries, particularly for distal lower extremity revascularization. However, approximately one-third of patients presenting for peripheral artery reconstruction have absent or inadequate saphenous veins due to prior use or harvest, small size or poor quality.¹ Therefore, vascular surgeons look to prosthetic bypass grafting alternatives typically involving expanded polytetrafluorethylene (ePTFE) grafts.

Unfortunately, due to progression of disease, technical failure, anastomotic intimal hyperplasia and graft thrombosis,² ePTFE grafts have shown less-than-desirable results in performance compared to autologous saphenous vein. In a review³ of vein and PTFE above-knee (AK) femoropopliteal bypasses, the 5-year primary patency rates were reported to be 74% and 39%, respectively. In the below-knee (BK) position, prosthetic bypasses have shown 1-year cumulative patency rates of 65%, declining to 29% by 2 years.⁴

By comparison, ePTFE performance is suboptimal, and only borderline acceptable in small-diameter applications such as BK tibial or peroneal bypasses. Thrombogenicity and intimal hyperplasia appear to be the principal mechanisms of failure when standard ePTFE grafts are used as arterial substitutes in low-flow, high-resistance vascular beds.⁵ Addressing these risks of graft failure by improving the thromboresistance of the luminal surface of the graft has much potential for enhancing the clinical performance of small-diameter prosthetic grafts.⁶

Potential Solutions

One potential strategy to reduce graft thrombogenicity and reduce intimal hyperplasia is to bind heparin to the endoluminal surface of the graft. Heparin, a heterogeneous mixture of sulfated polysaccharides, is a potent anticoagulant that inhibits thrombin and activated factors IX, X, XI and

XII. Heparin has a long history of clinical use to prevent and treat thrombosis and displays potent antiproliferative activity on vascular smooth muscle cells (SMCs) that is independent of its anticoagulant action.^{7,8} Inhibition of SMCs by heparin is mediated, at least in part, through interactions with cell receptors, growth factors, adhesion molecules and proteinase inhibitors.⁹

Heparin-coating technologies have been employed to reduce thrombogenicity in a number of medical devices. The benefits of bonding, or coating, heparin have been demonstrated in hemodialysis filters, vascular stents and cardiopulmonary bypass circuitry.¹⁰⁻¹²

Although various modalities exist to incorporate heparin onto a medical device surface, the resulting performance characteristics can be greatly affected by the precise heparin technology employed. Some of the ideal characteristics of a heparinized vascular graft would include uniformity of heparinization, retention of heparin on the graft flow surface and functional maintenance of its bioactivity.

One of the most clinically successful and innovative heparin-bonding methodologies has been the Carmeda BioActive Surface (CBAS; W.L. Gore & Associates, Inc., Flagstaff, Arizona).^{13,14} It is based on the covalent end-point attachment of heparin to a biomaterial surface, enabling maintenance of functional heparin bioactivity. This end-point attachment mechanism, or CBAS heparin immobilization, enables the heparin bioactive site to freely bind antithrombin III and maintain catalytic bioactivity (Figure 1).¹⁴ Such CBAS immobilization has been shown to result in a reduction of platelet deposition, a decrease in inflammatory responses,¹⁵⁻¹⁷ and a reduction of thrombogenicity.¹⁸⁻²²

Technology and Benefits

The Gore Propaten Vascular Graft (CBAS-ePTFE; W.L. Gore & Associates, Inc.) has shown convincing experimental evidence

From: W.L. Gore and Associates. **Address for correspondence:** Jennifer B. Recknor, PhD, W.L. Gore and Associates, P.O. Box 2400, Flagstaff, AZ. **E-mail:** jrecknor@wlgore.com.

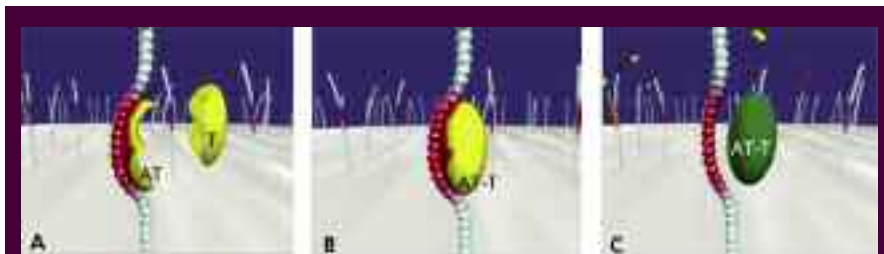


Figure 1. End-point covalent bonding of the Gore Propaten Vascular Graft keeps heparin anchored to the graft luminal surface over time. The heparin bioactive site remains free to interact with the blood. (A) Heparin molecules are bonded to the graft's luminal surface. The bioactive site of the heparin molecule binds to antithrombin (AT). (B) Antithrombin binds to thrombin (T); a neutral AT-T complex is formed. Thrombin loses its ability to catalyze the conversion of fibrinogen to fibrin. (C) The neutral AT-T complex detaches from the heparin molecule. The heparin bioactive site becomes available to again bind antithrombin.

In order to resist thrombus build-up, it is essential that heparin be present on the surface and retain its bioactive function. Stable, functional bioactivity resulting in improved graft thromboresistance has also been demonstrated by CBAS-ePTFE. Human explants at approximately 8 months and 3 years postimplantation have demonstrated heparin activity levels that were within the original manufacturing specifications for release of this product. These examples of heparin activity go beyond previous results shown in an earlier canine study⁶ and speak to the relative longevity of the bioactivity of heparin on the device surface.

that heparin bonding of ePTFE grafts using the CBAS technology results in a significant reduction in early platelet deposition and inhibits intimal hyperplasia at the anastomoses compared to untreated ePTFE.²³⁻²⁷ These effects have been demonstrated in a bilateral canine model²³ and a baboon aortoiliac bypass grafting model,²⁴ and were recently observed in a common carotid sheep model out to 6 months (Figure 2).²⁵

In addition to the reduction of platelet aggregation, improved graft patency and inhibition of intimal hyperplasia observed in the animal research, an absence of measurable systemic effects on hemostasis or development of HIT-inducing antibodies has also been demonstrated with CBAS-ePTFE in human *ex vivo* and *in vivo* studies.^{26,27} This evidence supports that the utilization of a proprietary end-point covalent bonding mechanism to achieve local thromboresistance at the graft surface avoids any systemic effects of heparin.

Conclusion

Heparin bonding of ePTFE grafts using the CBAS technology carries much promise to improve the clinical performance of prosthetic small-caliber bypasses, approaching the historical results achieved with autologous vein conduits. The available experimental evidence and emerging clinical results point to significant clinical benefits of the stable CBAS heparin immobilization on the CBAS-ePTFE vascular graft. The CBAS heparin-bonding technology provides important beneficial effects: sustained thromboresistance and antiproliferative properties with platelet inhibition. These benefits may explain the promising below-knee clinical results²⁸⁻³³ attained with the Gore Propaten Vascular Graft.

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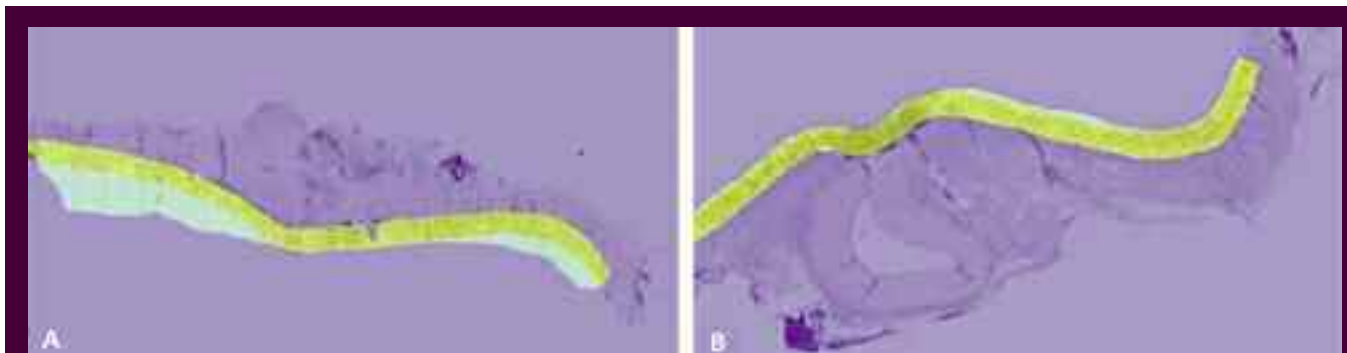


Figure 2. A) Standard PTFE: A micrograph demonstrating the use of the software BioPix (BioPix AB, Gothenburg, Sweden) shows intimal hyperplasia appearing in a turquoise color whereas graft material has a yellow color. (B) CBAS-PTFE graft: A micrograph demonstrating the use of the software Biopix shows a small brim of intimal hyperplasia appearing in a turquoise color, whereas graft material has a yellow color. Reprinted with permission.

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The ePTFE Evolution: Gore Propaten Vascular Graft

Knut P. Walluscheck, MD



Introduction

Autologous saphenous vein (ASV) is generally the preferred bypass material for treatment of patients with severe occlusive disease. In many patients requiring below-knee (BK) bypass, the ASV is unavailable or unsuitable for use. But there is an ever-growing group of patients for whom an ASV bypass is inadvisable due to increased risk of wound complications or infections associated with vein harvest or because they cannot tolerate the longer operating time that harvesting necessitates.^{1,2} Supported by advances in anaesthesiology, vascular surgery is offered increasingly frequently to high-risk patients. These patients in particular benefit from optimized operating time, even if ASV is available.

Previous studies have shown the poor patency of prosthetic grafts used in BK bypasses.³ The failure of a prosthetic bypass graft, especially one with the small diameter often used for crural or pedal access, may be due to deposition of thrombus, intimal hyperplasia, or progression of vascular disease.^{2,4} But there has been an expanded polytetrafluoroethylene (ePTFE) evolution. Efforts to reduce the thrombogenicity of implanted artificial surfaces have included the application of heparin.^{5,6}

To date, one of the most successful methods to provide and retain heparin on the surface of a prosthetic graft to achieve bioactivity has been the Carmeda BioActive Surface (CBAS) process (Carmeda AB, Upplands Väsby, Sweden), providing a single end-point covalent bond to immobilize the heparin molecule.⁷ After experimental and clinical studies applying the CBAS technology to different medical devices,⁶⁻¹⁰ several studies have been performed using a CBAS-ePTFE graft.¹¹⁻¹⁴ Since 2002, the CBAS-ePTFE graft (Gore Propaten Vascular Graft, W.L. Gore & Associates, Flagstaff, Arizona) has been commercially available for clinical use in Europe.

Clinical Performance of the CBAS-ePTFE Vascular Graft

Studies of the clinical performance of CBAS-ePTFE grafts in femoropopliteal (FP) and femorocrural (FC) bypasses have been reported in several published articles (Table 1).^{2,15-25}

Between 2003 and 2004 all patients who underwent an infrainguinal prosthetic bypass procedure in our department were included in our retrospective study¹⁵ published in 2005. All patients with no available ASV were treated with a CBAS-ePTFE graft (n=43). Above-knee (AK) bypasses (n=12) were performed in patients with disabling claudication and below-knee (BK) bypasses (n=31) in patients with rest pain or tissue loss. A Linton patch (n=20) was implanted in all cases with a crural anastomosis and, in a few cases, with BK popliteal anastomosis. There were no re-operations; no patients died during hospitalization or within 30 days.

Follow-up visits occurred at months 3, 6, 12, 18 and 24. Two years after surgery, 22% of the patients had died. Freedom of amputation was 98%. For AK bypasses, the 1- and 2- year primary patency rates were 91% and 68%, with similar secondary patency rates. For BK bypasses, the 1- and 2- year primary patency rates were 92% and 81%.

A further retrospective non-randomized study was carried out by Battaglia et al.¹⁶ and published in 2006. CBAS-ePTFE grafts (n=37) and ASV grafts (n=37) were implanted in infragenicular femoropopliteal and infragenicular infrapopliteal position. Prosthetic grafts were given when ASV was not available. Neither patches nor cuffs were used. Follow-up examinations were performed 1, 3, and then every 6 months after surgery. There were no differences in terms of graft occlusion and amputation between the two groups. The 1- and 2- year primary patency rates in CBAS-ePTFE and ASV groups were 78%/76% and 80%/80%, respectively.

From: Diako/Academic Hospitals, Flensburg, Germany.

Address correspondence to the Department of Vascular Surgery, Diako/Academic Hospitals, Knuthstraße 1, 24939 Flensburg, Germany; e-mail: kwalluscheck@kielheart.uni-kiel.de.



In 2005, Dorigo et al¹⁷ released a study comparing BK bypasses with CBAS-ePTFE (n=24), ASV (n=25) and standard ePTFE (n=21). There were no significant differences among these groups. However, patching of the proximal or distal anastomosis or endovascular treatment of the inflow-vessel was done in 12, 4, and 10 cases, applied to the groups. Early graft thrombosis, fewer than 30 days postoperatively, occurred in 5, 3, and 10 cases. Statistical analyses showed significantly better results for ASV and CBAS-ePTFE compared with standard ePTFE. But there was no significant difference between ASV and CBAS-ePTFE in early-graft thrombosis. The 18-month primary patency rates were 53% (ASV), 7% (CBAS-ePTFE) and 40% (standard ePTFE).

In 2008, Dorigo et al¹⁹ published longer term follow-up for CBAS-ePTFE with an inclusion of additional BK bypass patients in the study (n=34). The 2-year primary patency rate for BK bypasses was reported to be 81%. Limb salvage was calculated to be 84% at 2 years.

Bosiers et al²⁰ reported a prospective, multicenter trial with 86 patients treated with AK (n=55), BK FP (n=23) or FC (n=21) CBAS-ePTFE bypass. No cuffs or patches were implanted. There were no significant perioperative complications. The overall 1-year primary and secondary patency rates were 82% and 97%. The 1-year primary patency rate for AK bypasses was 84%. The primary patency for BK FP and FC bypasses was 81% and 74%, respectively.

In 2008, Dorrucchi et al¹⁸ presented a prospective study (n=27) with BK FP (n=20) and FC (n=7) CBAS-ePTFE bypasses. The mean follow-up time was 24 months. There were 2-year primary and secondary patency rates of 85% and 93% for the BK bypasses overall. The limb salvage rate was 96%.

Peeters et al²¹ included 153 infrainguinal CBAS-ePTFE bypass procedures (75 AK, 41 BK FP, 37 FC) in their study which was published in 2008. There was no use of additional techniques such as cuffs or patches. The 3-year overall primary and secondary patency rates were 72% and 77%. The primary patency rate for BK FP bypasses was 75%, 60% for FC bypasses. The 3-year limb salvage rate in patients with critical limb ischemia (CLI) was 86%.

A prospective, multicenter trial, enrolling 142 patients, with 87 AK and 52 BK CBAS-ePTFE bypasses, was published in 2009 by Hugl et al.²² The 1-year overall primary and secondary patency rates were 80% and 85% with a limb salvage rate of 96%. The primary patency rate for AK bypasses was 83%, for BK FP bypasses 74% and for FC 79%. The authors could show that the primary patency rate decreased depending on the number of patent run-off vessels from 84% (3 vessels) and 81% (2 vessels) to 73% (1 vessel).

Furthermore, female patients had significantly higher primary patency rates for BK bypasses than male patients (96% versus 68%). Patency rates for patients younger and older than 70 years were not statistically significantly different.

Daenens et al²³ presented in 2009 the largest single-center series of CBAS-ePTFE implantations to date, compared with ASV in a non-randomized retrospective study, as 240 patients were treated with a CBAS-ePTFE graft and 110 patients with ASV (n=350). An adjuvant technique, such as a cuff, patch or av-fistula was used in 18% of the synthetic grafts.

The primary patency rates for the CBAS-ePTFE grafts at 1-year and at 2 years were 92%/83% for AK bypasses, 92%/83% for BK bypasses and 79%/69% for FC bypasses. In the ASV group, the corresponding patency rates were 91%/80% for AK bypasses, 72%/72% for BK FP bypasses and 69%/64% for FC bypasses. The 2-year limb-salvage rates in the CBAS-ePTFE group were 92%/98%/87% and 100%/91%/96% in the ASV group. The authors concluded that there was no significant difference between patency rates of CBAS-ePTFE and ASV grafts.

Lösel-Sadee et al²⁴ reported the first 5-year results with CBAS-ePTFE grafts in 2009. In a retrospective study the outcome of 75 patients (n=30 BK popliteal, n=45 FC) was assessed. Five patients were implanted with a vein cuff. The 1-, 2-, 3-, 4- and 5-year primary patency rates were, respectively, 77%, 71%, 71%, 71% and undeterminable for the BK popliteal bypasses; and 64%, 57%, 50%, 50% and 50% for the FC bypasses. The 1-, 2-, 3-, 4- and 5-year secondary patency rates were, respectively, 88%, 83%, 83%, 83% and undeterminable for the BK popliteal bypasses and 87%, 78%, 72%, 72% and 72% for the FC bypasses. The limb-salvage rate was 84% at 5 years.

The latest report of CBAS-ePTFE clinical results was published by Pulli et al²⁵ in the *Journal of Vascular Surgery* in May 2010. Over 7 years, 425 patients (AK n=101/BK popliteal n=238/FC n=86) with critical limb ischemia (CLI) were treated with a CBAS-ePTFE graft and enrolled in an Italian multicenter registry. Adjunctive procedures at the distal anastomotic site were performed in 20%. The cumulative estimated 3-year primary and secondary patency rates were 61% and 70%. The limb-salvage rate was 83%.

The Impact of Adjunctive Procedures at the Distal Anastomotic Site

In some of the studies mentioned above the dedication of adjunctive procedures at the distal anastomotic site, such as the Miller cuff, Tayler patch, Linton patch or arteriovenous fistulas, was described.^{15,17,23-25} However, other studies disallowed these techniques,^{2,16,21} not necessarily leading to decreased results. In the majority of cases, adjunctive techniques have been applied at the distal anastomotic site of femorocrural bypasses due to

Table 1. Summary of Clinical Results of the Gore Propaten Vascular Graft for Below-Knee Bypasses

Author (Year)	Indication	No. of patients	Primary Patency Rate					Limb Salvage			
			1-year % (FP/FC)	2-year % (FP/FC)	3-year % (FP/FC)	4-year % (FP/FC)	5-year % (FC)	1-year % (FP/FC)	2-year %	3-year %	5-year %
Walluscheck, et al. (2005) ¹⁵	BK FP and FC	31	92	81	NI	NI	NI	NR	98	NI	NI
Battaglia, et al. (2006) ¹⁶	BK FP and FC	37	78	76	NI	NI	NI	NR	89	NI	NI
Bosiers, et al. (2006) ²⁰	BK FP and FC	44	81/74	NI	NI	NI	NI	87	NI	NI	NI
Dorigo, et al. (2008) ¹⁷	BK FP and Tibioperoneal trunk	34	81	81	NI	NI	NI	NR	84	NI	NI
Dorrucci, et al. (2008) ¹⁸	BK FP and FC	27	85	85	NI	NI	NI	NR	96	NI	NI
Peeters, et al. (2008) ²¹	BK FP and FC	78	86/71	79/60	75/60	NI	NI	90	90	86	NI
Hugl, et al. (2009) ²²	BK FP and FC	52	74/79	NI	NI	NI	NI	96	NI	NI	NI
Daenens, et al. (2009) ²³	BK FP and FC	154	92/79	83/69	NI	NI	NI	NR	98/87	NI	NI
Lösel-Sadée, et al. (2009) ²⁴	BK FP and FC	75	77/64	71/57	71/50	71/50	50	NR	NR	NI	84
Pulli, et al. (2010) ²⁵	BK FP and FC	324	75/66	67/57	61/52	NI	NI	87/82	86/80	83/77	NI

BK = below-knee; FP = femoro-popliteal; FC = femoro-crural; NI = not investigated; NR = not reported

the mismatch between a 6 mm prosthetic graft and a 2 mm to 3 mm often-calcified crural vessel.^{17,23}

But there was no study in which the distal anastomosis of femorocrural CBAS-ePTFE bypasses has been routinely performed with a patch or cuff, except our study.¹⁵ In all cases of femorocrural CBAS-ePTFE bypasses, we use the graft in combination with a distal Linton patch of bovine pericardium (Vascu-Guard, Synovis, St. Paul, Minnesota).

The bioactive surface of the CBAS-ePTFE graft provides excellent early and midterm patency results comparable with ASV in upper positions. But even for femorocrural bypasses the results are competitive, as shown by Daenens et al with a 2-year primary patency rate of 69% for femorocrural CBAS-ePTFE bypasses and of 64% for femorocrural ASV bypasses.²³ The researchers used adjunctive procedures at the distal anastomotic site in 37% of their FC bypasses. In our study, we could show a 2-year primary patency rate for BK bypasses (BK popliteal, n=7/FC, n=14) of 81%.¹⁵ In our opinion, the good results — especially regarding crural CBAS-ePTFE grafts — can be optimized by the stringent use of a patch of bovine pericardium, due to the specific material characteristics.

The CBAS-ePTFE graft is considered to be “an excellent alternative to autologous vein when it is not available” in almost all the above-named studies. Further, there are some points worth mentioning with regard to a significant number of patients, even if vein is available. First, the patients for these procedures are increasingly older at time of scheduling. Similarly, they are presenting with more co-morbid conditions. More high-risk patients with long occlusions not suitable for interventional therapy are presenting for surgery. These patients specifically benefit from anesthesiologic management in regional anaesthesia with short operation times.

Vein harvesting is time-consuming and produces an expanded wound area compared with the use of a prosthetic graft. The actuarial survival rate of these high-risk patients with cardiovascular diseases is low, and a significant number of patients will die with patent bypass in a short-term period.

The primary target is to achieve limb salvage and optimize quality of life for patients with severe CLI. In addition to using the CBAS-ePTFE graft for a patient who does not have a suitable vein, we consider the CBAS-ePTFE vascular graft to be a viable alternative for older patients with increased co-morbidity independent of vein availability. Further studies for this subgroup should be performed to evaluate this view.

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Treatment of Infrainguinal Critical Limb Ischemia Using a Heparin-Bonded ePTFE Graft: Mid-Term Results from a Multicenter Registry

Raffaele Pulli, MD, and Carlo Pratesi, MD



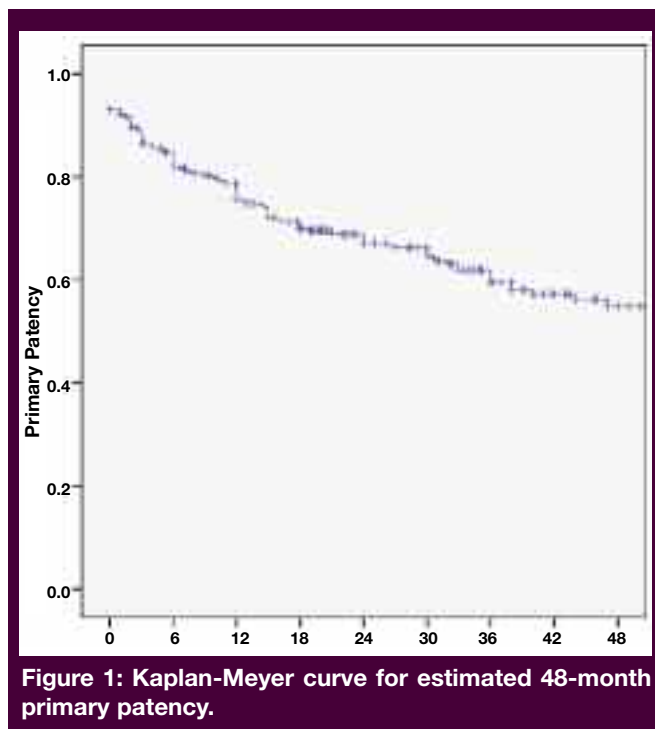
Abstract

We report a summary of our article¹ published in the May 2010 *Journal of Vascular Surgery* and presented at Annual Meeting of the Society for Vascular Surgery in Denver in 2009. The aim of this study was to evaluate early and mid-term results of above- and below-knee femoro-popliteal bypasses performed with a bioactive, heparin-treated ePTFE graft (Gore Propaten Vascular Graft, W.L. Gore & Associates, Inc., Flagstaff, Arizona) in patients with critical limb ischemia in a multicentric retrospective registry involving seven Italian vascular centers.

The idea of the Italian Registry started in 2007 after a presentation at the European Society for Vascular Surgery meeting in Madrid, Spain, where initial data from the centres of Florence, Catania and Mestre were collected and presented in a dedicated session. Since then, four more centers have been participating in and contributing to the registry. Further data were presented at the annual meeting of the Italian Society of Vascular and Endovascular Surgery in 2008 and 2009.

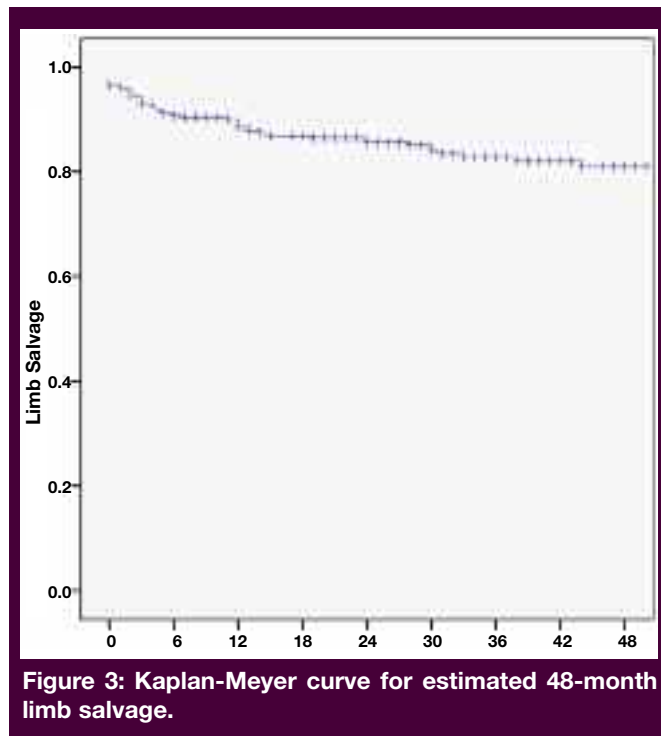
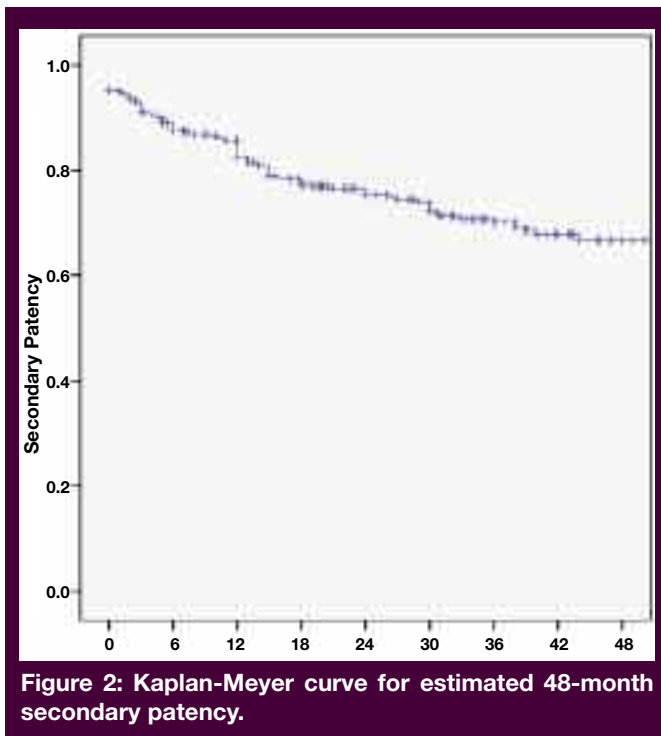
Introduction

Over a 7-year period ending in 2008, a heparin-bonded prosthetic graft (Gore Propaten Vascular Graft, W.L. Gore &



From: the University of Florence, Florence, Italy.

Address for correspondence: Raffaele Pulli, MD; Department of Vascular Surgery, University of Florence, Viale Morgagni 85, 50134, Florence, Italy. **E-mail:** rupulli@unifi.it.



Associates, Inc., Flagstaff, Arizona) was implanted in 425 patients undergoing lower limb revascularization for critical limb ischemia in seven Italian hospitals.

The choice to use this device was made on the basis of the surgeons' discretion and not only in the absence of a suitable vein. Data concerning these interventions were retrospectively collected in a multicenter registry with a dedicated database including main preoperative, intraoperative and follow-up variables.

Patient Group Profile

Patients were predominantly males (338 patients, 79%), with a mean age of 73.5 years (standard deviation [SD] 8.9 years). The indication for surgical intervention was the presence of critical limb ischemia in all patients (Rutherford class 4 in 230 patients, 54%; class 5 in 143 patients, 34%; and class 6 in the remaining 52, 12%).

Interventions were performed for occlusion of a native vessel in 315 cases, while 110 patients had a reintervention for the late occlusion of a prior open or endovascular femoro-popliteal intervention. In 186 cases (44%), 1 patent tibial vessel was present. The remaining 239 patients (56%) had 2 or 3 patent tibial vessels. Mean preoperative ankle-brachial index in the affected limb was 0.35 (SD 0.18).

Intervention Plan

Intervention consisted of a below-knee bypass in 324 patients (76%) and of an above-knee revascularization in the

remaining 101. In patients with below-knee bypass, distal target vessels were the popliteal artery in 238 cases, the tibioperoneal trunk in 38 cases and a tibial vessel in the remaining 48 cases (anterior tibial artery in 20 cases, posterior tibial artery in 23 cases and peroneal artery in 5).

All the patients received intraoperative administration of 30–70 IU/Kg of intravenous heparin at arterial clamping on the basis of the surgeons' preferences and habits.

Postoperative and long-term medical treatment consisted of single antiplatelet therapy in 221 cases, double antiplatelet therapy in 43 cases and oral anticoagulants in 161 patients.

Procedure Outcomes

There were 13 perioperative deaths, with a mortality rate of 3%. The cause of death was cardiac in 10 patients, while the remaining 3 patients suffered from a fatal pulmonary embolism, an ischemic stroke and sepsis, respectively. One instance of perioperative severe bleeding (requiring surgical revision at the distal anastomosis) occurred.

Early graft thrombosis occurred in 32 patients, with a cumulative 30-day graft patency rate of 92.5%. There were 18 early major amputations, with a 30-day major amputation rate of 4.2%.

Univariate analysis demonstrated that re-do surgery, a poor run-off score and the need for adjunctive distal procedures significantly affected early graft thrombosis, while only re-do surgery and poor run-off score increased perioperative amputation rates. Multivariate analysis confirmed that reintervention and poor run-

off score were independently associated with a higher risk of graft failure ($p=0.01$; 95% confidence interval [CI] 0.18–0.82; $p<0.001$; 95% CI 2.1–13.4), while none of the examined parameters were found to independently affect perioperative limb loss.

Follow-up Findings

Median duration of follow-up was 25.5 months (range 1–72 months); 420 patients (98%) had at least one postoperative clinical and ultrasonographic examination and 312 (73%) reached at least 1-year follow-up.

Mean ankle brachial index value during follow-up was 0.76 (compared to 0.35 preoperatively; $p<0.001$).

During follow-up, 50 deaths, 108 new graft thromboses and 35 major amputations occurred.

Cumulative survival rate at 48 months was 77%. Cumulative estimated 12-, 24- and 48-month primary patency rates were 75.5%, 67% and 55%, respectively (Figure 1). The corresponding 12-, 24- and 48-month data for secondary patency were 82.5%, 75.5% and 66% (Figure 2), and for limb salvage 88.5%, 85.5% and 81%, respectively (Figure 3).

At Cox regression analysis both redo surgery ($p=0.01$; 95% CI 0.4–0.9) and poor run-off score ($p=0.001$ 95% CI 1.2–2.4)

significantly affected estimated 48-month primary patency rates. Re-do surgery ($p=0.01$, 95% CI 0.31–0.88), poor run-off score ($p<0.001$, 95% CI 2.6–9.2) and preoperative clinical status ($p=0.02$; 95% CI 1–3.1) were also independently associated with lower-limb salvage rates.

Conclusion

Data from this large, retrospective registry confirmed that the Propaten heparin-bonded ePTFE graft provides good early and mid-term results in patients undergoing surgical treatment of critical limb ischemia. Excellent primary patency and limb-salvage rates could make this graft the initial choice in above-knee interventions. At the same time, its use in below-knee revascularizations may be considered in selected patients. Moreover, it could represent the optimal alternative to autologous saphenous vein when it is absent, unsuitable or of poor quality.

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Common Femoral Artery to Below-Knee Popliteal Artery Bypass with Gore Propaten PTFE Graft: Short-Term Results



Syed M. Hussain, MD, Jennifer L. Ash MD, Atif Baqai MD, Nabeel R. Rana MD

Introduction

Peripheral arterial disease (PAD) is increasing at an alarming rate and affects approximately 1 in 20 Americans. The U.S. Census Bureau predicts that in 2030 — when all baby boomers will be 65 and older — nearly 1 in 5 U.S. residents will be 65 or older. This age group is projected to increase to 88.5 million in 2050, more than doubling the 2008 figure of 38.7 million. Similarly, the 85-and-older population is expected to more than triple from 5.4 million to 19 million between 2008 and 2050.¹ Furthermore, there is predicted to be an increase in peripheral vascular procedures to 1.6 million, of which 1.2 million will be operative in nature.²

Infrainguinal bypass is used to save limbs that might otherwise require amputation, to treat ischemic rest pain or tissue loss and to improve walking distances in patients with severe life-limiting claudication. Contemporary practice has involved using synthetic conduit only when autologous vein is not available. As the patient population ages and the incidence of PAD increases, the availability of autologous vein conduit is decreasing. Many patients have already undergone vein harvest for coronary artery bypass grafting (CABG) or for a previous lower- or upper-extremity arterial bypass procedure. In addition, many vein conduits are not in adequate condition or of adequate size (at least 3 mm in diameter) for a bypass procedure.

Historically, the results of synthetic bypass grafts have been inferior to the results demonstrated by autologous vein. Notably, however, most studies comparing these two modalities of treatment are over 10 years old. Furthermore, none of these studies have assessed quality-of-life data or length of

stay in the hospital. Until recently, synthetic bypass grafts have made little technological advancement. Given these factors, one question remains: Is there a synthetic graft that provides comparable results to autologous vein in patency and limb salvage, and also decreases length of hospital stay and improves overall quality of life?

Review of Relevant Information and Literature

Historically, autologous vein has been the preferred conduit, especially for below-knee bypass procedures. In our experience, however, alternative conduits are increasingly becoming a necessity. As our patient population ages, we often see individuals who have no vein due to prior vein harvests, or have only suboptimal vein. Suboptimal vein (measuring <3 mm) or composite vein conduits have demonstrated dismal outcomes at best. Therefore, the search for an alternative, prosthetic conduit that performs as well as vein in the below-knee bypass position has become even more crucial.

Traditionally, graft patency and limb salvage have been looked upon as the major outcomes that determine the success of bypass grafts. We would argue that in addition to these factors, utilization of resources, operative time, length of stay and quality of life are also important predictors of not only bypass success, but also patient success. Moreover, the morbidity associated with vein harvests in an already-frail patient population cannot be underestimated when considering autologous vein as a conduit.

The heparin-bonded ePTFE graft (Gore Propaten Vascular Graft, W.L. Gore & Associates, Inc., Flagstaff, Arizona) became commercially available in the United States in November 2006. Several studies have demonstrated that the Gore Propaten vas-

From: The University of Illinois College of Medicine at Peoria. **Address for correspondence:** Syed M. Hussain, MD, Assistant Clinical Professor of Surgery, University of Illinois College of Medicine at Peoria, 5405 N. Knoxville Avenue, Peoria, IL 61614. **E-mail:** syed.m.hussain@heartcaremw.com.

Table 1. Breakout of patients according to Rutherford's classification of PAD.

Category	History	n=
0	Asymptomatic	0
1	Mild claudication	0
2	Moderate claudication	2
3	Severe claudication	23
4	Ischemic rest pain	22
5	Tissue ulceration (minor)	8
6	Tissue loss/gangrene	2

Table 2. Risk factors of patients evaluated.

Risk Factor	n=
Peripheral arterial disease	47
Diabetes	30
Tobacco use	47
Hypertension	55
Hyperlipidemia	52
Coronary artery disease	42
End-stage renal disease requiring dialysis	7

cular graft attains patency rates that are nearly comparable to autologous vein at 1 year, specifically in the below-knee popliteal position.

Peeters et al demonstrated in 2007 a 1-year patency of 71%, a 2-year patency of 60% and a 3-year patency of 60% in 37 patients in the below-knee position.³ Nevelsteen et al also demonstrated that year a 1-year patency of 79% and a 2-year patency rate of 69% in 97 patients in the below-knee position.⁴ Most recently, in 2010, Pulli et al reported midterm results from a multicenter registry that demonstrated a 2-year patency rate of 86% and a 3-year patency rate of 83% in the below-knee position.

Our experience has demonstrated similarly excellent patient outcomes for the Gore Propaten vascular graft in the below-knee position.

Design of Evaluation

We set out to evaluate the patency of the Gore Propaten vascular graft in the common femoral artery to below-knee popliteal artery bypass position. We performed a retrospective review of a prospectively maintained database from January 2007 to March 2010 and identified 57 patients who underwent 57 below-knee popliteal artery bypass procedures with the

Gore Propaten vascular graft during that period.

All the patients had a suitable common femoral artery and below-knee popliteal artery with at least one-vessel run-off. Thirty-seven men and 20 women underwent bypass. The average age was 70.3 years. The majority of the patients treated (n=45) presented with Rutherford class 3 or 4 PAD. Two patients presented with Rutherford Class 2, 8 presented with Class 5, and 2 presented as Class 6 (Table 1). Risk factors included previous PAD, diabetes, current tobacco use, hypertension, hyperlipidemia, coronary artery disease and end-stage renal disease requiring dialysis (Table 2).

Graft diameters implanted were 6 mm (n=44), 7 mm (n=6), and 8 mm (n=7). Follow-up was 100% in this group of patients. The average follow-up was 14.3 months, with a range of 3 to 39 months. Fifty-four of 57 patients were placed on 81 mg of aspirin daily. Three of the 57 had sensitivities or allergies to aspirin and were therefore not given aspirin.

It has been our practice to place all of our below-knee bypass graft patients who undergo procedures using prosthetic conduit on warfarin (Coumadin, Bristol-Myers Squibb, New York, New York). Fifty-four of 57 patients were placed on heparin or enoxaparin therapy postoperatively and were then bridged to therapeutic warfarin therapy (INR=2–3). Three of the 57 patients were not able to be placed on coumadin therapy and were instead placed on clopidogrel bisulfate, 75 mg daily.

The average length of stay was 3.7 days, with a range of 3 to 12 days. The average procedure time was 87 minutes (range of 79 to 153 minutes). Patients reported a return to full, normal activity at 26.6 days (range: 16 to 54 days). Primary patency at 12 months was 91.8% (52 of 57 grafts). Limb salvage at 12 months was 98.2% (56 of 57 grafts).

Complications included 1 failed graft at 28 months due to traumatic amputation secondary to injuries incurred in a motor vehicle collision; 2 thrombosed grafts at 7 and 9 months, both of which were successfully revised to tibial bypasses; and 2 patients with patent grafts who died during the follow-up period at 6 and 9 months. Four postoperative pneumonias and 2 postoperative urinary tract infections were also noted and successfully treated.

Eight patients presented in the early postoperative period with superficial wound infections. All 8 were treated successfully with local wound care.

Conclusion

The role of endoscopic vein harvesting techniques has yet to be determined in the realm of long-limb bypass procedures. Although we are acutely aware that the routine use of a prosthetic bypass graft in the below-knee position violates



most doctrines of vascular surgery, we believe that the Gore Propaten vascular graft data demonstrate results that may, for the first time, provide an acceptable alternative to autologous vein conduit.

In our experience, the Gore Propaten vascular graft serves as an excellent conduit for vascular bypass procedures at the below-knee popliteal artery position. The Gore Propaten bypass graft demonstrates acceptable short-term primary patency and limb-salvage rates, with relatively brief operative times, shortened hospital lengths of stay and rapid return to full function and normal daily activities.

Long-term follow-up and larger cohorts of patients are necessary to determine if the Gore Propaten vascular graft should be the conduit of choice for vascular bypass procedures at the below-knee popliteal artery position.

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Does Anastomotic Geometry Affect the Hemodynamics of PTFE Grafts?

Richard F. Neville, MD¹, Chris J. Elkins, PhD², Marcus T. Alley, PhD³, and Ryan B. Wicker, PhD⁴



Introduction

The use of a prosthetic graft for lower extremity bypass remains an option for many patients. Advantages include decreased operative morbidity, time, and minimization of incisions. Additionally, a significant number of patients in a limb salvage practice do not have autogenous tissue available for the bypass conduit.¹ Efforts to improve prosthetic graft performance include manipulation of anastomotic biology through autogenous tissue interposed at the distal anastomosis of the bypass in the form of a vein patch or cuff.²⁻⁵ Another approach involves improvement of graft performance through optimization of the hemodynamics related to the geometry of the anastomotic site. This paper describes the work first reported in the *Journal of Surgical Research* regarding the use of a magnetic resonance based, three dimensional model to study anastomotic hemodynamics.⁶

Model

Anastomotic flow patterns were studied for prosthetic graft models in a pulsatile flow system using magnetic resonance velocimetry (4D-MRV).⁷ The grafts used were commercially available 6 mm grafts; conventional PTFE (W.L. Gore and Associates, Flagstaff, Arizona) and pre-cuffed PTFE (Distaflo, Bard PV, Tempe, Arizona). Model configurations were chosen to study the anastomotic geometries most commonly used in current clinical practice; standard end-side, precuffed PTFE (Distaflo), and PTFE with a distal vein patch using PTFE graft material as the vein patch in order

to study the geometric effects on the hemodynamics of this configuration.⁸

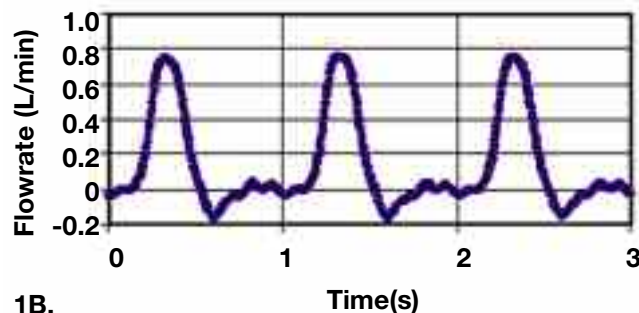
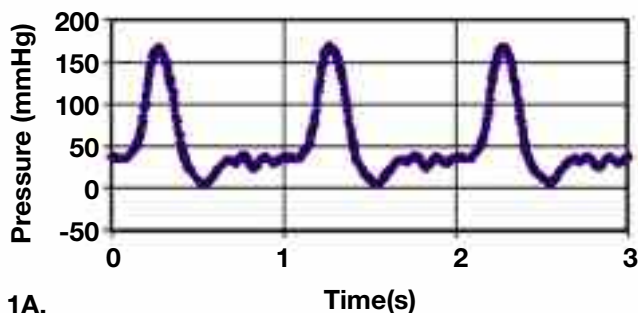
The ePTFE grafts were sewn onto silicone tubes acting as the recipient tibial artery with 6-0 Prolene suture. Silicon tubing was chosen with a size (4mm ID) and compliance to mimic a tibial artery as compared to the rigid glass tubing used in other reports. A custom pulsatile pump and tunable flow setup were used to create triphasic flow rate waveforms. Blood was simulated with a solution of 40% glycerol and a trace amount of gadolinium in distilled water. Pressure and flow rate were monitored in the flow delivery system proximal and distal to the bypass graft models. The pump was set to 70 beats per minute and the periods of the systolic and diastolic waveforms were set to 0.34s and 0.51s, respectively. The pressure varied between approximately 50 and 175 mm Hg with a minimum of 0 mm Hg corresponding to the negative flow between systole and diastole (Figures 1A and 1B).

In each model, the silicone tube was clamped a standard distance proximal to the distal anastomosis to represent an occluded proximal target artery. The models were imaged using a 4D-MRV technique implemented in a 3-Tesla MRI scanner (G.E. Healthcare, Newark, Delaware) using a standard protocol. Software (EnSight, Computational Engineering International, Apex, North Carolina) was used to visualize the three dimensional flow fields. Isosurfaces visualized the internal geometry of the models and included features such as the suture lines between ePTFE grafts and the 4 mm silicone

From: 1. Division of Vascular Surgery, Georgetown University Hospital, Washington, DC; 2. Department of Mechanical Engineering, Stanford University, Stanford, California; 3. Department of Radiology, Stanford University, Stanford, California; 4. Department of Mechanical Engineering, University of Texas at El Paso, El Paso, Texas.

Address for correspondence: Richard F. Neville, MD, Division of Vascular Surgery, Georgetown University Hospital, 3800 Reservoir Road, 4 PHC, Washington, DC 20007. **E-mail:** neville@gunet.georgetown.edu.

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Flow rate and pressure generated by pulsatile pump systems monitored in the flow delivery system proximal and distal to the bypass graft phantoms. (1A) Flow rate waveforms. (1B) Pressure waveforms.

tubes. Streamlines visualized the path of the fluid. The streamlines are curves that are tangent to measured velocity vectors in each specific time phase. These velocity vectors deliver quantitative data in three dimensions. Analysis of the flow patterns focused on the anastomotic regions prone to the development of intimal hyperplasia as identified in the literature; the toe, floor, heel and hood.⁹

Results

General observations

Flow patterns from the streamline images generated by velocity vector analysis were examined at the toe, heel, and hood regions of the anastomosis during various points in the pulsatile cycle (Figure 2). Regions of flow separation were evident representing chaotic, low velocity vectors with prolonged residence time. This was especially true of the separated regions at the hood and heel of the anastomosis. Depending on the specific anastomotic geometry, high velocity flow impinged on the recipient vessel floor opposite the toe with varying velocities before turning to flow through the distal native vessel. This resulted in an area of flow impingement and a stagnation point where the flow was noted to split distally and proximally.

Conventional end-to-side ePTFE

The straight end-to-side anastomosis created a reduced angle of impingement on the opposite vessel floor and a stagnation point with minimal secondary flow. There was a small region of slow recirculation at the heel of the anastomosis. At the toe of the anastomosis, there was a small area of flow separation (Figure 3). During flow deceleration at the beginning of diastole, flow separation increased at the graft hood and the recirculation region in the heel increased. The stagnation point shifted more distally along the recipient vessel wall and the separation region at the toe increased.

At the peak of retrograde flow, the vectors changed direction and the separation region in the hood grew, but flow separation at the toe disappeared. The retrograde flow swept across the vessel floor and impinged on the heel. This maintained a small vortex of recirculation and slow flow between the heel and the floor.

Pre-Cuffed ePTFE

The pre-cuffed anastomosis created a stagnation region on the recipient vessel floor with high normal stresses and strong secondary vortices in the distal flow stream. There was slow, chaotic flow in the vortex at the heel of the anastomosis (Figure 4).

A region of flow separation also developed at the top of the graft hood with a large separation at the toe of the anastomosis. As the flow moved distally, the secondary vortices swept fluid from the vessel floor, up the sides of the vessel, and into the toe region. As the flow decelerated in diastole, the separation regions in the hood and toe increased, and a large vortex formed in the heel of the anastomosis. Velocities in the vortex were decreased with chaotic, three-dimensional flow. This is consistent with increased particle residence time in the vortex at the heel of the anastomosis. The vortex continued to expand throughout the pulsatile cycle.

ePTFE with Simulated Distal Vein Patch

As in the pre-cuffed model, the distal vein patch anastomotic geometry created strong secondary flow in the distal anastomosis and recipient vessel. There was a small vortex near the heel, and a minimal flow separation due to the bulge in the hood created by the patch (Figure 5).

There was also flow separation at the toe, but strong secondary flow filled this region. This rapid flow extended distally for several graft diameters beyond the suture line between the patch and native vessel. The region of slow flow

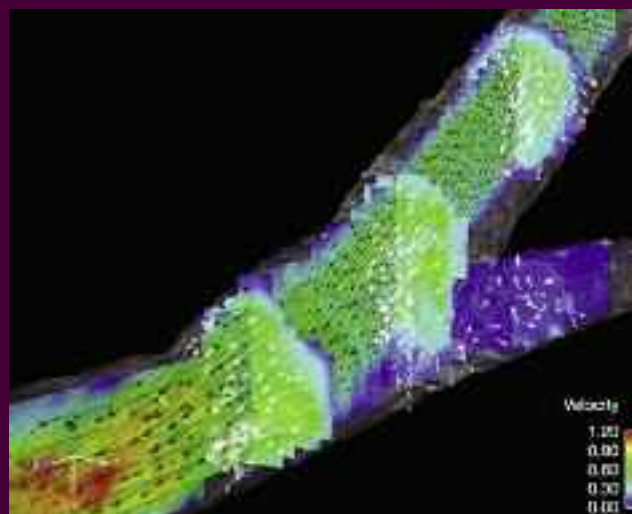


Figure 2. Oblique 3D view of the model during systole. Streamwise-vertical and spanwise-vertical planes show contours of velocity. Vectors are black in the streamwise-vertical plane and white in the other planes. These vectors show the pointwise fluid velocity and direction.

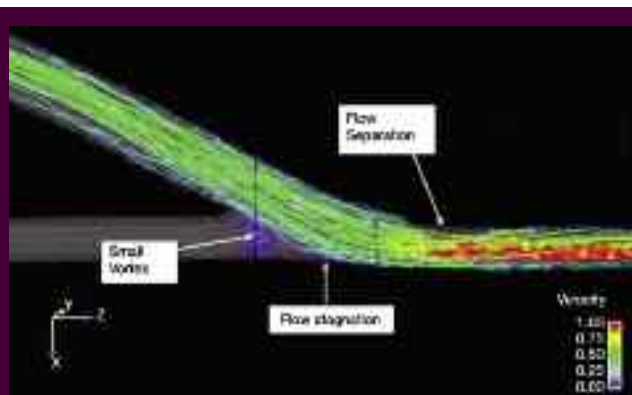


Figure 3. Conventional end-to-side ePTFE anastomosis — systolic acceleration. Flow travels straight through anastomosis. Heel has stagnant flow. Separation occurs at toe and secondary flow fills in the flow 2–3 vessel diameters distally, and secondary flow fills in the flow 2–3 vessel diameters distally.

near the heel remained small with a correspondingly small vortex. However, flow separation did occur in the hood to a greater degree than with the straight configuration.

The flow separation at the toe increased as the secondary flow weakened with deceleration. Although the angle of impingement was similar to the pre-cuffed geometry, the flow patterns with the DVP anastomotic geometry approximated the straight end-to-side configuration.

Discussion

Magnetic resonance velocimetry has been previously used to produce velocity measurements in a complex three-dimensional domain.¹⁰ Analysis of velocimetry data produces velocity vectors, streamlines, and isosurfaces that visualize hemodynamic patterns using pulsatile flow in anastomoses of varying geometry. We applied this technique to study the flow patterns in the anastomoses currently used in vascular surgical practice.

MR velocimetry involves a three dimensional, quantitative assessment of hemodynamic factors thought important to the success of lower extremity bypass. Prior models to define anastomotic hemodynamics have been two dimensional, qualitative models with idealized geometries. These prior models have relied on optically clear, rigid components that result in a two-dimensional particulate analysis of flow patterns in noncompliant tubes. This study used actual bypass graft material in a non-rigid system resulting in flow rates and pressure waveforms that mimic physiologic, pulsatile flow conditions. Hemodynamic differences with varying anastomotic geometries were captured in three dimensions using this technique. Areas of flow separation, recirculation, and vortex formation were evident during streamline visualization. Additionally, flow vectors indicated velocity and direction at points in the anastomotic site.

Attempts have been made to elucidate the relationship between hemodynamics and graft function. Norberto used a canine model to study the hemodynamics of cuffed grafts and found that graft compliance did not play a prominent role in the reduction of the hyperplastic response often responsible for graft failure.¹¹ Archie performed a fluid dynamics analysis using computational models of distal anastomotic sites with and without a vein cuff.¹² The presence of a vein cuff reduced the potentially detrimental changes in near wall residence time and shear stress by shifting hemodynamic abnormalities to interface between the ePTFE and the vein cuff. Ojha measured wall shear using a photochromic tracer method.¹³ These in vitro experiments implicated a number of potential hemodynamic stimuli for intimal hyperplasia including mean wall shear stress (WSS), wall shear rate (WSR), spatial wall-shear stress gradients (WSSG), and temporal wall-shear stress gradients.¹⁴

Ku et al proposed an oscillatory shear index (OSI) which measures the tendency for shear stress to reverse from its mean direction as an important parameter in optimal hemodynamics.¹⁵ The effect of mean wall-shear stress was studied by How using near-wall velocity vector measurements to determine wall shear stress. In this work, the addition of a vein cuff led to a decreased area of low shear stress in the recipient artery of the anastomosis.¹⁶

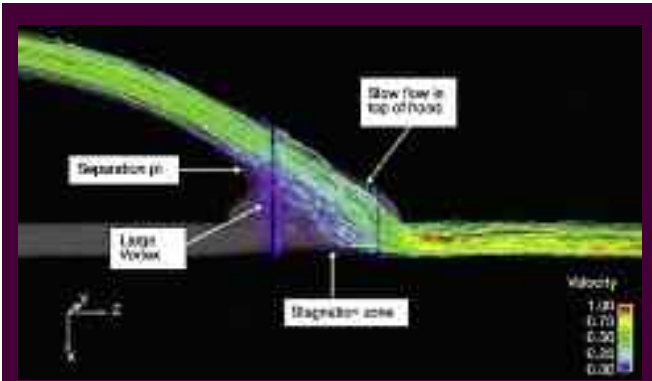


Figure 4. Precuffed ePTFE anastomosis — systolic acceleration. Due to large area of the cuff, the flow slows down before accelerating back into the native vessel. Heel has slow flow. Toe region has high velocity and complex flow since it is fed by secondary flow circulating from the impingement zone on the floor, up the vessel sides, and into the toe region.

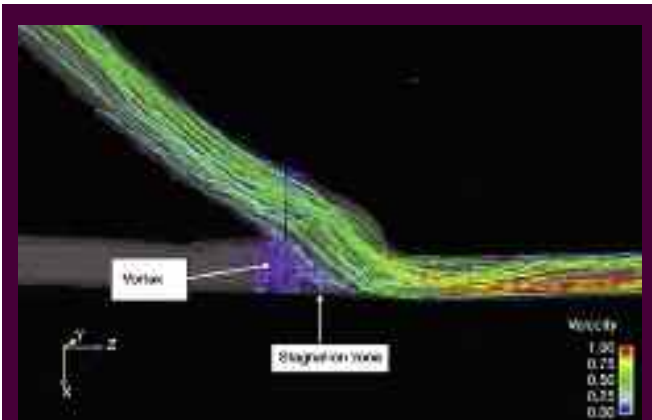


Figure 5. Distal vein patch anastomosis — systolic acceleration. Flow turns as it enters the anastomosis creating a 45° impingement angle. This creates an impingement line along the vessel floor and strong secondary flows shown by streamlines that hit the floor, turn upward, and curve into the toe separation region.

Keynton examined the effect of wall shear stress in a canine carotid model. The authors identified levels of wall shear (1500 1/s) above which there was no hyperplasia and levels below which over 92% of the hyperplasia occurred (350 1/s).¹⁷ Loth studied hyperplasia in a canine iliofemoral PTFE bypass model.¹⁸ Hyperplasia formed on the graft hood and along the suture line especially in the anastomotic sinus at the heel. These areas correlate with the flow separation noted in the MRV analysis. Loth proposed that flow fluctuation in the graft hood was proliferative due to flow separation while the flow fluctuations on the recipient vessel floor

at the toe were less harmful due to variability in the stagnation point.

Longest and Kleinstreuer performed a computational study with a model for biological stimulation of hyperplasia.¹⁹ The model was based on near-wall residence time of blood, platelet activation, and surface reactivity and was able to predict hyperplasia formation in agreement with in vivo observations. Calculations for both pre-cuffed and straight configurations showed regions conducive to hyperplasia in the toe, graft hood, and the anastomotic heel. In the pre-cuffed anastomosis, this resulted in a large area in the heel with slow flow, recirculation and high NWRT. This was noted to a lesser degree in other regions of the pre-cuffed anastomosis. These computational findings coincide with the MRV images in the current study.

The MRV images and streamlines in this study indicate that there are different velocity and flow pattern produced by anastomoses of varying geometry. The conventional end-to-side configuration results in a small vortex at the anastomotic heel, decreased flow separation in the graft hood, and decreased flow separation at the toe. Minimal secondary flows at the toe of the conventional anastomosis result in decreased surface reactivity and less time for particle-wall interaction.

The pre-cuffed ePTFE graft creates flow patterns with increased flow separation in the hood of the graft and at the toe of the anastomosis, especially during the diastolic phase of the pulsatile cycle. The pre-cuffed configuration creates a large vortex at the anastomotic heel with chaotic velocity vectors. Velocity vectors in the heel vortex demonstrate low velocity and disordered flow patterns.

These areas of increased flow separation and vortex formation would seem to be disadvantageous and correlate with noted areas of intimal hyperplasia formation.¹⁶ There was no evidence of the high-velocity uniform flow that would maintain an advantageous high-shear stress environment. The distal vein patch anastomosis demonstrated flow separation and vortices with magnitude between those in the straight and precuffed configurations. The distal vein patch geometry resulted in a small vortex at the heel. This pattern was closer to the straight graft hemodynamic pattern as opposed to the precuffed geometry.

Conclusion

Magnetic resonance velocimetry produces three dimensional velocity measurements with sufficient accuracy and resolution to quantitatively analyze hemodynamics in anastomotic geometries. The velocity vector fields and calculated streamlines demonstrate the effects of anastomotic geometry on hemodynamics. Flows generated by different graft

configurations were captured with marked differences noted between standard and pre-cuffed anastomotic geometries. The findings support a conventional end to side anastomosis with a low incidence angle using a straight graft as producing favorable hemodynamics as compared to a cuffed configuration. The distal vein patch configuration approximates the conventional, straight anastomotic pattern. This MR technology has an imaging capability to study aspects of graft hemodynamics in vitro with possible in vivo applications in the future.

Note

Figures originally published in Neville RF, Elkins CJ, Alley M, Wicker RB. Hemodynamic comparison of differing anastomotic geometries using magnetic resonance velocimetry. *J Surg Research* January 1, 2010 [epub ahead of print].

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Nonhealing Ulcer of the Toe and Use of Heparin-Bonded Graft in Treatment

Edward Y. Woo, MD



Introduction

Historically, below-knee popliteal and infrageniculate prosthetic bypasses have been met with very poor patency results. This case report examines the use of a novel heparin-bonded graft in the treatment of a nonhealing ulcer of the toe.

Case Report

A 79-year-old female presented with a non-healing ulcer of her right second toe. This condition had been ongoing for approximately 6 weeks, with no signs of healing. Her past medical history was significant for coronary artery disease, diabetes mellitus, hypercholesterolemia, hypertension and peripheral vascular disease. She had a past surgical history including coronary artery bypass grafting and multiple podiatric procedures. Her ulcer was managed by a podiatrist for over a month, but no progress had been made.

A work-up was instituted. Ankle-brachial indices were 0.12 on the right and 0.45 on the left. An angiogram demonstrated a complete occlusion of her superficial femoral artery and popliteal artery. The peroneal artery had segmental occlusions, and the posterior tibial artery was completely occluded. An anterior tibial artery did reconstitute in the mid-calf and formed a dorsalis pedis artery. Given the long-segment occlusions of the superficial femoral and popliteal as well as severe infrageniculate disease, endovascular options were ruled out. Vein mapping was performed as shown in Figure 1.

The patient was taken to the operating room. Her greater saphenous, lesser saphenous, and cephalic veins were explored. However, all veins were small and sclerotic and unsuitable for use as conduits. As a result, the decision was made to use the Gore Propaten heparin-bonded PTFE graft as a conduit. A femoro-anterior-tibial bypass was performed. From a technical

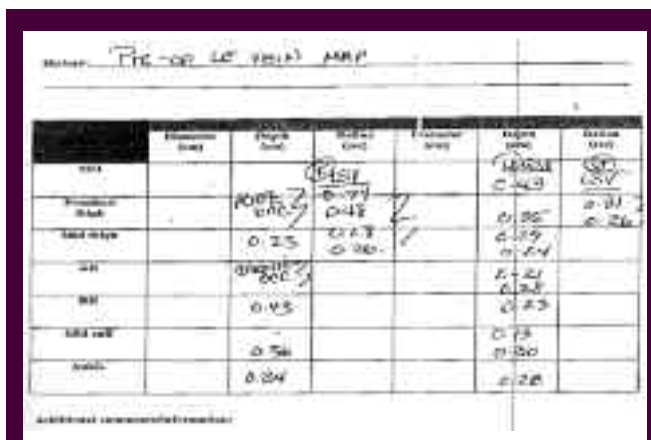


Figure 1. Vein mapping of 79-year-old female subject.

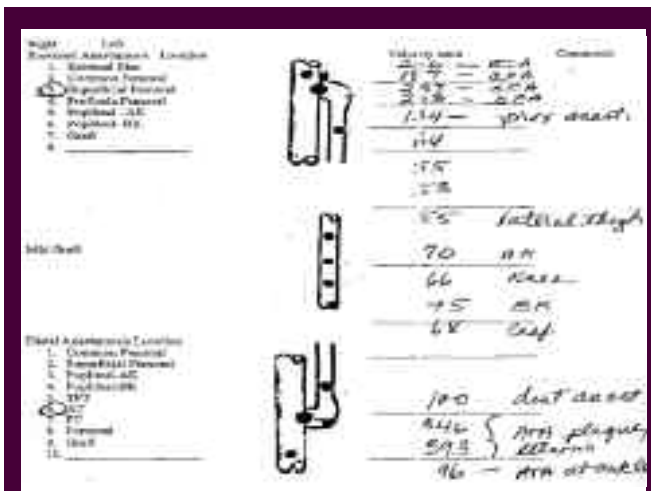


Figure 2. Patency at 1 year as demonstrated by graft duplex.

From: the Hospital of the University of Pennsylvania University of Pennsylvania Health System.

Address for Correspondence: Edward Y. Woo, MD; Vascular Laboratory/Division of Vascular Surgery and Endovascular Therapy; 4 Silverstein Pavilion; Hospital of the University of Pennsylvania, University of Pennsylvania Health System; 3400 Spruce Street; Philadelphia, PA 19104. **E-mail:** edward.woo@uphs.upenn.edu.

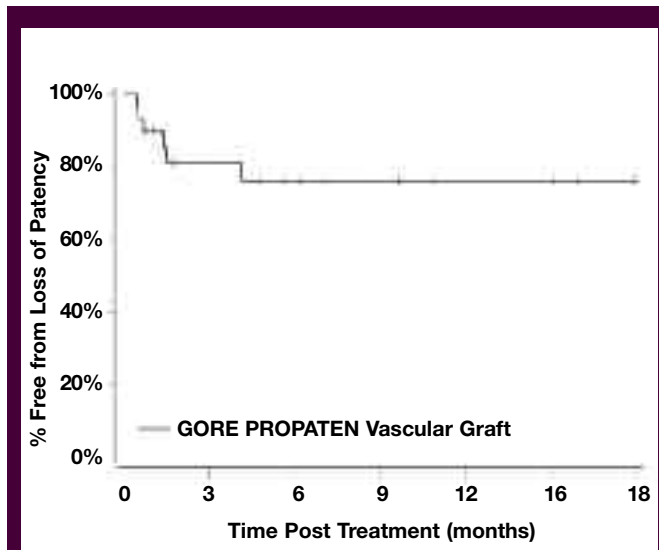


Figure 4. Primary patency of below-knee popliteal and infrapopliteal bypasses.

This patient did well postoperatively and was discharged home uneventfully. Her ulcer healed in a few weeks. Graft surveillance was performed at 1 month and then at 6-month intervals. At the 1-year mark, a graft Duplex demonstrated a patent graft (Figure 2). However, the target vessel appeared to have a stenosis and a CT angiogram was performed (Figure 3). This demonstrated a widely patent graft, anastomoses and the target vessel. It has now been more than 2 years since the patient had the operation, and the graft remains widely patent with no interventions.

standpoint, we always make an oblique incision in the groin for exposure of the femoral artery. This allows for better healing.

A counter-incision is made over the anterior compartment to expose the anterior tibial artery. The prosthetic graft is then tunneled subfascial from the groin to the anterior tibial artery. This ensures that the graft stays deep throughout its course and does not take a subcutaneous route. It also allows for closure of a muscle layer over the graft in the calf. Although it was not needed in this case, a sartorius muscle flap can be used for groin coverage. These extra layers are helpful in preventing infection, especially when there is wound breakdown.

Discussion

This case highlights the Gore Propaten heparin-bonded graft, which has demonstrated markedly better results when compared to historical controls. At our institution we have performed more than 68 implants in various positions, with an overall patency rate of 94% at 30 days and 86% at 18 months. Furthermore, we have performed 29 bypasses below the knee (popliteal/infrageniculate). The patency for this group at 30 days was 90% and at 18 months 76% (Figure 4). Because of these improved results, we now use the Propaten graft in any position and any time we use a prosthetic PTFE graft.

Infra-Inguinal Arterial Bypass With Propaten: How I Do It

Niren Angle, MD, RVT, FACS



Abstract

The advent of endovascular therapy has spurred a revolution in lower-extremity revascularization for claudication or critical-limb ischemia over the last decade. Although endovascular treatment for lower-extremity arterial disease has advanced tremendously, bypass surgery as a whole continues to exhibit longer durability than endovascular interventions. Despite the better patency rates of bypass surgery, the procedure's morbidity — especially morbidity with wound-healing — limits enthusiasm on the part of some practitioners. Overall, however, vein remains the superior conduit for lower-extremity bypass surgery, particularly infrapopliteal bypass.

Heparin-bonded ePTFE (Gore Propaten Vascular Graft, W.L. Gore & Associates, Flagstaff, Arizona) is a novel synthetic conduit wherein heparin molecules are end-point covalently bonded to the ePTFE and, therefore, do not get eluted off with pulsatile blood flow. Literature would suggest that Propaten has better 1- to 2-year primary patency than historically has been the case for lower-extremity prosthetic bypasses.¹ The objective of this article is to describe my technical method of performing lower-extremity bypass with the ePTFE graft.

Patient Selection

For an above-knee femoropopliteal bypass, I prefer Propaten over saphenous vein, as the patency rates are comparable. The ideal situation for the use of Propaten, in my opinion, is for an infrapopliteal bypass wherein there is not adequate vein, and the lesion falls into the TASC C or D category. Assuming a primary endovascular approach is unsuccessful, a bypass with Propaten is then an option.

Technique

The operation can be performed under general anesthesia

or continuous spinal/epidural anesthetic. The epidural can then be maintained for the initial 48 to 72 hours for pain control. However, in my experience, a properly done PTFE bypass usually lets physicians discharge most patients within 72 hours — and some, particularly patients with above-knee femoro-popliteal bypass, within 24 to 48 hours.

With either method, the patient is administered preoperative antibiotics, then the lower extremity is prepped and draped from the umbilicus down to the foot. I use Ioban (3M, St. Paul, Minnesota) for draping of the surgical site, particularly with prosthetic graft material.

The common femoral artery is exposed through a 3- to 4-inch incision from the inguinal ligament down to the groin crease. This is carried through the skin and subcutaneous tissue using electrosurgery, and the femoral sheath is then opened.

The extent of exposure of the common femoral artery depends on the degree of disease at the femoral bifurcation. If there is significant profunda femoris disease, then the arterial exposure needs to be more extensive than if the profunda is disease-free. The common femoral artery, the superficial femoral artery (SFA), and the profunda are also encircled with Silastic vessel loops.

Above-Knee Popliteal Artery Bypass

For an above-knee popliteal artery exposure, an incision is made on the medial aspect of the thigh above the knee (Figure 1). To facilitate this exposure, a cotton roll is placed under the calf, and the knee is partially flexed. An incision is made on the medial aspect of the thigh below the vastus medialis and carried down through the muscle fascia.

The sartorius muscle is reflected inferiorly and dissection is carried out past the fatty tissue close to the posterior aspect of the femur. The adductor tendon is then appreciated as the popliteal artery exits Hunter's canal. The popliteal artery is then exposed for a length of approximately 5 to 6

From: The University of California, San Diego Health Sciences.

Address for correspondence: Niren Angle, MD, RVT, FACS, UCSD Medical Center — Hillcrest, 200 West Arbor Drive, San Diego, CA 92103. **E-mail:** nangleka@gmail.com.

cm and encircled with Silastic loops. It is very important to use monopolar electrosurgery as little as possible when dissecting around the popliteal artery because the saphenous nerve travels intimately with the artery; injury or transection of the saphenous nerve or of the sartorial or anterior branch can result in anesthesia of the anterior leg.

The patient is then given 100 units/kg of heparin intravenously and, simultaneously, a Gore tunneler is used to tunnel a 6 mm Propaten (non-ringed) graft from the groin to the above knee popliteal fossa in a subsartorial tunnel. The tunnel is created by blunting clearing space on the anterior aspect of the SFA into the popliteal fossa. The Propaten graft is then tunneled through with the sheath of the tunneler.

The common femoral artery is then clamped with an angled DeBakey clamp, as proximal as necessary, as it exits under the inguinal ligament. The SFA is then clamped with an angled DeBakey clamp and a profunda clamp is used to occlude the profunda femoris artery.

An 11 blade is used to create an arteriotomy and is extended with a Potts scissors. If there is a significant plaque that is amenable to an endarterectomy, then an endarterectomy is performed. The graft is then cut and shaped appropriately with a tonsil clamp to match the arteriotomy. It is important to emphasize that the geometry of the graft anastomosis must be such that the graft takes a lazy course as it originates from the artery. This requires that the angle of the cut on the graft be less than 45 degrees.

Once the anastomosis is completed — but not yet tied down — the last three suture loops are loosened with a fine nerve hook. The artery is flushed antegrade and retrograde, but only once the graft is clamped with a Fogarty shodded clamp. The lumen is flushed with heparinized saline, and the distal clamp on the profunda is released to fill the lumen with blood. Under the continuous retrograde bleeding, which distends the lumen, the suture line is tied down. The proximal clamp is then released to restore flow through the native system.

The popliteal artery is then clamped in a similar manner. I tend to prefer using Yasargil clips for occluding the popliteal artery. If the SFA is occluded, one option is to perform an end-to-end anastomosis. Alternatively, the most commonly done anastomosis is an end-to-side anastomosis (Figure 2). My preference is to perform an end-to-end spatulated anastomosis in all cases due to the more favorable hemodynamics of such a procedure. The concern about compromising retrograde flow is largely theoretical.

I perform the anastomosis with a running 6-0 Prolene suture and once again, after the native artery is flushed antegrade and retrograde, under continuous retrograde bleeding, the suture line is tied down. Flow is then restored in the

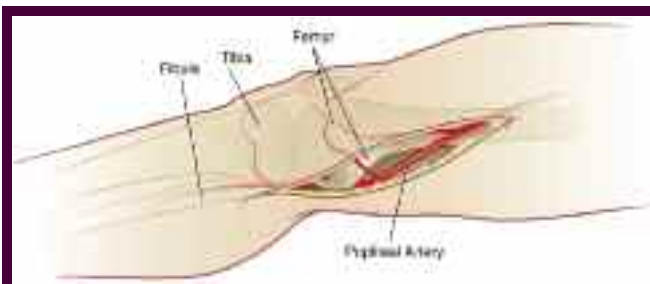


Figure 1. For an above-knee popliteal artery exposure, an incision is made on the medial aspect of the thigh above the knee.

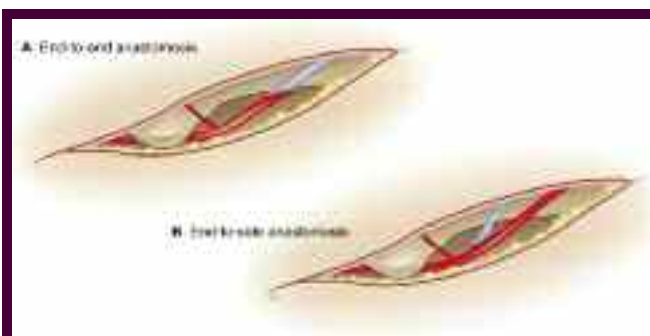


Figure 2. If the SFA is occluded, one option is to perform an end-to-end anastomosis. Alternatively, the most commonly done anastomosis is an end-to-side anastomosis.

native popliteal artery. The heparin is routinely reversed with protamine sulfate. Once hemostasis is ensured, the incision is closed with layers of 3-0 Vicryl for the subcutaneous tissues and 4-0 Monocryl for the skin.

Below-Knee Popliteal Artery Bypass

The proximal exposure for the femoral artery is done the same way as described above. The below-knee popliteal artery is exposed in the standard fashion with an incision below the knee on the medial aspect of the leg. The skin and muscle fascia are opened using electrosurgery, and the medial head of the gastrocnemius is retracted posteriorly bluntly.

The popliteal fossa is entered and the popliteal vein is retracted to expose the artery. The popliteal artery is flanked by paired veins that are virtually fused to the artery. The artery must be separated from the flanking veins sharply and the artery encircled with vessel loops. The graft is then tunneled in the manner described above and the arterial anastomosis performed with a running 6-0 Prolene suture.

Tibial Artery Bypass

For purposes of conciseness, the technique of individual tibial artery exposure will not be described here. Once the



artery in question is exposed based on the pre-operative arteriogram, the proximal anastomosis is performed as previously described.

If the tibial artery is very soft, clamping with Yasargil clips is a decent option. Each tibial artery has venae comitantes that are very fragile; dissecting these veins can be treacherous. Bleeding from these veins is very troublesome and usually results in ligation of the veins themselves. For this reason and also for calcified tibial arteries, I prefer to use a tourniquet for inflow occlusion. Cracking the plaque on these tibial arteries can be very risky and can compromise the outflow artery.

After the proximal anastomosis is done, the tourniquet is placed above the knee. An Esmark bandage is used to exsanguinate the limb from the foot to the knee, then the tourniquet is inflated to roughly twice the patient's systolic blood pressure.

I open the tibial artery with an 11 blade that is used to serially score the arterial wall until the lumen is entered. A Dietrich-Potts scissors is then used to extend the arteriotomy. The graft is then cut and shaped to length; it should be noted that the arteriotomy should be at least 3 to 4 cm. The graft is then pulled to length and sutured in an end-to-side and fashioned with 7-0 Prolene.

The native artery is then forward and back-bled, the graft flushed and reclamped and the lumen flushed with heparinized saline. Under continuous retrograde bleeding from the artery, the suture line is tied down and flow is then restored into the native artery. Hemostasis is obtained and the incisions closed in the standard fashion.

The tourniquet technique is the most atraumatic of techniques for arterial anastomosis; I recommend its use for any infrapopliteal bypass in diabetics and in non-diabetics. Occasionally one will encounter arteries that, despite the tourniquet, are impossible to occlude. In these cases, one can use intraluminal flowresters.

Conclusion

Prosthetic bypass with Propaten appears to provide a reasonable alternative when suitable vein is not available and endovascular approaches have failed or are inadequate. The geometry of the anastomosis is critical for graft patency, and atraumatic, careful handling of the artery is critical for good short-term outcomes.

I put the patients on 48 hours of low-dose, unfractionated intravenous heparin for its anti-inflammatory properties, then stop the heparin. I do not routinely place patients with prosthetic bypasses on warfarin. Aspirin plus clopidogrel is my regimen of choice for tibial bypasses, though admittedly without supporting data.

If autogenous vein is available, this remains the gold standard for arterial reconstruction. If the vein is of poor quality, is inadequate or absent, then the use of Propaten for lower-extremity arterial reconstruction is a good alternative.

Ringed grafts, in my opinion, are rarely necessary and for infra-inguinal bypasses, the 6 mm diameter of the Propaten graft is the proper choice. For axillo-femoral or femoro-femoral bypass, 8 mm grafts are more appropriate.

The proper reconstruction of the arterial system must be considered in the context of the age of the patient, the functional goal of the operation, the options for conduit and the patient's ability to undergo extensive rehabilitation. A comprehensive assessment of the patient will help guide the most appropriate therapy of the patient with lower-extremity arterial disease.

Reference

1. Pulli R, Dorigo W, Castelli P, et al; Propaten Italian Registry Group. Midterm results from a multicenter registry on the treatment of infrainguinal critical limb ischemia using a heparin-bonded ePTFE graft. *Journal of Vascular Surgery* 2010;51:1167-1177.

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83 General Warren Blvd., Suite 100
Malvern, PA 19355
www.hmpcommunications.com