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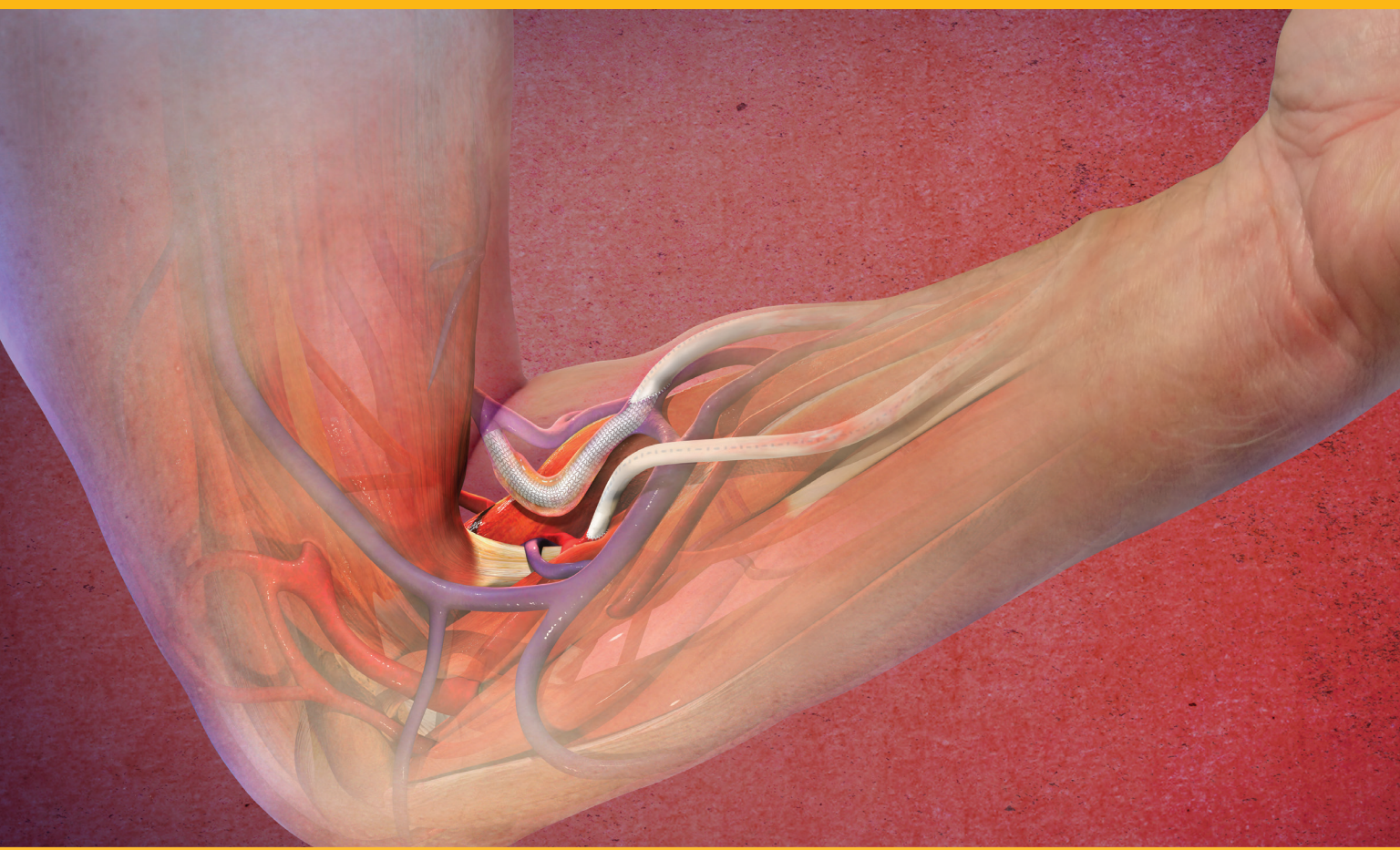

A review of how experts are managing the challenges of dialysis access.

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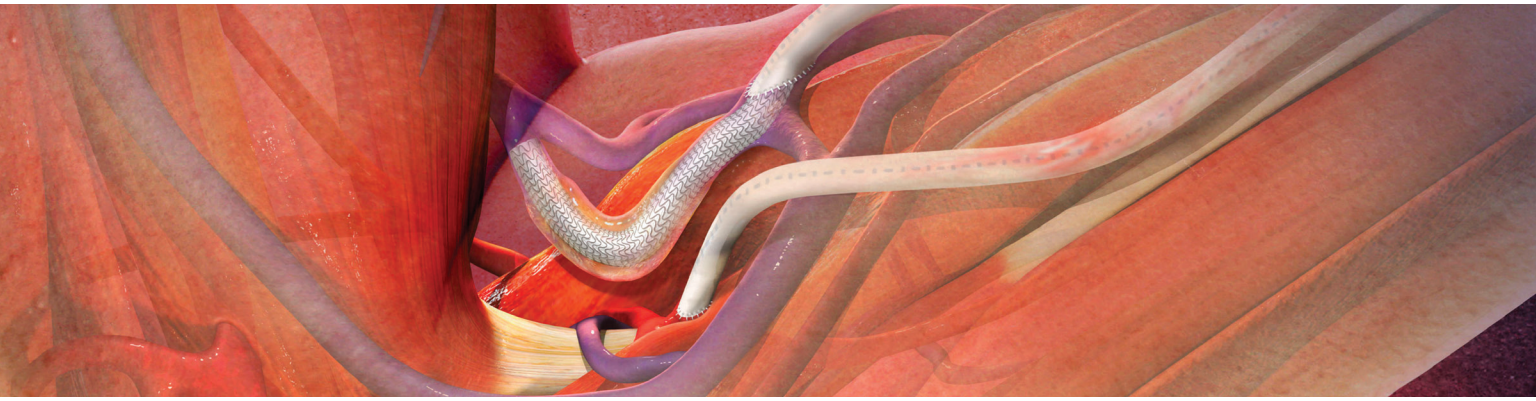

Bound to Perform: GORE PROPATEN Vascular Graft and CBAS Heparin Surface Technology

The role of grafts having end-point attached heparin in maintaining patency.

BY RICHARD NEVILLE, MD, AND JENNIFER RECKNOR, PHD

The Fistula First initiative mandates the construction of an autogenous arteriovenous fistula (AVF) as the primary choice for hemodialysis access. However, certain clinical scenarios remain that are best suited for a prosthetic arteriovenous graft (AVG). These scenarios include patients lacking suitable vein for or lack of maturation of an AVF. In these cases, a prosthetic AVG, most commonly expanded polytetrafluoroethylene (ePTFE), is indicated to establish permanent hemodialysis access despite a historic record of inferior primary and secondary patency compared to AVFs. Prosthetic AVGs are prone to thrombosis due to increased thrombogenicity and stenosis or occlusion as a result of an accelerated myointimal hyperplastic response. This myointimal hyperplastic occlusive process most commonly forms at the AVG-venous anastomosis due to hemodynamic flow disturbances, as well as the biologic response to the anastomotic construction.

The reasons for suboptimal performance with prosthetic grafts are biological and hemodynamic. Expanded PTFE grafts are more thrombogenic than autogenous conduits, with increased platelet adhesion and activation of the coagulation cascade.[1] Increased thrombogenicity at the graft surface results in thrombosis especially when blood flow falls below the critical thrombotic threshold. Late graft failure due to myointimal hyperplasia usually occurs 6 to 24 months after graft implantation. This hyperplastic response is the result of smooth muscle cell migration and proliferation, primarily at the toe and heel of the anastomosis, causing a reduction in lumen area, reduction in flow, and subsequent graft occlusion. The hemodynamic factors of shear stress and compliance mismatch have been implicated in prosthetic graft failure. However, an animal study addressing compliance did not prove compliance to be a significant factor in the formation of the hyperplastic response.[2] Anastomotic turbulence, oscillating shear forces, near wall residence time, and flow separation have been suggested as mechanisms of graft failure due to hyperplasia.[3]

IMPROVING PROSTHETIC GRAFT PERFORMANCE

The major cause of failure for prosthetic AVGs is thrombosis or significant stenosis due to neointimal hyperplasia. There have been biological and hemodynamic manipulations used in attempts to affect these failure mechanisms. In terms of hemodynamics, cuffed AVGs have been used involving stretch or non-stretch AVGs with the addition of a vein cuff. In terms of biological manipulation, AVGs having end-point attached heparin (CBAS Heparin Surface; Gore & Associates) have been utilized for hemodialysis access and reported better clot free survival than standard ePTFE alone. Even though follow-up in the series by Davidson et al was short, at less than 6 months for 38% of patients, 78% clot-free survival for the AVGs having the CBAS Heparin Surface versus 58% clot-free survival for the standard ePTFE at 1 year follow-up was reported.[4] There have been differences in

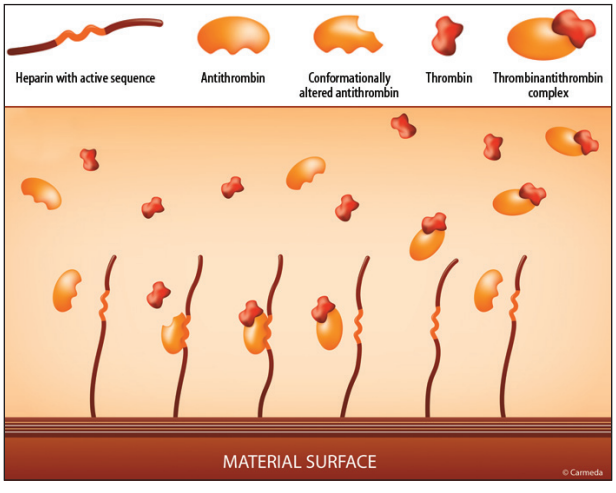

Figure 1. Illustration of CBAS Heparin Surface showing the material surface, base coating, and end-point attached heparin. Also shown are the reactants antithrombin, conformationally altered antithrombin, thrombin, and the inactive thrombin antithrombin complex.

neointimal hyperplasia between standard and heparin bonded graft use for dialysis access documented in animal models showing that compliance may play a role as shown by Gessaroli et al.[5] Therefore, potential solutions to improve the performance of a prosthetic graft for dialysis access includes affecting thrombogenicity through heparin bonding or affecting the development of myointimal hyperplasia by optimizing anastomotic compliance and hemodynamics.

CBAS Heparin Surface Technology and Benefits

One of the most clinically successful and innovative heparin bonding methodologies has been the CBAS Heparin Surface.[6,7] It is based on covalent end-point attached heparin to a biomaterial surface, enabling maintenance of functional heparin bioactivity. The end-point attachment mechanism, used in the CBAS Heparin Surface, preserves the heparin-active site and thus enables binding of the clotting factor inhibitor, antithrombin III (Figure 1).[7] Just as heparin functions in the solution phase, immobilized CBAS heparin is also catalytic. It is not consumed in the reaction by which antithrombin inhibits clotting factors such as thrombin. This retention of catalytic activity and the fact that the heparin is covalently attached and noneluting provides the potential for long-term immobilized heparin functionality clinically. The CBAS Heparin Surface can be applied to most medical device materials.[8] The coating is thin yet durable, usually in the range of hundreds of nanometers. When stored properly, CBAS-coated devices have an acceptable shelf life of at least 4 years. The CBAS coating can be sterilized by ethylene oxide, one of the common methods of device sterilization, without losing its mode of action. Furthermore, some of the key clinical performance benefits of end-point attachment of heparin on the CBAS Heparin Surface have been demonstrated in broad application, including extracorporeal circuits, vascular stents, ventricular assist devices, and ePTFE vascular grafts. The CBAS Heparin Surface has clinically shown a reduction of platelet deposition, a decrease in inflammatory responses,[9-11] and a reduction of thrombogenicity.[12-16]

Although there are many approaches for binding heparin to devices,[17] different immobilization techniques can affect the functional activity of the immobilized heparin. Immobilization of heparin to the surface alone does not necessarily ensure thromboresistance of that surface. Heparin can be bound by covalent attachment to material surfaces in different ways that adversely affect heparin's functional properties.[18] In contrast to covalent end-point attachment as employed in the CBAS Heparin Surface, heparin covalently bound by multipoint attachments along the heparin molecule can interfere with the critical pentasaccharide sequence in heparin known to be essential for its anticoagulant activity. Even end-point attachment of heparin can be performed in different ways and, generally, will not result in the unique functional properties[19] of the CBAS Heparin Surface. Each heparin-coating technology is individual and must therefore be judged according to its specific clinical performance. Tanzi[20] and Jordan[21] provide a relevant review of heparin and alternative technologies for improving biocompatibility of device materials.

The CBAS Heparin Surface has been in clinical use for nearly 25 years. It is the most widely published of all commercially available technologies of its type, providing evidence of the CBAS Heparin Surface hemocompatibility and biocompatibility benefits for short-term and permanent product applications, with few if any adverse events reported. More than 400 publications and studies have examined the hemocompatible properties of the CBAS Heparin Surface in controlled in vitro blood contact models or in vivo animal models and clinical studies. The continued commercial clinical application of this surface is based on a decade long track record of proven usefulness of this technology for improving the hemocompatibility of devices used for cardiovascular treatment.

The GORE ePTFE Vascular Graft with the CBAS Heparin Surface, the GORE PROPATEN Vascular Graft, was designed to improve the properties of vascular grafts with regard to thrombosis and, as a result, the clinical patient outcomes for cardiovascular disease treatment. The CBAS Heparin Surface is bound to the luminal surface of the GORE PROPATEN Vascular Graft. The CBAS Heparin is retained on the graft flow surface, is uniform in nature, and its functionality is maintained. With several hundred thousand GORE PROPATEN Vascular Grafts implanted worldwide, this graft has been reported to be widely used in contemporary practice.[22] In animal models and clinical applications, evidence has suggested that the GORE PROPATEN Vascular Graft is superior to uncoated grafts with patency rates comparable to autologous veins in humans.[23-26] By substantially reducing acute graft thrombosis within weeks after implantation, the CBAS Heparin Surface on the GORE PROPATEN Vascular Graft provides beneficial effects that standard ePTFE, control grafts do not.[27] The CBAS Heparin Surface has improved the clinical performance of prosthetic small-caliber vascular graft bypasses and has an important role in the management of lower extremity occlusive disease, with up to 4-year primary patency and limb salvage rates for the GORE PROPATEN Vascular Graft approaching historical results achieved with autologous vein conduits.[28-31] Furthermore, the CBAS Heparin Surface on the GORE

PROPATEN Vascular Graft has evolved to a clinically powerful technique for the hemodialysis patient resulting in a 20% improved clot-free survival at 1 year.[4] Other medical devices having the CBAS Heparin Surface that are used in peripheral vascular reconstruction and/or dialysis applications include the GORE ACUSEAL Vascular Graft, the GORE HYBRID Vascular Graft, and the GORE VIABAHN Endoprosthesis.

LOWER LIMB EXPERIENCE WITH CBAS HEPARIN: GORE PROPATEN VASCULAR GRAFT

The available worldwide experimental evidence and published clinical results point to significant durable clinical benefits of the CBAS covalent end-point attached heparin on the GORE PROPATEN Vascular Graft, imparting improved thromboresistance to the graft surface. The CBAS Heparin Surface may improve prosthetic graft performance by decreasing luminal thrombosis and the formation of myointimal hyperplasia. Reduced platelet deposition has been demonstrated in animal and human models as well as reduced thrombus formation on the inner surface of the graft.[25-27,32] A reduction in myointimal hyperplasia at the anastomotic site has also been demonstrated in animal models.[25,32,33]

Clinical trials in the lower extremity have supported these findings with improved patency rates as compared to historic controls of standard ePTFE. This is especially important in the below-knee position for tibial bypass in the lower extremity. Clinical bypass results with GORE PROPATEN Vascular Grafts have been described in nonrandomized, retrospective trials from Europe.[34,35] Although these trials included a limited experience with tibial bypass, they reported results superior to those obtained using standard ePTFE with 1 year patency for below knee popliteal bypass in the 80% range and 68% patency at 3 years. A retrospective comparison between the GORE PROPATEN Vascular Graft and saphenous vein grafts (SVG) for below-knee bypass demonstrated higher patency rates for the GORE PROPATEN Vascular Graft conduit although without reaching statistical significance, and concluded that the GORE PROPATEN Vascular Graft should be routinely considered for below-knee bypass.[28] Peeters reported 2 year patency rates of 73% for below-knee bypass and 69% for tibial bypass using heparin bonded ePTFE.[36] Patency specifically for tibial bypass was reported by Lösel-Sadée and Alefelder, who found 64% patency at 1 year for tibial bypasses using the GORE PROPATEN Vascular Graft.[37] Comparing the GORE PROPATEN Vascular Graft and vein for below-knee bypass, Battaglia and colleagues noted that vein graft patency was significantly better in patients with single-artery runoff and more severe symptoms at initial presentation.[38] Dorigo et al compared primary patency for in situ vein, standard PTFE, and the GORE PROPATEN Vascular Graft in a below knee bypass experience with patency rate at 18 months of 75% for vein, 40% for standard PTFE, and 53% using the GORE PROPATEN Vascular Graft. Early thrombosis was not significantly different between vein and the GORE PROPATEN Vascular Graft. However, patency results remained inferior compared to saphenous vein conduit.[39] Similar results were obtained on a larger scale as reported by the Italian Registry Group, with GORE PROPATEN Vascular Graft patency of 75% at 1 year and 61% at 3 years.[40]

In more recent podium presentations and publications, it was reported that GORE PROPATEN Vascular Grafts had improved clinical performance over standard ePTFE, especially in the most challenging patient populations.[41,42] Prospective and retrospective studies have led to the conclusion that peripheral arterial disease treatment using the GORE PROPATEN Vascular Graft is a clinically acceptable, safe alternative to treatment with native vein, especially disadvantaged vein.[29] The Scandinavian GORE PROPATEN Trial prospectively evaluated the GORE PROPATEN Vascular Graft across 11 centers in patients with chronic limb ischemia.[42] The GORE PROPATEN Vascular Graft was randomized against Stretch ePTFE Vascular Grafts in femoropopliteal (above-knee and below-knee) or femoral-femoral bypasses and demonstrated statistically significant improvement versus ePTFE in primary patency, secondary patency, and in patients with critical limb ischemia. It was determined that as severity of disease increases, the benefit of the GORE PROPATEN Vascular Graft increases.[42]

In a retrospective analysis of prospectively collected data, 112 tibial bypasses (62 GORE PROPATEN Vascular Graft, 50 SVG) were compared.[43] All GORE PROPATEN Vascular Graft bypasses were performed using an autologous vein patch at the distal anastomosis. At 1 year, the GORE PROPATEN Vascular Graft had a primary patency of 75.4% and SVG patency of 86.0% with the GORE PROPATEN Vascular Graft group including more reoperative procedures (45% vs 26%). There was no significant difference in primary patency due to gender, race, or diabetes mellitus. Results showing comparable primary patency and limb salvage rates with SVG at one year demonstrate that the GORE PROPATEN Vascular Graft is an effective alternative choice for patients with absent or poor quality saphenous veins that need a tibial bypass. The GORE PROPATEN Vascular Graft has emerged as the choice over arm vein, especially in the ESRD patient who needs upper extremity vein for dialysis access, and over composite short saphenous vein given the increased dissection required and length of conduit.

CONCLUSION

End-point attachment of heparin on ePTFE grafts using the CBAS Heparin Surface 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 Surface immobilization on the GORE PROPATEN Vascular Graft. The CBAS Heparin Surface provides important beneficial effects, which include sustained thromboresistance and reduced platelet attachment. These benefits may explain the promising below-knee and dialysis access clinical results attained with the GORE PROPATEN Vascular Graft, as well as the potential of other products utilizing the CBAS Heparin Surface technology. ■

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GORE® ACUSEAL Vascular Graft and Early Cannulation

Perspective on the potential patient care paradigm shift.

BY MARC H. GLICKMAN, MD

The number of patients starting dialysis with a central venous catheter (CVC) has not appreciably changed in the last decade; the percentage ranges from 78% to 82%.[1-3] There are many reasons for this lack of change in the CVC incident rate, including lack of early referrals, patient noncompliance, and an inability to undergo adequate and timely surgical intervention. Although attempts have been made to change these factors, the incidence of CVCs still remains high in the United States. The high morbidity and mortality rates associated with catheter dialysis are often noted within the first 90 days of starting dialysis.[4] Infection is the second most common cause of death in the hemodialysis population.[5] For this reason, the possibility of using an early cannulation graft for dialysis is intriguing in that reducing the time to catheter removal or avoiding catheters could have a positive impact on the dialysis population. This impact could result in a reduction in infections, improving mortality and morbidity in these patients, and possibly reducing the incidence of central vein stenosis.

A new graft developed by Gore & Associates is a trilayer expanded-polytetrafluoroethylene (ePTFE) graft composed of an inner layer of ePTFE bonded with CBAS Heparin Surface, a middle elastomeric layer, and an outer layer of ePTFE (Figure 1). Although there are reported cases of early cannulation with standard ePTFE grafts, hematoma formation and excessive bleeding are the major reasons that these standard grafts should not be cannulated within hours or days of implantation.

The GORE ACUSEAL Graft allows for early cannulation and is provided in three lengths. This includes a 6 mm × 40 cm graft for primary graft implant and a 6 mm × 10/20 cm graft for arteriovenous graft revisions. The use of the GORE ACUSEAL Graft for revisions due to infection or pseudoaneurysmal formation allows for extensive repair without the need for placement of temporary catheters, as this new graft may be accessed immediately without any increase in infection or hematoma formation (Figure 2).

A new 4 to 7 mm tapered GORE ACUSEAL Graft is on the horizon. The hope, as with any tapered graft, is that the incidence of steal will be reduced and allow for use in very high-risk steal patients.

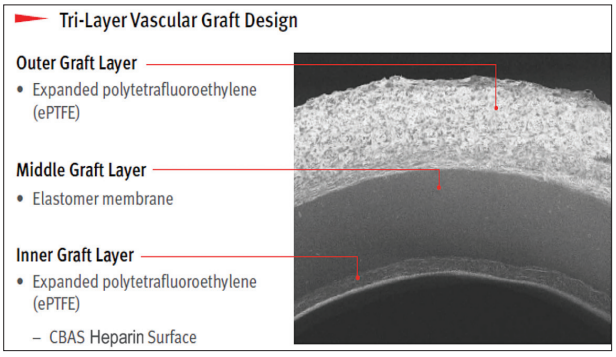


Figure 1. This is a scanning EM of the GORE ACUSEAL Graft demonstrating the three layers of the graft. The middle elastomer layer provides the "low-bleed" state of the graft.

SURGICAL IMPLANTATION

As opposed to other early cannulation grafts, the GORE ACUSEAL Graft does not have any particular tunneling needs. A Kelly Wick Tunneler (Bard Peripheral Vascular) or Sheath Tunneler (Bard Peripheral Vascular) may be used to tunnel the graft into position. Due to the slightly larger outer diameter (8.8 mm), a slightly larger sheathed tunneler needs to be used rather than the standard, commonly used devices.

The GORE ACUSEAL Graft has a strong radial force, and there has been no evidence to date of any kinking or compression of the graft. Sewing of this graft to the vessels is not mechanically different from sewing standard ePTFE grafts. Care should be taken to ensure that the arterial anastomosis is not overly large, staying within the 5 mm size. No special care is needed for the venous anastomosis. Surgeons find this graft easy to use and quite malleable in its handling properties, including a reduction in suture line bleeding (Figure 3).

One observation is how these grafts incorporate into the subcutaneous tissue. There are two different types of tissue incorporation. The majority of grafts become incorporated into the surrounding tissues like other ePTFE grafts. A subset of grafts, upon dissection, does not appear to be completely incorporated. This nonincorporation does not mean the graft is infected. To date, none of the nonincorporated

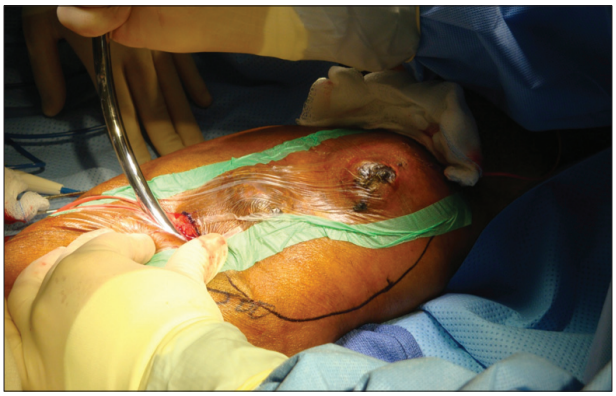
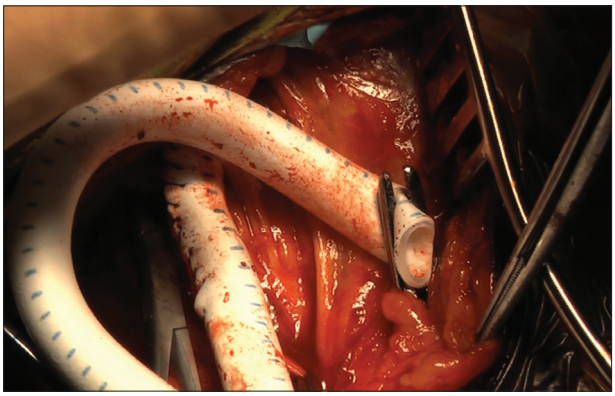


Figure 2. Tunneling of the graft and bypassing a large infected cannulation site.



(Courtesy of Eric Chernia, MD.)

Figure 3. This graft is easy to use and malleable in its handling properties. Tunneling with a large clamp/forcep may be less traumatic.

grafts has become infected. Therefore, if there are no signs of infection (ie, sepsis or purulence), then the nonincorporation does not mean infection, and the graft should remain in place. This is a new concept and a very important observation seen primarily in African American women.

EARLY CANNULATION GUIDELINES

Educating and working with the dialysis unit is an important first step in achieving good results with an early cannulation graft. Many of the staff members in dialysis units are not familiar with cannulating grafts in the early postoperative period, and educating the nursing staff is important for success. Many of the units' staff members may be resistant, but once they have experience, they will accept the concept of early cannulation, knowing the catheter will be able to be removed sooner.

Suggested guidelines for accessing early cannulation grafts include prepping the cannulation site with a bacteriostatic solution, having the nurse/technician wear sterile gloves, and using a 17 gauge dialysis needle for the first three sessions within the first 2 weeks of implantation, whichever comes first. The literature suggests using lower flows up to 250 mL/min as opposed to high flows up to 400 mL/min that are used later in a graft's history.[6] This means after a graft has been cannulated successfully three times, the higher normal flow rates can be used. However, our experience has shown that using near-normal flow does not increase any complication rate of early access with this device. The suggested lower flows are thought to reduce both turbulence and stresses on the venous anastomosis.[4] Some European dialysis units use the sterile glove technique, and this has resulted in an overall lower infection rate in their graft population.

It is important to note that the GORE ACUSEAL Graft is a low-bleed graft. This means that light pressure needs to be placed on the decannulation site for 10 to 15 minutes. The GORE ACUSEAL Graft is not a no-bleed graft; therefore, this light, constant pressure is needed to avoid any hematoma formation, particularly in the first weeks after implantation. Educating the dialysis unit staff is important regarding these patients in order to achieve excellent and successful results.

Catheter removal protocols vary from institution to institution. In certain European institutions, a slightly different and more aggressive approach is used than in most centers in the United States. For patients who already have catheters, these are removed the evening before the placement of the GORE ACUSEAL Graft. The graft is then cannulated within 24 hours of placement. These patients have a reduced incidence of seeding of the graft by an indwelling catheter. However, most centers in the United States use a slightly more conservative approach. If a patient already has a catheter, most centers wait for three consecutive dialysis sessions before removing it.[7] Although this is not totally "catheter avoidance," it does allow for a marked reduction in catheter dialysis days. This is still important and does shift the paradigm to reduce catheter-dependent dialysis days. As one obtains more experience with this new graft, we may be able to be more aggressive in avoiding long-term catheter placement by using temporary catheters for urgent dialysis and then switching promptly to this early cannulation graft.

PATIENT SCENARIOS WITH THE GORE ACUSEAL GRAFT

Case 1

A 76-year-old African American man presented to the emergency department with congestive heart failure and an elevated creatinine level. This patient was in stage 4 end-stage renal disease but was reluctant to undergo placement of any permanent access. The patient received a temporary dialysis catheter, 3 days of aggressive dialysis, and venous mapping. Venous mapping did not show any evidence of suitable veins.

The patient underwent placement of an upper arm straight GORE ACUSEAL Graft from the brachial artery to

(Continued on page 30)

Expanded Treatment Options With ePTFE Vascular Grafts Having CBAS Heparin Surface for Hemodialysis

Selection of best patient-centered dialysis access, using new and old technology, yields excellent outcomes: follow-up of 254 grafts.

BY INGEMAR DAVIDSON, MD, PHD; JOHN R. ROSS, MD; MICHAEL GALLICHIO, MD; AND DOUGLAS SLAKEY, MD, MPH

Disagreements surround the management of dialysis access patients, including proper selection of the dialysis modality (ie, hemodialysis [HD] vs peritoneal dialysis [PD]), type and surgical site selection, timing of access placement, and who places the access. The lack of and the difficulty of performing randomized studies with multiple confounding factors in a heterogeneous and rapidly changing end-stage renal disease (ESRD) population partly explains the dialysis access conundrum. The rapidly developing and competing technologies, socioeconomic forces, wide spectrum of the professional experience, and bias add to the multivariate and complex nature of dialysis access.[1]

INCONSISTENT OUTCOMES

In general, published dialysis access data are plagued by great variability. Reported outcome data are often influenced by study selection design bias and device variability. The large variability in outcomes is exemplified in Figure 1, in which dialysis graft function at 12 months after surgery varies from 10% to 78%.[2-15] This variability likely has many contributing components, such as the poorly defined but powerful "center effect," in which local system factors like dialysis access team training, technical skills, professional dedication, and bias and institutional support profoundly affect outcomes. Two recent blinded randomized studies by the Dialysis Access Consortium underscore the generally poor outcomes reported for both the grafts and native veins used for dialysis access.[14,15] One serious confounding bias in these studies is that PD is not considered or included in the selection process.

Graft thrombosis is the most common dialysis graft dysfunction. In 90% of thrombosed grafts, the underlying pathology leading to thrombosis is neointimal hyperplasia at the venous anastomosis associated with turbulent flow.[16] This phenomenon is largely prevented by an end-graft to end-vein anastomosis configuration. The end-graft to end-vein anastomosis can be accomplished by a new

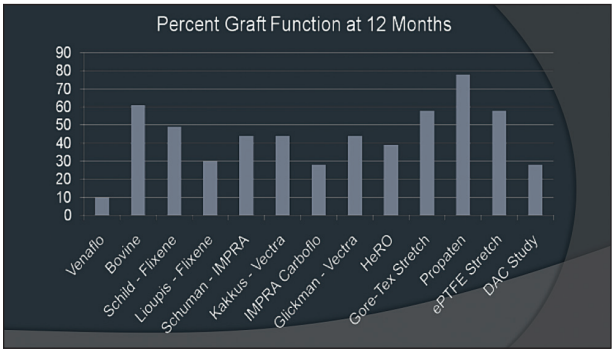


Figure 1. Published graft function outcome data at 1 year varies between 10% and 78%.

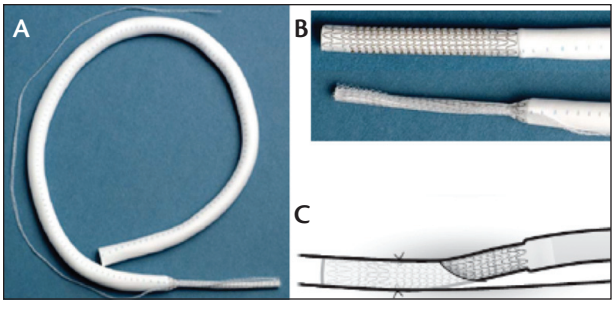


Figure 2. The GORE Hybrid Vascular Graft, with end-point attached heparin, has a 5 or 10 cm length nitinol-reinforced segment that is placed into a vein by pulling a deployment line (A). The nitinol segment (available in 6, 7, 8, and 9 mm diameters) is shown before and after deployment (B). End-graft to end-vein endoluminal anastomosis (C).

graft design in which the nitinol end is deployed into the vein (Figure 2).

Other etiologies occurring alone or in combination with intimal hyperplasia may contribute to graft thrombosis. These include poor arterial inflow caused by an arterial stenosis (atherosclerosis calcification plaques) commonly seen in patients with chronic kidney disease who also have diabetes, hypertension, and a history of cigarette smoking.[17]

Poor access inflow may also be seen in patients with impaired cardiac function, such as myocardial infarction, congestive heart failure, low blood pressure during and between the dialysis sessions, decreased blood volume, and dehydration, all of which may precipitate access thrombosis.[18,19]

Central venous and/or superior vena cava stenosis, uniformly caused by central venous catheters (CVCs), may not be associated with graft thrombosis but rather arm swelling. Cannulation difficulties then become a contributing factor to thrombosis from perigraft hematoma compression. A previous history of CVC placement is the most important risk factor for the development of central venous stenosis. Multiple CVCs and long dwell times increase the probability of stenosis.[20]

When no anatomical explanations are found, hypercoagulable states are investigated for increased platelet activity common in renal patients, as well as elevated serum fibrinogen, von Willebrand factor, factor VIII, C-reactive protein, and the presence of anticardiolipin antibodies and/or lupus antibodies.[21,22] In some cases, the patient may have one or more elevated clotting factors.[22]

CBAS HEPARIN SURFACE TECHNOLOGY

The proprietary CBAS Heparin Surface was developed by Carmeda AB, a company in Sweden that is a wholly owned subsidiary of W. L. Gore & Associates, Inc. Heparin, a polysaccharide anticoagulant, is bonded directly to the luminal surface of expanded polytetrafluoroethylene (ePTFE) grafts. The proprietary end-point attachment mechanism (CBAS Heparin Surface) serves to anchor heparin molecules to the luminal surface, allowing for prolonged retention of heparin's intrinsic bioactive properties. Antithrombin (AT), a coagulation inhibitor that circulates in the blood, serves as the mechanism of action and binds to the active site of the heparin molecule. Thrombin, a coagulation protein, binds to the AT and loses its ability to convert soluble fibrinogen into insoluble strands of fibrin. The CBAS heparin catalyzes (up to 1,000 fold) the inactivation of thrombin by antithrombin.[23] It is not consumed nor destroyed in this reaction. Controlled animal studies and isolated clinical explants demonstrate prolonged persistent heparin bioactivity.[24,25]

HEPARIN BONDED (CBAS HEPARIN SURFACE TECHNOLOGY) GRAFTS AND STENT-GRAFTS ON THE US MARKET

- GORE PROPATEN Vascular Graft 4 to 7 mm tapered configuration for dialysis and 6 mm straight for peripheral vascular surgery.
- Nitinol end-graft to end-vein (GORE Hybrid Vascular Graft).
- Stent-graft for peripheral and venous anastomosis revision stenting (GORE VIABAHN Endoprosthesis with Heparin BioActive Surface).
- GORE ACUSEAL Vascular Graft for early cannulation.

In vitro experiments have demonstrated the antithrombotic properties of CBAS Heparin Surface technology. For example, there is a > 80% platelet adhesion inhibition compared to the control.[25,26] Heparin has a potent antiproliferative effect on vascular smooth muscle cells. Animal studies have repeatedly confirmed that the CBAS Heparin Surface of the GORE PROPATEN Vascular Graft prevents neointimal hyperplasia in the ePTFE graft portion but not in the native vein distal to the graft-vein anastomosis.

There is a general consensus that the grafts having end-point attached heparin stay patent despite low flow secondary to stenosis and other pathology, partly explaining the higher intervention-free survival rate. This fact allows more time for interventions to take place, such as balloon angioplasty and stenting.

The available vascular grafts and stent-grafts having end-point attached heparin are depicted in the *Heparin Bonded (CBAS Heparin Surface Technology) Grafts and Stent-Grafts* sidebar. The 4 to 7 mm tapered GORE PROPATEN Vascular Graft is designed for hemodialysis access and has characteristics similar to the stretch graft. Clinical trials have demonstrated the enhanced patency of the GORE PROPATEN Vascular Grafts in peripheral surgery over the standard ePTFE. The unique, stable, proven CBAS Heparin Surface technology maintains the anticoagulant activity of heparin.[26]

THREE DATA SETS FROM ONE INSTITUTION

A prospective, nonrandomized, single-center study compared the 4 to 7 mm heparin bonded ePTFE vascular grafts (N = 73) (GORE PROPATEN Vascular Graft) to 4 to 7 mm standard ePTFE grafts (N = 67) between January 1, 2007, through October 1, 2009. Hospitals initially restricted graft use due to cost, and the GORE PROPATEN Vascular Grafts were selected only for difficult "high-risk" patients, most commonly with several past failed access procedures. At 12 months, 65% of the

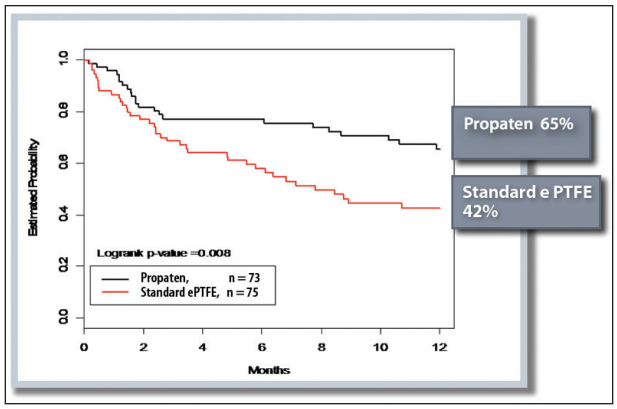


Figure 3. Heparin bonded ePTFE grafts (Propaten) had a 23% clot-free (intervention-free) survival benefit over the standard ePTFE grafts.

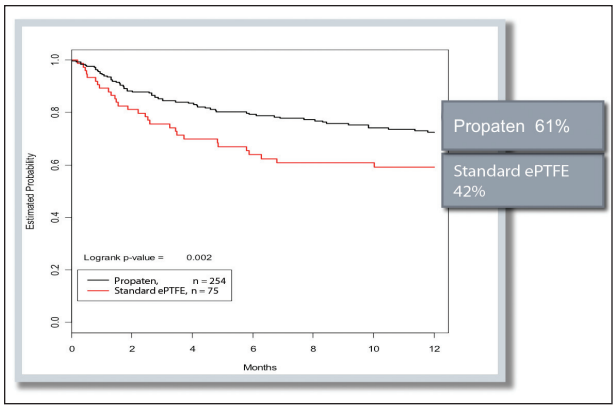


Figure 4. Clot-free (intervention-free) survival at 12 months for 254 heparin bonded ePTFE grafts (Propaten) had a 19% benefit (*P* = .002) over the standard stretch ePTFE graft.

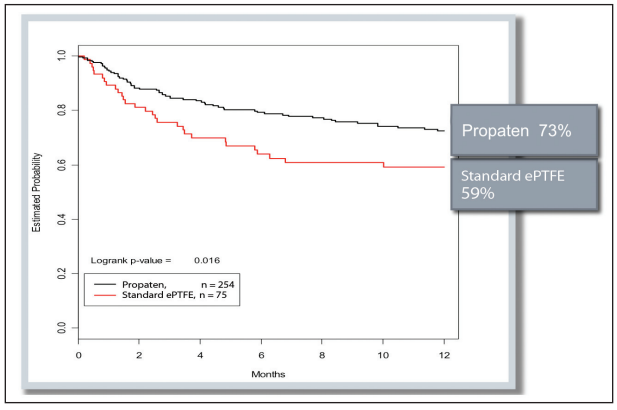


Figure 5. Graft survival at 12 months for 254 heparin bonded ePTFE grafts (Propaten) had a 14% benefit (*P* = .016) versus 75 control patients receiving a standard ePTFE graft.

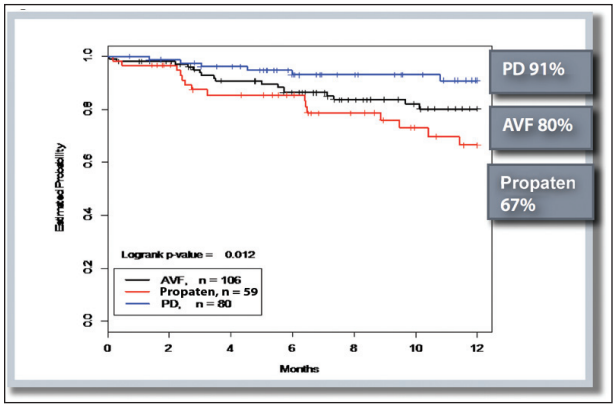


Figure 6. The clot-free (intervention-free) survival rates for peritoneal dialysis, AVF, and heparin bonded ePTFE grafts (Propaten) were 91%, 80%, and 67%, respectively.

GORE PROPATEN Vascular Grafts (Propaten) remained clot-free compared to 42% of the standard ePTFE grafts, a 23% benefit (*P* = .008) (Figure 3).[2]

Since mid 2008, the GORE PROPATEN Vascular Graft was made freely available, explaining the recent larger GORE PROPATEN Vascular Graft cohort. With the larger GORE PROPATEN Vascular Graft cohort of 254 implants, intervention-free and graft survival continued to show a 19% (*P* = .002) and 14% (*P* = .016) benefit over the historic control, respectively (Figures 4 and 5).

These outcome data are further supported by a recent dialysis access experience for the calendar year of 2012, including 393 access procedures. PD and HD accounted for 81 (33%) and 166 (67%) of new dialysis access cases, respectively. Revisions accounted for 38% of the procedures. Of the HD cases, 106 (65%) were native vein arteriovenous fistulas (AVFs), and 59 (35%) were GORE PROPATEN Vascular Grafts in a loop configuration.

One year patient survival was similar for PD and native vein AVFs (98%) and PTFE grafts (92%; [NS]). Patients receiving grafts were, on average, 6 years older (or 58 years of age) compared to 52 years of age for the PD and AVF patients. The freedom from intervention survival rates for PD, native vein AVFs, and GORE PROPATEN Vascular Grafts were 91%, 80%, and 67%, respectively (Figure 6). Although PD provided the highest access function survival rate of 91%,[27] the relative ease of revisions and thrombectomy of the grafts provided similar or slightly better graft survival (85%) at 1 year compared with native vein AVFs (81%; [NS]) (Figure 7).

SUMMARY

With the selection philosophy of doing the right thing for every patient at all times, dialysis access treatment outcomes are optimized for each patient. Access function at 1 year in excess of 90% was achieved with PD, followed by GORE PROPATEN Vascular Grafts of 85%, and native vein AVFs of 81%. GORE PROPATEN Vascular Grafts had an approximate 20% improvement in clot-free (intervention-free) survival over standard ePTFE grafts at 1 year. ■

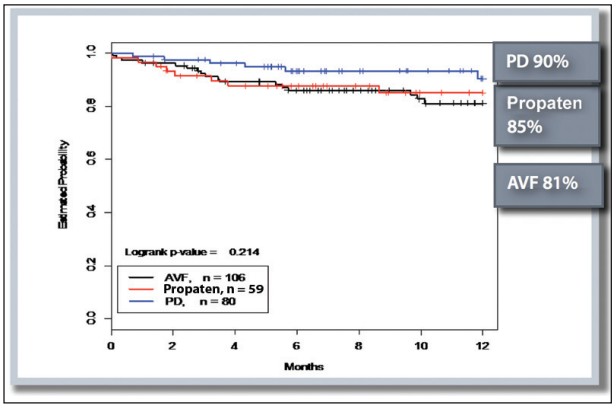


Figure 7. One year dialysis access function was highest for PD at 90%. Because of the relative ease to re-establish function of thrombosed grafts compared to native vein AVFs, the heparin bonded ePTFE grafts (Propaten) had similar or slightly better graft function at 1 year compared to AVFs of 85% and 81%, respectively.

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Challenging Hybrid Cases: How We Do Them

How the GORE Hybrid Vascular Graft can be used to treat complex dialysis cases.

BY SHAWN M. GAGE, PA-C, AND JEFFREY H. LAWSON, MD, PHD

The primary intent of the GORE Hybrid Vascular Graft is to create a sutureless end-to-end vascular anastomosis, possibly reduce intimal cell proliferation, and improve flow hemodynamics in the outflow track of arteriovenous access or arterial bypass circuits. The expanded polytetrafluoroethylene (ePTFE) transition to stent-graft (nitinol-reinforced section) design creates an end-to-end anastomosis and maintains laminar flow from the graft conduit into the recipient vessel.[1] Extensive fluid and flow dynamics testing suggests that this design significantly reduces the vessel wall shear stresses conveyed on the outflow track when compared to a conventional end-to-side, sutured anastomosis (Figure 1).[2,3] Presently, there are no peer-reviewed clinical data that prove altering the outflow dynamics with this device has truly had an impact on the genesis of neointimal hyperplasia or overall graft patency. However, as in the case of most novel technology, ideas for new and innovative applications are often discovered, and as such, there has been success with expanded application of the GORE Hybrid Graft in various cases and complex situations.

The GORE Hybrid Graft has been used for complex vascular access, peripheral bypass, carotid reconstruction, and renal and mesenteric artery reimplantation during aortic debranching surgery.[4-6] In this article, we describe two cases in which we used the GORE Hybrid Graft to address challenging situations in complex dialysis access.

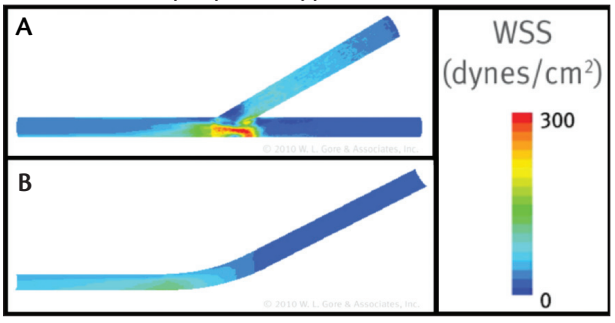

Figure 1. Computational fluid dynamics testing comparing conventional end-to-side anastomosis (A) to GORE Hybrid Graft (B), which demonstrates significant reduction in wall shear stresses with the GORE Hybrid Graft endoluminal anastomosis. The model depicts 600 mL/min flow, 4.8 mm anastomosis at a 30° angle.

CASE 1

A 53-year-old African American man on hemodialysis for more than 15 years presented with frequent thrombosis of his right upper arm graft. Previously, he had an ePTFE graft placed to salvage a basilic vein transposition fistula on the anteromedial aspect of the upper arm. Subsequent to failure, that access was then salvaged by placing a GORE Hybrid Vascular Graft with a 7 mm × 5 cm Nitinol Reinforced Section (NRS) from the brachial artery to the axillary vein that had become dysfunctional secondary to intimal hyperplasia and severe venous outflow stenosis just beyond the anastomosis. Additionally, a GORE VIABAHN Endoprosthesis (8 mm × 5 cm) was used to extend the outflow by overlapping it with the NRS of the GORE Hybrid Device.

The patient's GORE Hybrid Graft had been working extremely well for nearly 3 years until he developed frequent clotting episodes, which required multiple thrombectomy procedures. When the most recent angiograms were reviewed, they revealed a very mild narrowing of the outflow vein just beyond the GORE VIABAHN Endoprosthesis and no significant technical issues within the graft. The mild narrowing did not seem to be flow limiting, but it was noted that the patient had discontinued his antiplatelet therapy several months previously in addition to having newly developed hypotension after dialysis. His antiplatelet therapy was reinitiated, as was midodrine to support his blood pressure in an attempt to prevent future thrombotic events.

Unfortunately, the patient presented to clinic 1 month later having thrombosed his graft despite the previously prescribed therapy. The decision was made to thrombectomize the graft in an open fashion so as to expand the potential options for revision. The GORE Hybrid

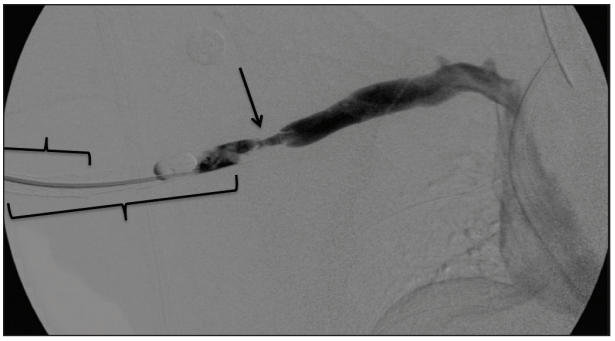

Figure 2. Intraoperative angiogram, before second GORE Hybrid Graft placement. Previous Hybrid NRS (top bracket) and previous Gore VIABAHN Device (bottom bracket). Severe stenosis central to the GORE Hybrid Graft NRS (arrow).

Graft was accessed via surgical exposure distally, near the arterial anastomosis, and the inflow was successfully thrombectomized using a compliant thrombectomy balloon. We attempted thrombectomy of the venous limb but had significant difficulty crossing the cannulation segment. We were able to eventually traverse the cannulation segment with a wire and directional catheter, but attempts at thrombectomy were unsuccessful. Angiography of the venous outflow identified aggressive stenosis of the outflow vein just central to the NRS of the previous GORE Hybrid Graft and VIABAHN Device (Figure 2).

Due to our inability to satisfactorily thrombectomize the entire graft, we decided to once again salvage this right upper arm access site by placing a new GORE Hybrid Graft. At this point in the patient's dialysis access history, he had had three previous concentric grafts in the right upper arm, with each new graft being placed just lateral to the last. Geometrically speaking, placing a new graft just lateral to the previous, in this case, would have been more technically challenging and would have likely exposed the graft to a mechanical complication such as kinking or torsion. As such, we decided to place the new GORE Hybrid Graft medial to the previous three grafts.

An incision was made in the axilla proximal to the venous anastomosis from the previous graft (through which the currently thrombosed GORE Hybrid Graft had been inserted). We identified the thrombosed GORE VIABAHN Device within the axillary vein. The vein and stent-graft were transected, and the new 7 mm × 10 cm GORE Hybrid Graft was inserted under direct visualization into the previously stented axillary vein. Completion angiography noted successful treatment with the 10 cm NRS, but there was a residual stenotic segment just central to the GORE Hybrid Graft. Extension of the NRS with an 8 mm × 5 cm GORE VIABAHN Device provided an excellent final result (Figure 3). Finally, the GORE Hybrid Graft was tunneled distally (and medial to the previous grafts), utilizing the cuff of the previous graft for arterial inflow. A graft-to-graft anastomosis was completed using a 5–0 GORE suture (1:1 ratio, needle-to-suture diameter). The patient returned to the vascular clinic 2 weeks after the procedure with a well-functioning arteriovenous graft (Figure 4).

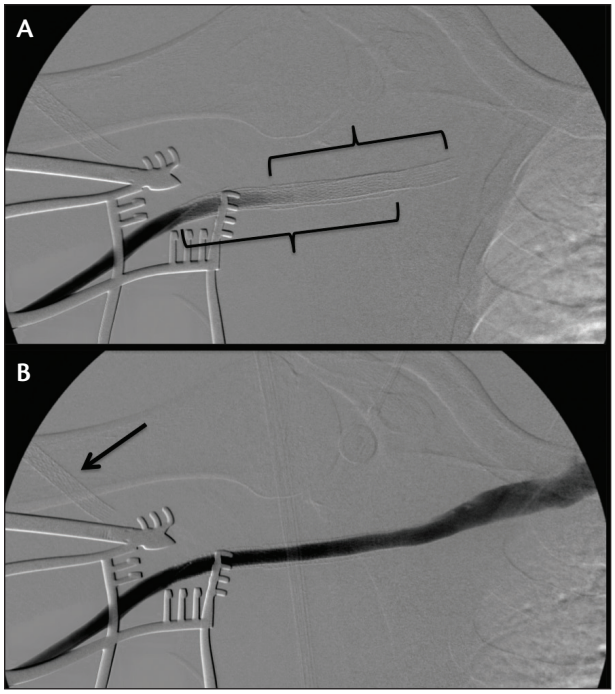

Figure 3. After second GORE Hybrid implant (A): 10 cm NRS (bottom bracket) overlapping with extension of 5 cm GORE VIABAHN Device (top bracket). Successfully treated venous stenosis after GORE Hybrid Graft deployment with patent central veins noted (B). Previously placed Hybrid NRS and VIABAHN Device (transected) (arrow).

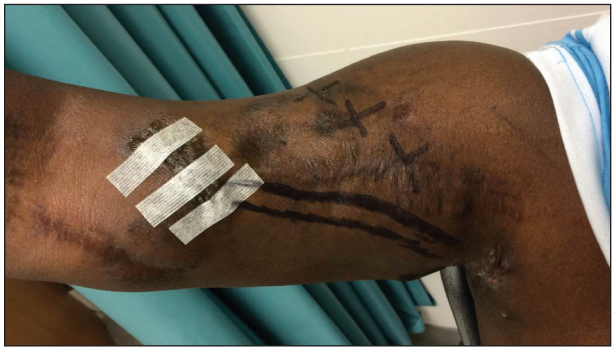

Figure 4. Two weeks postprocedure. Four concentric grafts in the right upper arm with an "X" to denote each. The outlined, and most medial graft, is the new, functional GORE Hybrid Graft.

CASE 2

A 56-year-old African American woman was seen 18 months after placement of a right upper extremity hemodialysis reliable outflow (HeRO) graft (Hemosphere/CryoLife, Inc.) for central venous occlusion. She presented to the vascular clinic with new development of a right upper extremity firm fluid collection in the right axilla in the region of the arterial anastomosis (Figure 5). She did not report fever, chills, or tenderness, and the graft was otherwise working extremely well for hemodialysis. The graft had recently thrombosed and was successfully thrombectomized at an outpatient vascular access center just weeks before. Based on exam, the working diagnosis was weeping syndrome (graft ultrafiltration), but the timing did not make sense for a classic presentation. Typically, weeping syndrome occurs near the arterial anastomosis immediately after graft implantation due to failure of the plasma proteins to seal the air interstices of an ePTFE graft.

At the time of the initial HeRO Graft implantation, there was a strong concern for the development of steal syndrome due to the small arterial anatomy of the patient, so the graft segment of the HeRO Graft was replaced with a 4 to 7 mm tapered graft. We presumed that it had not been appreciated that the graft was tapered and that the operators, thinking that an acquired arterial stenosis had developed, treated this region with balloon angioplasty at the time of graft thrombectomy, thus overstretching and damaging the ePTFE, which allowed plasma to leak from the graft to develop a large collection.

The patient was taken to the operating room for evacuation of fluid and gelatinous material and stent-graft placement in the most proximal 5 cm of the graft adjacent to the arterial anastomosis, our treatment of choice for weeping syndrome (Figure 6). The patient presented to the clinic 2 weeks later with complete reaccumulation of fluid at the site. To date, we had never observed this degree of fluid reaccumulation after treating weeping syndrome. This made us concerned that fluid was still leaking around the stent-graft due to lack of apposition of the stent to the graft wall secondary to the tapered configuration of the graft or incomplete deployment of a slightly oversized stent (Figure 7).

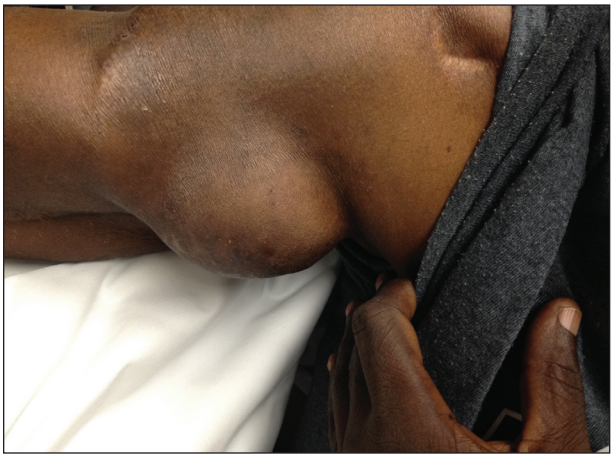

Figure 5. Right upper extremity graft ultrafiltration fluid collection over arterial anastomosis weeping syndrome.

Access abandonment was considered; however, the patient had no further options due to her central vein occlusion and limited inflow. We had already decided to proximalize her inflow from the brachial to the axillary position and to use a tapered graft at her initial operation to avoid steal syndrome. We were determined to maintain her current inflow, as this was virtually the patient's last option for access salvage. In order to preserve her inflow, we decided to use the GORE Hybrid Graft to create a sealed, sutureless, arterial anastomosis between the previously placed stent-graft and the GORE Hybrid Graft.

So as to avoid damaging the stented portion of the graft, a compliant balloon was inserted through the graftotomy and inflated for arterial control. The existing tapered graft was transected from around the balloon catheter and removed. The 6 × 50 mm GORE Hybrid Graft was then inserted into the previous graft and

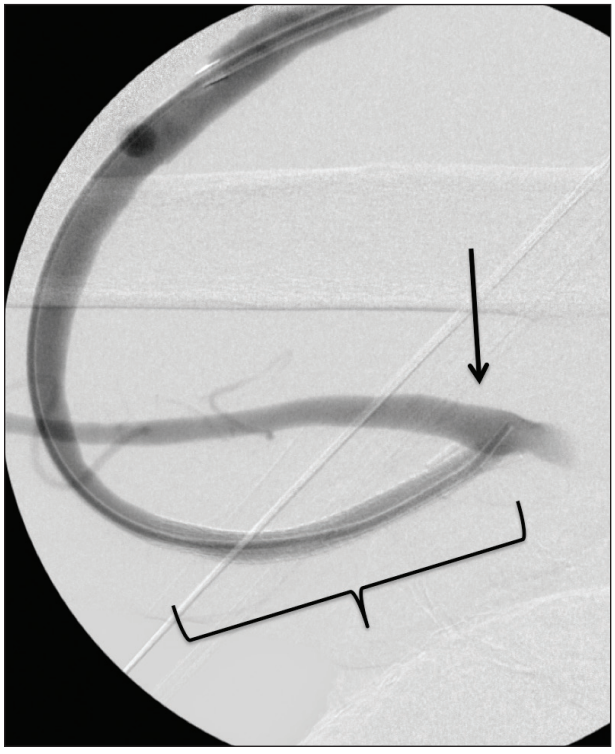

Figure 6. Completion angiogram from the first operation to repair weeping syndrome (stent-graft, bracket; arterial anastomosis, arrow).

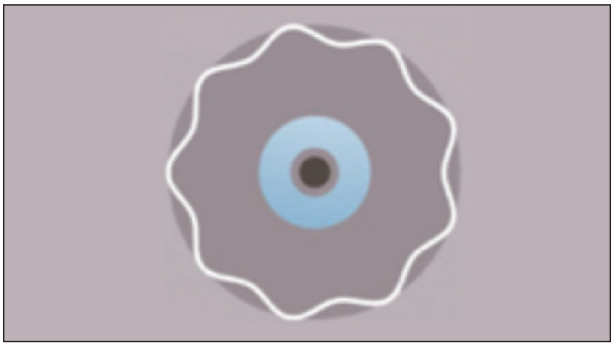

Figure 7. Incomplete deployment and nonapposition of oversized stent-graft within vessel.

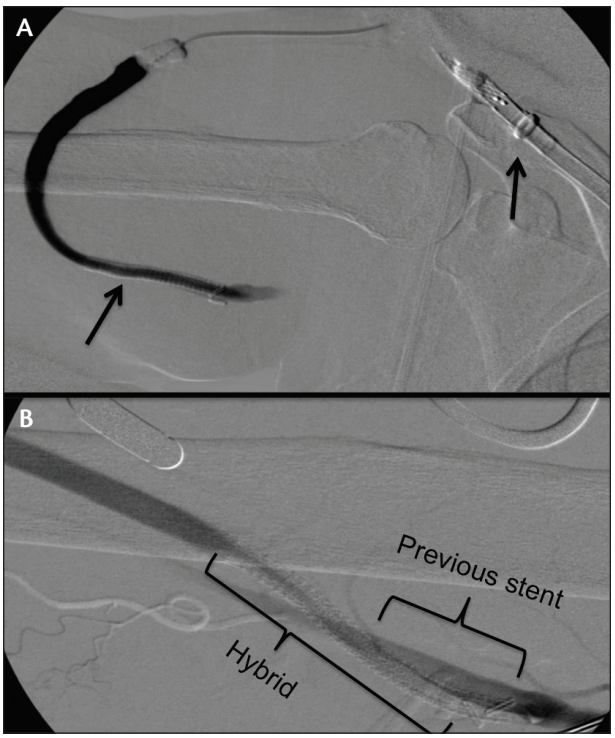

Figure 8. Previously deployed stent-graft within 4- to 7 mm tapered graft before stent transection (left arrow); HeRO Graft titanium connector (right arrow) (A). Completion angiogram of deployed GORE Hybrid Graft within transected stent-graft (B).

stented segment and deployed (Figure 8). The GORE Hybrid Graft was tunneled, the HeRO Graft cannulation segment was interposed and replaced with the GORE Hybrid Graft, and a graft-to-graft anastomosis was created near the titanium connector of the HeRO Graft venous outflow component. Once again, the plasma-rich gelatinous material was evacuated from around the original arterial anastomosis, irrigated, and closed. The patient presented at the clinic 2 weeks after the operation with a well-functioning HeRO Graft/GORE Hybrid Graft, without evidence for graft ultrafiltration.

CONCLUSION

These cases demonstrate the expanded utility of the GORE Hybrid Graft to rapidly accomplish a sutureless end-to-end anastomosis in challenging cases in which limited alternative options exist. The utility of this goes far beyond improvement of the flow dynamics at the anastomosis and recipient vessel. The graft has become an effective adjunct in complex and often convoluted vascular cases in which we now have an improved ability to treat patients in the most effective way: open surgery, endovascular therapy, or a hybrid combination of the two. As such, the GORE Hybrid Graft takes advantage of both conventional open vascular graft and endovascular stent technologies and maintains the current trajectory and natural evolution toward minimally invasive and cutting-edge vascular surgery. ■

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Stent-Graft Sizing for AV Access Creation and Revision Procedures

Wall apposition is not necessary for quality results.

BY JOHN R. ROSS, MD

Creating and maintaining a functional vascular access in many hemodialysis patients remains a significant challenge due to an increasingly complicated end-stage renal disease patient population with significant comorbidities and multiple previous failed arteriovenous (AV) access attempts. Many of these patients may not be suitable candidates for creation of an AV fistula, and an AV graft (AVG) may be the preferred method of AV access creation.[1] Although it is essential to create a functional access and attempt to maintain that access as long as possible, it is also imperative to plan each patient's possible revision strategy.

This article describes sizing and positioning of the GORE VIABAHN Endoprosthesis and the GORE Hybrid Vascular Graft (Gore & Associates) for AV access creation and revision procedures. My experience, recent clinical data, and computational fluid dynamics (CFD) studies have demonstrated that a lack of vein wall apposition at the distal tip of stent-grafts placed in an outflow vein are not necessary in order to provide quality long-term results.

CREATION STRATEGIES: INFLOW, OUTFLOW, CONDUIT

When creating an access, there are three components that must be carefully considered: the inflow, the outflow, and the conduit. There must be adequate inflow to sustain flow in an access and, similarly, adequate outflow to accept the blood going through the conduit. When choosing a synthetic conduit, the patient must be evaluated in terms of anatomy, location, and size of their veins and arteries, previous access history, and the potential need for early cannulation. The configuration of the conduit must also be considered. One conduit of choice, especially for the complex patient, is the GORE Hybrid Graft.

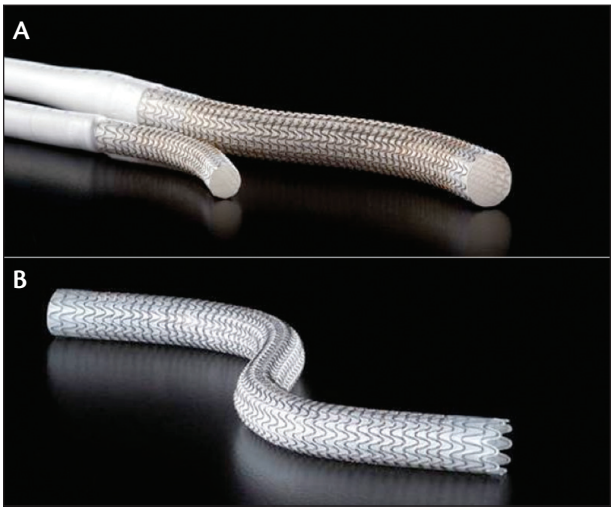

Figure 1. The GORE Hybrid Vascular Graft (A) and the GORE VIABAHN Endoprosthesis (B).

The GORE Hybrid Graft is an expanded polytetrafluoroethylene (ePTFE) graft with a Nitinol Reinforced Section (NRS) on one end (Figure 1A). The GORE Hybrid Graft includes the CBAS Heparin Surface, consisting of covalent end-point attached heparin on the luminal surface. The constrained NRS can be deployed into a vessel, resulting in a sutureless end-to-end anastomosis. The venous anastomosis can be performed with a minimally invasive, over-the-wire technique. This technique allows one to access the adequate outflow vein in patients with challenging anatomy and/or deep vessels.

REVISION STRATEGIES: ESTABLISHING A NEW OUTFLOW

Formation of neointimal hyperplasia at the venous anastomosis remains the most common cause of AVG failure, many times requiring multiple interventions to

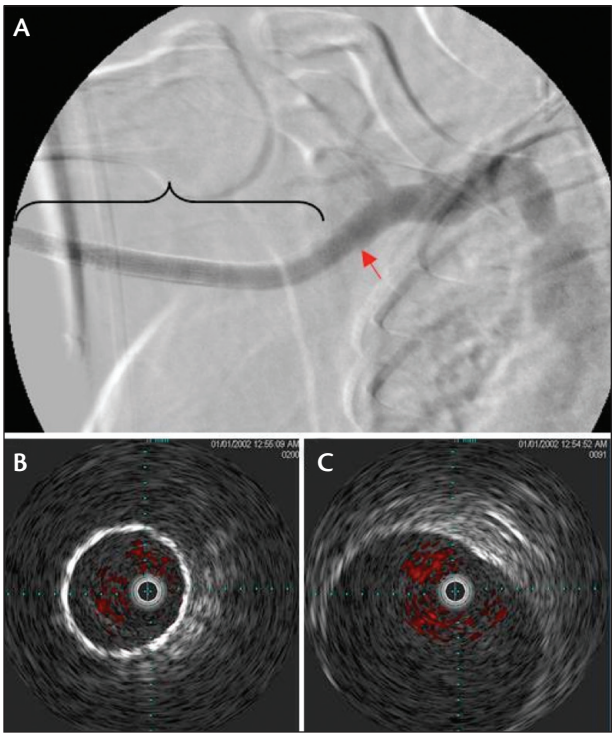

Figure 2. Case example of the GORE VIABAHN Device (bracket) extending an AV access graft into a larger outflow vein (arrow). The angiographic view demonstrates little-to-no backflow observed (A). Intravenous ultrasound visualizes the smaller-diameter cross-section of the GORE VIABAHN Device (B) as compared to the outflow vein (C).

maintain graft patency.[2] If an AVG fails due to outflow stenosis or thrombosis, the use of the GORE VIABAHN Device should be considered. The GORE VIABAHN Device is constructed with a durable, reinforced, biocompatible, ePTFE liner attached to an external nitinol stent structure (Figure 1B). It is indicated for the treatment of stenosis or thrombotic occlusion at the venous anastomosis of synthetic AV grafts.

STENT-GRAFT SIZING CONSIDERATIONS

The strategy for sizing a stent-graft, whether in the arterial system or the venous system, has historically been to oversize with respect to the recipient vessel. Data demonstrate that, in the arterial system, the GORE VIABAHN Device should be oversized by 5% to 20%, but that oversizing by more than 20% results in decreased patency rates.[3]

While it is recommended to oversize a stent-graft to the recipient vessel by 5% to 20% to ensure adequate anchoring, in the venous system, I always ensure that the size of the distal tip of the stent-graft (or NRS of the HVG) is smaller than the adequate outflow vein, providing robust flow through the device and good long term results (Figure 2). Of course for stent-grafts, I first ensure that I have adequately sized to

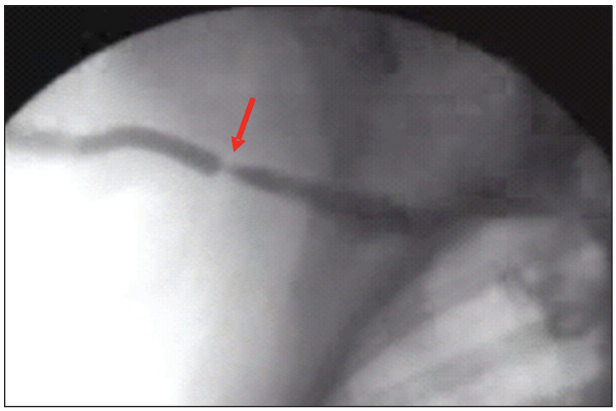

Figure 3. Example of oversizing a stent-graft in the venous system by more than 20%, resulting in acute spasm at the end of the stent-graft (red arrow).

the inflow in order to gain wall apposition for anchoring of the device and to prevent migration. In my experience, oversizing the outflow in the venous system can produce an acute spasm at the end of the stent-graft (Figure 3) and/or rapid end-stent stenosis, resulting in poor long-term outcomes. It is unclear whether this phenomenon is due to improved hemodynamics, lack of foreign body response, larger outflow considerations, and/or some other response.

CLINICAL OUTCOMES OF LANDING IN A LARGE OUTFLOW VEIN

I choose to use the GORE VIABAHN Device as a de novo treatment for strictures > 2 cm long or those that do not respond well to percutaneous transluminal angioplasty (PTA). In my experience, the longer strictures tend to have a high recurrence rate. Short strictures that either have a high-grade stenosis or that immediately rebound after PTA also tend to have a high recurrence rate. In those instances, the natural history of the AV access has declared itself to be unresponsive to PTA, and that patient is destined for frequent visits to the operating room unless an alternative treatment method is chosen. The GORE VIABAHN Device will change the natural history of that access by excluding the compromised vein from the AV access circuit. In my experience, the outcomes of the device tend to be more durable than other endovascular techniques and should work for the majority of patients with large outflow veins for at least 9 to 12 months before recurrence.

The durability of the GORE VIABAHN Device, however, can be affected by the choice of landing zone. Often, I will seek to not only overcome the stricture but also reach an outflow vein > 9 mm or at least 1 mm greater than the device, as demonstrated in Figure 2. The longer length options of the GORE VIABAHN Device allow the device to reach larger healthy vessels without the need for placing multiple devices.

The GORE Hybrid Vascular Graft adds significant options, particularly when creating an access in a patient with a violated axilla. This is a patient with an axilla that has had multiple explorations with multiple grafts in place and/or a patient with a massively obese arm. The GORE Hybrid Graft is also a valuable tool when a patient does not have an adequate target vein in the axilla but has an adequate outflow vein higher up toward the chest wall.

The GORE Hybrid Vascular Graft comes with an NRS of four different diameters (6, 7, 8, and 9 mm) and in two lengths (5 and 10 cm). The appropriate diameter and length of the NRS should be chosen based on where the tip of the NRS will land in the adequate outflow vein. If the vein where the tip of the NRS will land is > 9 mm in diameter, I will use the 9 mm Hybrid configuration. If the vein (where the tip of the NRS will land) is 9 mm in diameter, I will choose an 8 mm diameter NRS, and so on. It is important to recognize that, while the tip of the NRS may be undersized to the vein and not have wall apposition, the majority of the length of the NRS of the GORE Hybrid Vascular Graft is typically sized to the vein according to the Instructions for Use (IFU) recommendation of 5% to 20% oversizing, ensuring adequate anchoring to the vessel wall. The 10 cm length NRS is usually chosen for deep axillary procedures in order to reach the adequate outflow.

OTHER POSITIONING AND LANDING ZONE CONSIDERATIONS

When the GORE VIABAHN Device and the GORE Hybrid Graft are used in the axillary region, some may have concerns that blocking the venous return with the stent-graft (or NRS of the GORE Hybrid Graft) may cause edema or arm swelling. Due to the rapid and extensive collateralization of the venous system, I do not hold this concern and have not had any significant problems with arm swelling or edema after placing these devices in the axillary region.

In addition to diameter sizing, it is also critical to position and land the stent-graft (or NRS of the GORE Hybrid Graft) properly within the vein. This positioning consideration includes the concentricity of the vessel with the device. It is important to attempt to ensure that positioning of the stent-graft (or NRS) is straight into the larger vein, centered down the "barrel" of the large vein (Figure 2), so that the outflow is directed "inline" with the host vein. If the tip of the stent-graft is directed at an angle, the high-pressure arterial flow will impinge on the native vein and may cause significant vessel trauma and/or intimal hyperplasia development.

Valves are another critical consideration in selecting an adequate landing zone for the device. In my experience, landing inside or within 1 cm proximal to the valve can lead to rapid endothelial buildup at the edge of the device. I choose to cross the valve by at least 1 cm to avoid this potential failure mode (Figure 4).

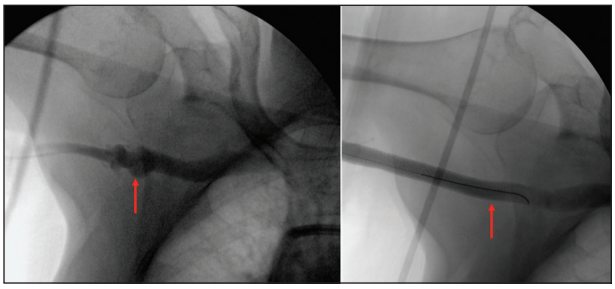

Figure 4. Example of appropriate landing of the NRS of the GORE Hybrid Graft beyond a vein valve. The red arrows indicate the valve and tip of the NRS.

THE GORE REVISE CLINICAL STUDY

Results from the Gore REVISE clinical study support the previously described process of care strategy for my practice. A subset of the subjects in the study had an outflow vein with a diameter at least 1 mm greater than the implanted GORE VIABAHN Device (n = 49). For those subjects, the target lesion and circuit primary patency was 62% and 48% at 6 months, respectively, with an access secondary patency of 77% at 2 years.[4] These outcomes represent an improvement over the rest of the study cohort, albeit not statistically significant. These results demonstrate that similar clinical success, similar to what I have experienced with the GORE VIABAHN Device, can be achieved without stent-graft wall apposition to the outflow vein.

OBJECTIONS TO SIZING METHODOLOGY

Migration, the ability to declot, and flow disturbance are three common objections to placing a device at a graft anastomosis that is smaller than the outflow vein. These three objections, however, have not been demonstrated to be a clinically significant issue with either the GORE Hybrid Graft or the GORE VIABAHN Device when landing in a large outflow vein.

Migration is a logical objection because the opportunity to gain wall apposition is reduced if the stent-graft "jumps" forward during deployment. This is not a concern for the GORE Hybrid Graft because the NRS is attached to the graft. The unique design and deployment system of the GORE VIABAHN Device relies on a single pull of a deployment line as opposed to a push-pull mechanism. The result is highly accurate and consistent placement of the device that does not lend itself to jumping forward during deployment. Proper upstream sizing as well as accurate delivery are tantamount to preventing migration. Once deployed, both the graft and

the stenosis provide enough vessel wall surface area to allow the device to anchor in place and prevent spontaneous migration. No device jumping or spontaneous migration was reported for the entire Gore REVISE clinical study, including a subset of the subjects who had an outflow vein with a diameter at least 1 mm greater than the implanted GORE VIABAHN Device.

Standard declotting techniques are still applicable for devices that are smaller in diameter than the outflow vein. However, care should be taken with mechanical thrombectomy when transitioning from the device to the vein. Catching the exposed edge of the GORE VIABAHN Device with the mechanical thrombectomy device can lead to an adverse event and potential device destruction.

Flow disturbance is observed when there is an increase in turbulence associated with high velocity flow exiting the stent-graft into the larger open vein. However, the presence of disturbed flow is not enough to result in access dysfunction. The disturbed flow has to result in a significant increase in wall shear stress (WSS) for a hyperplastic and/or thrombotic response to be initiated.[6-11] In the next section, the impact of wall apposition on WSS of the outflow vein will be explored via a CFD model.

COMPUTATIONAL FLUID DYNAMICS

WSS Generated By a Stent-Graft Without Wall Apposition Versus With Wall Apposition

Elevated WSS has been correlated with remodeling of the vasculature in the form of neointimal hyperplasia as well as the formation of thrombus.[6-11] The remodeling is thought to be a mechanism to restore the WSS within the veins to the physiological range between 1 to 6 dyn/cm^2.[7] Thus, by creating a stenosis, the blood flow can be reduced and with it the WSS. The development of neointimal hyperplasia is confounded by the variability associated with the oscillatory nature of blood flow between the WSS of 15 to 75 dyn/cm^2.[10] However, beyond 75 dyn/cm^2, the impact of WSS on both neointimal hyperplasia and the activation of thrombosis pathways becomes significant.[6,7,11]

Engineers at Gore & Associates created a computational fluid dynamics (CFD) model study to understand the impact of flow disturbances on WSS. In this study, AV access hemodynamics in two outflow geometries (Figure 5) were compared using three-dimensional CFD simulations. Both geometries—generated using SolidWorks (Dassault Systèmes, S. A.)—had a graft inlet diameter of 7 mm and a vein outlet diameter of 11 mm, as illustrated in Figure 5. It was assumed that the upstream venous return was completely occluded by a stenosis such that the flow at the graft inlet was equal to the flow at the vein outlet. Also, the simulated placement of the stent-graft across the anastomosis was down the "barrel" of the vein, as shown in Figure 2.

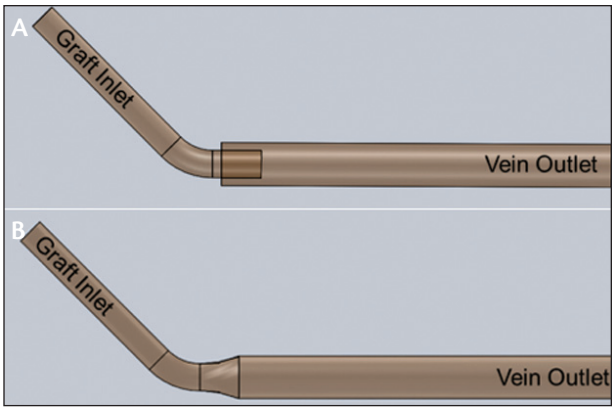

Figure 5. Two access geometries associated with AV access were modeled computationally. The two outflow geometries utilized for the CFD: one without wall apposition (A) and the other with wall apposition (B).

Ansys Fluent software (Ansys, Inc.) was used to obtain the numerical solution for the two cases. The simulated fluid was blood under Newtonian conditions with a density of 1,050 kg/m^3 and a dynamic viscosity of 3.7 cP. The CFD analyses used a prescribed pulsatile inlet flow waveform.[12] The inlet flow rate waveform had a peak flow rate of 1.6 L/min, a mean flow rate of 1.2 L/min, and a time period of 0.85 seconds.

Velocity vector plots are presented at four time points in the cardiac cycle (at 0.1, 0.4, 0.55, and 0.7 seconds) on the central plane for both the geometries (Figure 6). These time points include peak systole (0.4 seconds) and diastole (0.55 seconds), which correspond to the highest and lowest inlet velocities, respectively.

In Figure 6A, it was observed that the higher velocities occur on the bottom of the outflow, distal to the bend the stent-graft takes into the vein. It was seen that a recirculation region exists downstream of the stent-graft, mainly at peak systole and diastole. At the other time points (0.1 and 0.7 seconds), it was observed that the recirculation region was smaller comparatively. The recirculation region varies in intensity over the cardiac cycle, which is an indicator that little to no fluid is retained or pooled in that region past a single cardiac cycle. Figure 6B shows the result for a stent-graft with wall apposition to be similar to the straight stent-graft without wall apposition. Recirculation regions were observed in Figure 6B, and the intensity of the recirculation zones vary over the cardiac cycle. However, the recirculation region was observed to extend closer to the center of the vein, leading to a greater region of recirculation as determined qualitatively.

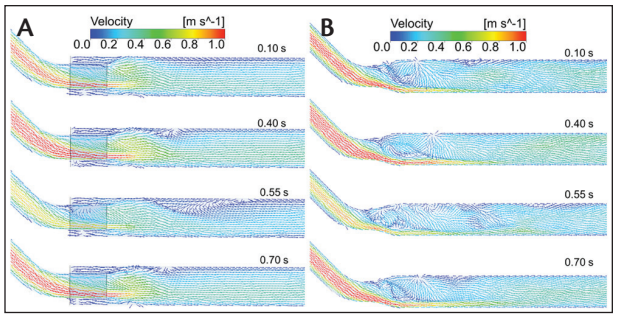

Figure 6. CFD outputs of velocity vector plots on the central plane at four representative time points in the cardiac cycle: outflow without wall apposition (A) and outflow with wall apposition (B).

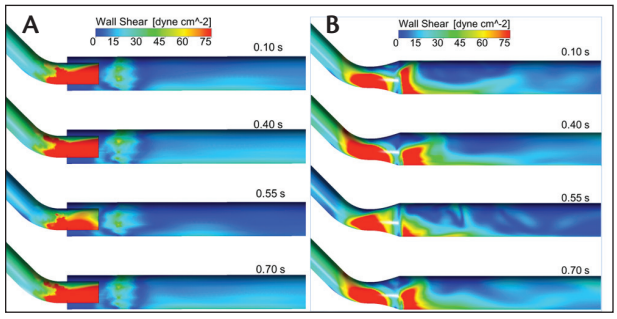

Figure 7. CFD outputs of the WSS contour plots at four representative time points in the cardiac cycle: outflow without wall apposition (A) and outflow with wall apposition (B).

WSS contour plots are presented at the four representative time points in the cardiac cycle for both the geometries in Figure 7. The plots show that the highest WSS is found along the bottom of the stent-graft, distal to the bend the graft takes into the vein for both configurations.

As expected, the highest WSS (> 75 dyn/cm^2) corresponded to the location that had the highest velocity gradients and primarily occurs within the stent-graft. However, in Figure 7A, the WSS dissipated below 75 dyn/cm^2 once the flow transitioned from the stent-graft without wall apposition to the larger outflow vein. By comparison, the configuration with wall apposition in Figure 7B demonstrated high WSS both in the stent-graft and the vein. In this scenario, the maximum WSS was 185 dyn/cm^2, and high WSS was maintained throughout the entire cardiac cycle. The results suggest that a device with a diameter less than the outflow vein may actually reduce the WSS experienced by the vein relative to devices that match the vein diameter.

CONCLUSION

More and more patients are presenting with multiple failed AV access attempts, and these complex patients pose significant challenges when we try to create a functional access. Once a functional access has been created, it is important to strive to keep that access patent as long as possible while also planning the future revision strategy. Whether creating a new access in the violated axilla with the GORE Hybrid Graft or using a GORE VIABAHN Device to revise the outflow vein of a failed AVG, my experience, clinical data, and CFD studies suggest that vein wall apposition of the stent-graft outflow component is not necessary for successful long-term results of the AV access circuit. ■

John R. Ross, MD, is Medical Director of the Dialysis Access Institute in Orangeburg, South Carolina. He has disclosed that he receives research funding from W. L. Gore & Associates, Inc. Dr. Ross may be reached at jrrsurgery@aol.com.

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Summary of the Gore REVISE Clinical Study

This nationwide study reports on the safety and effectiveness of the GORE VIABAHN Endoprosthesis for the treatment of stenoses and thrombotic occlusions involving venous anastomoses of hemodialysis grafts.

BY THOMAS VESELY, MD, AND ANTHONY RODRIGUEZ, PHD

All arteriovenous access circuits, whether native vein or prosthetic graft, will inevitably fail due to the development of neointimal hyperplastic stenoses. These smooth muscle cell lesions obstruct blood flow and thereby decrease the efficiency of hemodialysis and increase the risk of access thrombosis. The etiology of neointimal hyperplastic stenosis is complex and multifactorial.[1] Vascular stenoses develop in response to vascular injury and to endoluminal stresses applied to the blood vessel wall. Surgical creation of an arteriovenous access circuit causes acute traumatic injury at vascular anastomoses, and the high rate of blood flow (> 800 mL/min) through the circuit induces chronic injury to blood vessels in hemodialysis fistulas and grafts.[2] The majority of chronic hemodialysis patients will experience a problem with their arteriovenous access circuit during the first 12 months after access placement.

Balloon angioplasty remains the standard of care for the endovascular treatment of neointimal hyperplastic stenoses obstructing blood flow in hemodialysis fistulas and grafts.[3] However, the true effectiveness of balloon angioplasty remains questionable. Recent prospective studies have reported postangioplasty patency rates that were less than the expected patency rates described in national guidelines.[4,5] The availability of ultra-high-pressure angioplasty balloons has improved technical success, but these results may be short-lived due to delayed elastic recoil of the blood vessel wall. Autonomic contraction of smooth muscle layers within the blood vessel wall can cause restenosis within minutes or hours after a successful angioplasty procedure (Figure 1). Because of its ease of use for both the patient and physician and a low procedural complication rate, balloon angioplasty remains the standard of care for treating neointimal hyperplastic stenoses.

Bare-metal stents are used in the treatment of venous anastomotic stenoses, but patency rates are often no better than with balloon angioplasty alone.[6] Bare-metal stents have proven useful for treating restenosis due to elastic recoil and for managing angioplasty-induced vascular rupture and vascular dissection.[7] A metal stent can maintain full expansion of the blood vessel lumen that produces tamponade to control bleeding and optimizes blood flow to reduce turbulence through the hemodialysis fistula or graft. However, expansile forces exerted by the metal stent may exacerbate neointimal hyperplasia, and stents with

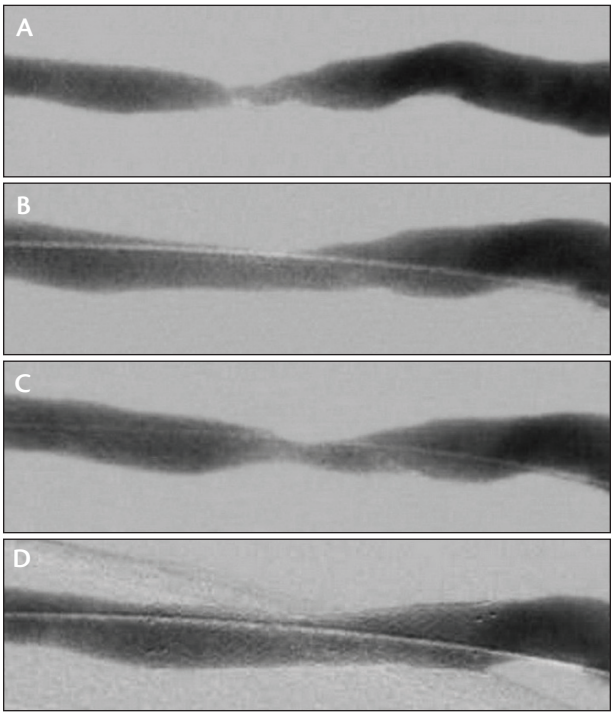

Figure 1. Severe stenosis of the cephalic vein (A). A good result immediately after balloon angioplasty (B). Restenosis 30 minutes later due to elastic recoil (C). A good result after placement of a metal stent (D).

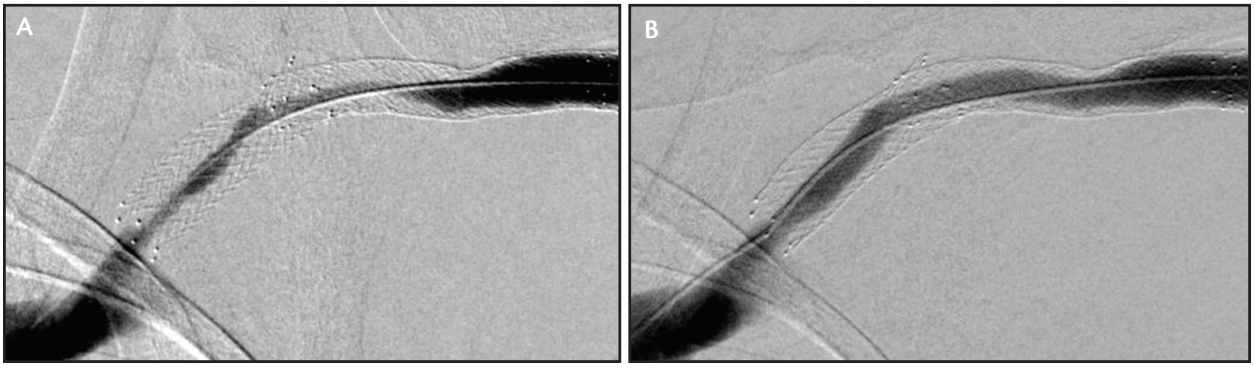

Figure 2. Severe stenosis within bare-metal stents in the upper cephalic vein (A). A good result immediately after balloon angioplasty (B).

an open-mesh design are porous to cellular proliferation. Progressive ingrowth of neointimal hyperplasia through the metal mesh creates in-stent restenosis that obstructs blood flow through the arteriovenous access circuit (Figure 2). In summary, a metal stent can provide an effective short-term treatment for neointimal hyperplastic stenosis and other vascular problems, but long-term patency is often no better than with balloon angioplasty alone.[8]

Despite decades of clinical research, an effective, long-lasting treatment for neointimal hyperplastic stenoses remains elusive. Advancements in biomaterials and stent-graft design may provide a technological solution. A stent-graft provides endoluminal support to resist muscular contraction of the blood vessel wall plus a nonporous, biocompatible barrier to prevent cellular ingrowth and in-stent restenosis. Vascular stent-grafts can provide effective and durable treatment for neointimal hyperplastic stenoses causing obstruction of hemodialysis fistulas and grafts. Ideally, a stent-graft should be sufficiently flexible to conform to variable anatomy and safely cross joint spaces (Figure 3). Because of the superficial location of most arteriovenous access circuits, self-expanding stent-grafts are preferable to balloon-expandable stent-grafts when used in hemodialysis fistulas and grafts.

In 2008, the FDA approved the first stent-graft for use as a primary treatment for venous anastomotic stenosis involving a polytetrafluoroethylene (PTFE) hemodialysis graft. Continuing advancements in stent-graft materials and design have improved biocompatibility, durability, and ease of use for a variety of vascular applications. Clinical experience has demonstrated that stent-grafts work well in treating neointimal hyperplastic stenoses, delayed elastic recoil, and other vascular problems that commonly occur along arteriovenous access circuits. However, the true clinical effectiveness of using stent-grafts to treat these problems has not been sufficiently substantiated to justify broad use of these expensive medical devices. Self-expanding stent-grafts are considerably more expensive than standard angioplasty balloons, ultra-high-pressure angioplasty balloons, or bare-metal stents. The cost effectiveness of using stent-grafts for hemodialysis access applications continues to be a subject of considerable debate. The data analysis described herein of the Gore REVISE clinical study will support the assertion that use of the GORE VIABAHN Device provides significant clinical benefit while reducing the overall cost of maintaining arteriovenous access.

THE GORE REVISE CLINICAL STUDY

The Gore REVISE Clinical Study (REVISE study) is a prospective randomized comparison of balloon angioplasty versus the GORE VIABAHN Device (with CBAS Heparin Surface) (Gore & Associates) as primary treatment for venous anastomotic stenosis causing dysfunction or thrombosis of a PTFE hemodialysis graft. Unique features of the REVISE study include enrollment of patients with thrombosed hemodialysis grafts and use of the GORE VIABAHN Device across the elbow joint. Few published studies have reported success rates after using stent-grafts for these common problems.

During the study enrollment period, 293 patients with dysfunctional (56%) or thrombosed (44%) PTFE hemodialysis grafts were enrolled and followed at 31 study sites throughout the United States. The etiologies of hemodialysis graft dysfunction included a low rate of blood flow, elevated venous pressure, or prolonged hemostasis time. Fifty percent of the study patients underwent balloon angioplasty, and 50% of patients were treated with balloon angioplasty plus a GORE VIABAHN Device. The patients were followed for 2 years after the date of the treatment procedure.

The demographic distribution of the 293 subjects enrolled in the REVISE study was reflective of the

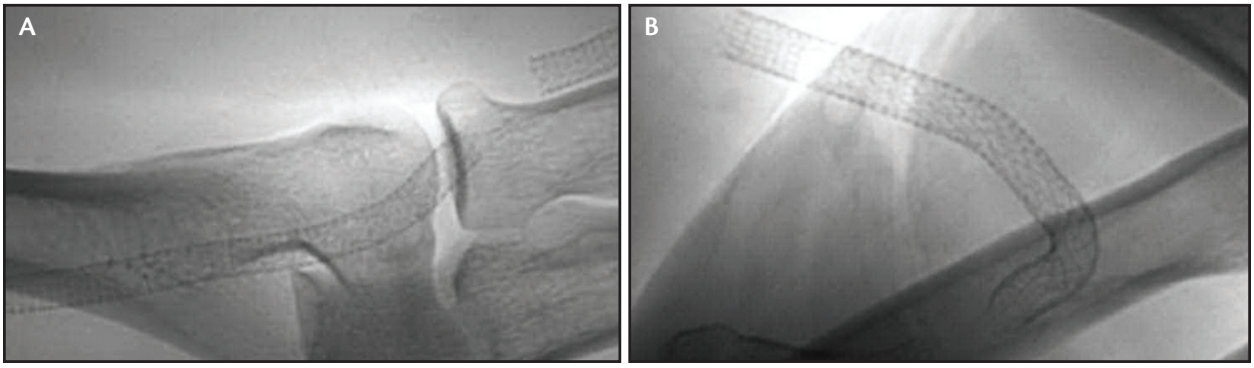

Figure 3. GORE VIABAHN Device positioned across the elbow joint (A). With tight flexion of the elbow joint, the GORE VIABAHN Device maintains an open lumen (B).

United States hemodialysis patient population. The study patients were an average age of 62 years and were primarily women (52%), African American (51%), and diabetic (65%). Their average time undergoing chronic hemodialysis therapy was 3.9 years, and the average age of their PTFE hemodialysis graft was 2.1 years. The majority (62%) of study patients had undergone previous interventions at the graft's venous anastomosis (target lesion).

The target lesion was defined as a stenosis causing > 50% luminal narrowing at the venous anastomosis, or within 30 mm of the venous anastomosis, of a dysfunctional or thrombosed PTFE hemodialysis graft. All study patients underwent thorough fistulagraphy to evaluate and measure the target lesion and to identify other vascular stenoses along the arteriovenous access circuit. Patients with a significant (> 50%) secondary stenosis could be enrolled in the REVISE study if the entirety of the second stenosis was: (1) located more than 30 mm from the target lesion, (2) < 50 mm in length, and (3) had < 30% residual stenosis after angioplasty. Per study protocol, patients with a symptomatic central venous stenosis were excluded from enrollment.

All 293 study patients were initially treated with angioplasty. Upon full inflation of the angioplasty balloon at the target lesion, the patient was randomized to undergo treatment using either balloon angioplasty alone or balloon angioplasty plus a GORE VIABAHN Device. The operating physician could treat the target lesion using any type and size of angioplasty balloon. Before undergoing randomized treatment, the two groups of patients had similar characteristics of their target lesions; the mean percentage stenosis (74% vs 73%) and the mean length (24 vs 22 mm) of the target lesions were nearly identical.

At the discretion of the operating physicians, patients randomized to treatment with balloon angioplasty alone could undergo additional angioplasty until clinical success was achieved. Larger-diameter and/or higher-pressure angioplasty balloons could be used when appropriate. The 148 patients randomized to treatment using balloon angioplasty alone had a mean number of 2.1 balloon inflations at the venous anastomosis of their hemodialysis grafts.

Study patients randomized to the GORE VIABAHN Device group underwent placement of an appropriate-size device as described in the instructions for use document. The device was landed at least 1 cm into the graft and 1 cm into healthy vein. The device diameter was chosen based on 5% to 20% oversizing to the graft diameter, regardless of the vein diameter.

Nearly all (98%) of the 145 patients randomized to balloon angioplasty plus a GORE VIABAHN Device had successful treatment of their venous anastomotic stenosis using only one GORE VIABAHN Device.

Patients enrolled in the REVISE study were followed for a period of 2 years or until surgical revision or abandonment of the target lesion, the venous anastomosis of the hemodialysis graft. During the 2-year follow-up period, each patient's hemodialysis graft was managed according to local protocols. Specific management of restenosis, new stenoses, or any other problems with each patient's hemodialysis graft was determined by local nurses and physicians. The intent of the REVISE study was to obtain information and results that are reflective of real-life vascular access care provided to the majority of hemodialysis patients.

RESULTS OF THE REVISE STUDY

The REVISE study is the first prospective study of stent-grafts for this application that included patients with thrombosed hemodialysis grafts. The inclusion of patients with thrombosed grafts is important because it is commonly believed that these patients often have worse outcomes after any treatment. Nearly one-half of the patients (44%) enrolled in the REVISE clinical study had a thrombosed PTFE hemodialysis graft.

TABLE 1. THE GORE REVISE CLINICAL STUDY OUTCOMES

	Angioplasty + GORE VIABAHN Device Group	Angioplasty Group
Effectiveness Population*	N = 131	N = 138
At 6 months		
Target lesion primary patency†	53%	36%
Circuit primary patency‡	43%	29%
At 24 months		
Access secondary patency	69%	67%§
Repeat interventions at the target lesion	2.7	3.7
Nonthrombotic subjects at 6 months¶		
Target lesion primary patency	65%	46%
Circuit primary patency	50%	36%
Thrombotic subjects at 6 months		
Target lesion primary patency	36%	24%
Circuit primary patency	34%	22%

**Statistical comparisons of the intent-to-treat population for the primary end-points were similar to the effectiveness population.*
†Statistical comparison between the two treatment groups reported a P value of .008.
‡Statistical comparison between the two treatment groups reported a P value of .035.
§Secondary patency was maintained with 61 additional stents or stent-grafts (53 VIABAHN Devices).
¶The treatment benefit of the GORE VIABAHN Device was statistically similar between dysfunctional and thrombotic subjects for both target lesion and circuit primary patency (P = .792; P = .768).

As reported in Table 1, patients who were in the group treated with balloon angioplasty plus a GORE VIABAHN Device had statistically superior primary patency rates at the target lesion at 6 months when compared to treatment using balloon angioplasty alone (53% vs 36%; *P* = .008). Patients treated with a GORE VIABAHN Device also had better primary patency of the entire arteriovenous access circuit at 6 months (43% vs 29%; *P* = .035). At 24 months, there was no statistical difference in the secondary patency rates between the GORE VIABAHN Device group and the angioplasty alone group (69% vs 67%).

However, the 148 patients initially treated with balloon angioplasty alone needed 61 stents or stent-grafts (53 of which were GORE VIABAHN Devices) to maintain secondary patency of their hemodialysis grafts during the 2-year follow-up period. These patients also needed 43% more angioplasty and twice as many surgical revisions to maintain hemodialysis graft patency for 2 years. If the use of stents and stent-grafts was considered a loss of secondary patency, the results for the angioplasty alone group would drop from 67% to 35%. Thus, the GORE VIABAHN Device was necessary to maintain secondary patency in both treatment arms.

Results of the REVISE study substantiate the belief that graft thrombosis portends shortened patency, whether treatment was with balloon angioplasty or balloon angioplasty plus a GORE VIABAHN Device. Study patients with dysfunctional hemodialysis grafts had better target lesion primary patency at 6 months compared to patients with thrombosed grafts, whether receiving a GORE VIABAHN Device (65% vs 36%) or balloon angioplasty alone (46% vs 24%). Use of a GORE VIABAHN Device improved primary patency for both groups of patients, dysfunctional grafts and thrombosed grafts, compared to balloon angioplasty alone. Based on these superior results, the FDA approved use of the GORE VIABAHN Device for treatment of both dysfunctional and thrombotic hemodialysis grafts.

The 2-year results from the 293 patients enrolled in the REVISE study provide interesting information about this patient population. Study patients who had no previous interventions at the target lesion had similar results, whether treated with balloon angioplasty alone or balloon angioplasty plus a GORE VIABAHN Device. Study patients who had at least one previous intervention at the target lesion had better primary patency rates at 6 months after

treatment with the GORE VIABAHN Device compared to treatment using only balloon angioplasty (54% vs 29%). These results suggest that the GORE VIABAHN Device is a good option if a second intervention is needed at the target lesion. However, the REVISE study also showed that early use of a GORE VIABAHN Device significantly reduced the number of additional interventions at the target lesion compared with the angioplasty alone group (2.7 vs 3.7; $P = .009$) and along the arteriovenous access circuit (3.7 vs 5.1; $P = .053$) needed to maintain 2-year secondary patency of the hemodialysis graft.

By reducing the number of reinterventions, it is estimated that use of a GORE VIABAHN Device could provide a cost reduction of approximately $2,000 per patient.

Twenty-five patients had a GORE VIABAHN Device positioned across their elbow joint. The 6-, 12-, and 24-month primary patency rates at the target lesion were 72%, 56%, and 32%, respectively. The 6-, 12-, and 24-month secondary patency rates were 95%, 95%, and 83%, respectively. During the 2-year follow-up period, there were no reported fractures of the GORE VIABAHN Device, and the long-term patency rates were superior to treatment of a venous anastomotic stenosis using balloon angioplasty alone.

SUMMARY

The REVISE study demonstrated that the use of a GORE VIABAHN Device to treat venous anastomotic stenosis provided superior patency and fewer reinterventions when compared to balloon angioplasty alone. Early results of the REVISE study suggest that early use of a GORE VIABAHN Device is a cost-effective method to maintain long-term patency of a dysfunctional or thrombosed hemodialysis graft. ■

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Crossing the Point of Flexion in the Antecubital Fossa

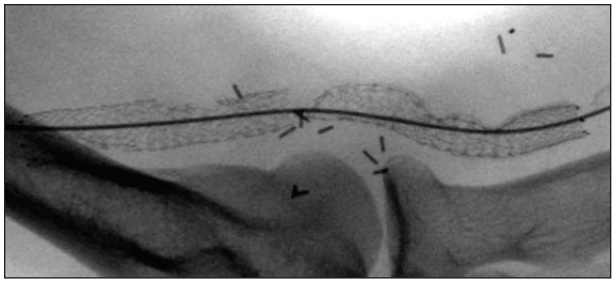
Using the GORE VIABAHN Endoprosthesis for long-term access patency.

BY WILLIAM DAVANZO, MD

Crossing the antecubital fossa with a stent or stent-graft to treat a dysfunctional or thrombosed graft can be a cause for concern for most interventionists. Some stent-grafts will kink when the arm bends, which can lead to a thrombotic occlusion.[1] Bare-metal stents tend to have enough flexibility to avoid kinking, but the mechanical strain from repeated flexion can potentially compromise the structure of the device (Figure 1). The only alternatives are frequent angioplasty or graft abandonment, neither of which is ideal for the patient.

The GORE VIABAHN Endoprosthesis (Gore & Associates) has proven to be both flexible and durable when crossing the antecubital fossa. The device resists kinking even when the arm is bent (Figure 2). Most importantly, I have not experienced any device fracture even under repeated flexion. My experience was validated by the absence of fractures reported over the entire 24-month study period of the Gore REVISE Clinical Study (REVISE), including the 25 subjects who required a device to cross the antecubital fossa. The data suggest that this device does not tend to fracture under repeated flexion, which results in a clinically significant issue.[2]

I describe a single case experience, as well as the population data from REVISE for the placement of the GORE VIABAHN Device across the antecubital fossa. The case highlights the direct impact the device can have on the life of a patient's arteriovenous (AV) access graft, while the REVISE data validate the decision to use the device across the elbow.



(Image courtesy of Thomas Vesely, MD.)

Figure 1. Bare-metal stent crossing the antecubital fossa, with fracture.

CASE STUDY

A 36-year-old woman with end-stage renal disease for just over 2 years was referred to our hospital for what was originally thought to be a thrombosed access. Upon examination, she was found to have a faint bruit and a weak thrill in her left forearm graft.

The patient was not diabetic, but she had a history of hypertension, which was thought to be the cause of her renal disease. Her current and only vascular access was a left forearm loop, expanded polytetrafluoroethylene, tapered 4 to 7 mm graft using the brachial artery for inflow and the cephalic vein for outflow. Before this visit, she had a history of three thrombotic events of the graft in 23 months, each of which were successfully treated interventionally with percutaneous thrombectomy and angioplasty of the venous anastomosis. The most recent event was 4 months before the visit.

The patient had a healthy cephalic vein for a potential upper arm fistula that could have provided a better working access with less frequent thrombosis. However, I wanted to attempt to alter the natural history of the current access through endovascular means to prevent the need for a central venous catheter while retaining future options. Also, prolonging the life of the current access was particularly important, given the patient's young age and potential need for long-term dialysis.

The patient was screened for the REVISE Study. She met all of the inclusion/exclusion criteria and consented for participation in the clinical trial.

The patient was then taken to the angiography suite, where she was prepped in the standard fashion. A 7 F short sheath was inserted into the venous section of the graft, and angiographic images were obtained with multiple views. The films revealed a clinically significant lesion of the venous anastomosis measuring 24 mm in length originating at the venous anastomosis and 75% stenosed (Figure 3A). She also had a distal cephalic arch

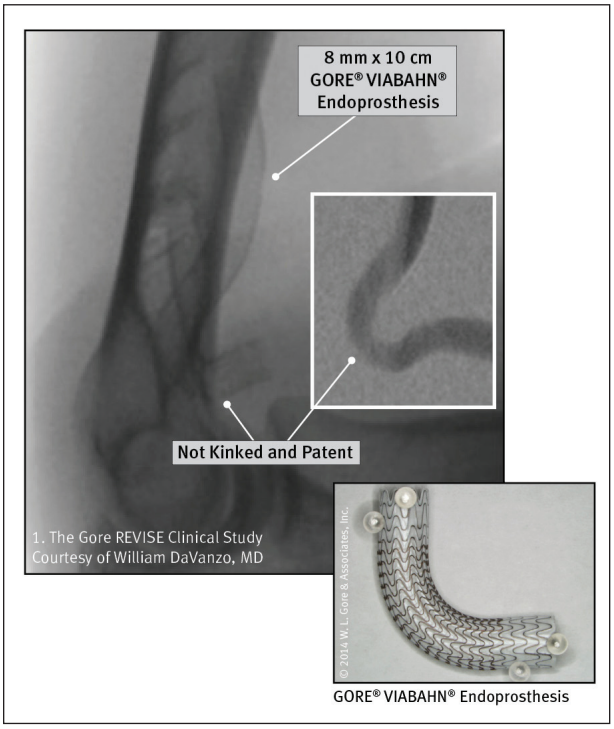


Figure 2. GORE VIABAHN Device crossing the antecubital fossa with flexion. Note patency of the device without kink.

stenosis of 53% that was 25 mm long. Angioplasty was performed with a 7 mm × 8 cm balloon, followed by an 8 mm × 4 cm balloon. Both balloons were inflated to 16 atm for 60 seconds, resulting in a 21% residual stenosis. This met the study requirement for successful treatment of a secondary lesion. The remainder of the dialysis circuit was patent; the arterial anastomosis was < 50% stenosed and was not treated.

The target lesion was then addressed. An 8 mm × 8 cm balloon was used to perform angioplasty on the lesion, requiring 26 atm of pressure for 60 seconds to remove the balloon waist. A 25% residual stenosis was seen, and the patient was randomized to the GORE VIABAHN Device group. The 7 F sheath was exchanged for an 8 F sheath, and an 8 mm × 5 cm GORE VIABAHN Device was used to treat the lesion. The 8 mm diameter device was chosen to ensure anchoring into the 7 mm outflow of the graft. The device crossed the antecubital fossa and landed in the cephalic vein, measuring 10.6 mm at the distal edge of the device (Figure 3B). The device crossed the flexion point of the vein by approximately 1 cm, and the lumen of the device remained open at that flexion point with the arm bent. The patient successfully dialyzed through the access the following day.

Three days later, she reported to the dialysis clinic with a thrombosed access. Thrombectomy was performed through the graft, the device, and the native cephalic vein. The arterial anastomosis was found to be > 50% stenosed. A 7 mm angioplasty balloon was used to perform angioplasty on the lesion. The GORE VIABAHN Device was found to be widely patent (Figure 3C).

At the 30-day follow-up interval, the patient was found to have been discharged from the dialysis unit after multiple missed treatments. We were unable to contact the patient, and she was terminated from the clinical trial as "lost to follow-up."

The patient was referred back to our clinic for decreased vascular access flow on hemodialysis, 33 months later. The access had not been intervened on in the interim. She was taken to the angiography suite and was found to have an arterial anastomosis stenosis, which was treated. The GORE VIABAHN Device crossing the antecubital fossa was found to be minimally stenosed (Figure 4A).

The patient was again referred back for poor access flow 39 months after initial implantation and was found to have a pulsatile access on exam. Angiography was performed, demonstrating advancement of the secondary cephalic arch lesion. The original implant was widely pat-

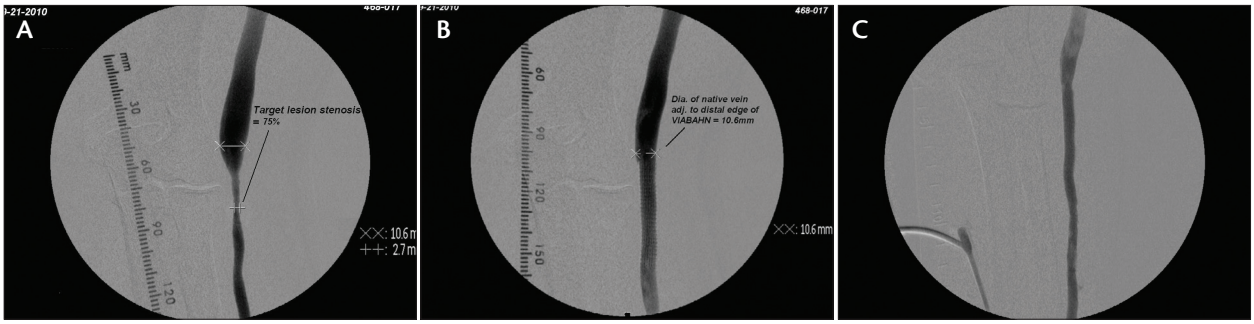


Figure 3. Prestent angiography (A). Note the anastomosis is with the cephalic vein, and the target lesion crosses the antecubital fossa. Poststent angiography showing 8 mm × 5 cm GORE VIABAHN Device placed across the antecubital fossa (B). Note the large-caliber cephalic vein (10.6 mm) for the landing zone. The patient returned with thrombosed AV access (C). The GORE VIABAHN Device was unremarkable.

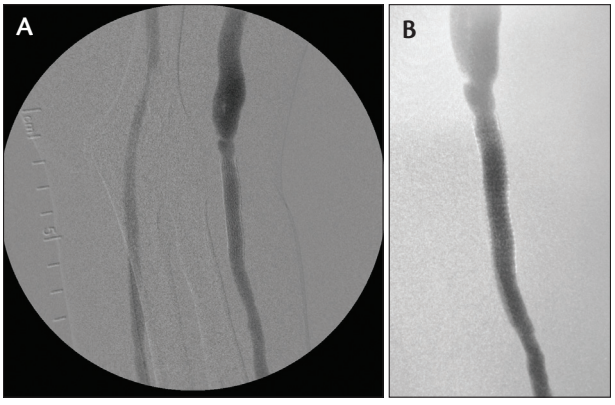


Figure 4. The patient was referred back at 33 months (A) and 39 months (B). Note the GORE VIABAHN Device was minimally stenosed.

ent (Figure 4B), and the cephalic arch lesion was successfully treated with an off-label placement of a stent-graft.

CHOOSING THE LANDING ZONE

The location of the outflow edge of the device is an important consideration when crossing the elbow. The placement can affect both outcomes and future potential access opportunities. In this procedure, many options are available to the operator, such as crossing the median cubital vein as a means for using the basilic vein or placement in the cephalic vein crossing the elbow completely or landing at the elbow crease. Each decision can provide a successful outcome for the patient with the GORE VIABAHN Device but can also come at the cost of preventing a future access.

The interventionist must also consider which vein is being used as the landing zone for the stent-graft when addressing the best scenario for the patient's future. If the anastomosis is within the cephalic vein past the median cubital, the only consideration for device choice becomes the size of the vein distal to the anastomosis. When considering the basilic vein, it is useful to evaluate the entire vein to determine whether it may be more appropriate than the cephalic for a future fistula. If so, crossing the median cubital vein and diverting the access to the basilic vein with a stent-graft may serve the patient well in the future.

In this case, an 8 mm device was used in the initial procedure to size 5% to 20% larger than the graft, per the instructions for use. However, the GORE VIABAHN Device was landed in a vein measuring 2.6 mm larger than its nominal diameter (Figure 3B). I believe this scenario contributes to the long-term patency of the device and reduction in the progression of stenosis at the outflow. When possible, I choose to land the device in a larger outflow vein, provided future access sites will not be compromised. My personal experience with this sizing strategy is in fact supported as safe and effective by the REVISE Study data.[2]

In the case described, I opted for a shorter device in the patient to maintain as much venous real estate as possible for a future upper arm cephalic fistula. This decision resulted in the device landing only a centimeter past the flexion point (Figure 3). Alternatively, a longer device would have more completely extended past the flexion point of the elbow (Figure 2). However, the patient in Figure 2 received the shorter device due to the characteristics of the stenosis, not in order to cross the flexion point. If the shorter device had landed in the point of flexion, a longer device would have been more appropriate. In such a case, I would choose to land the device only 1 cm past the flexion point while preserving as much healthy vein as possible. Excess length would have been extended distally into the graft, provided that cannulation zones could be avoided. In this location, the GORE VIABAHN Device still retains excellent flow and does not kink, despite the proximity of the flexion point to the end of the device.

DISCUSSION

Lesions that are found near the antecubital fossa can be difficult to manage. Angioplasty has been the therapeutic modality of choice for lesions in this area. When angioplasty has failed, the options to maintain a working access are limited to stents or surgical revision of the venous anastomosis. The choice for using stents for repair of the venous anastomosis has been debated. Bare-metal stents have not been adequate solutions for the venous anastomosis or crossing the antecubital fossa, as they are prone to stent fracture (Figure 1) and in-stent tissue growth.[3,4] Use of other stent-grafts across the antecubital fossa has typically been avoided based on clinical data[5] or warned against in the device's instructions for use.

Alternatively, the GORE VIABAHN Device has the flexibility, durability, and the indication to successfully treat lesions across the antecubital fossa. In my experience, the device does not compress or kink when the extremity is flexed (Figure 2) as compared with other stent-grafts, which kink under the same anatomic manipulations.[1] Also, I have not experienced a GORE VIABAHN Device fracture when placed across the elbow, and no fractures were reported in the REVISE Study.[2] The device is a valuable tool in maintaining access function in even the most challenging lesions.

This case study highlights how the GORE VIABAHN Device can be effectively placed across the elbow to restore and maintain long-term access function. Typically, a patient who is thrombosing at this frequency does not

have much hope for long-term durability of his or her AV graft. However, the treatment of the venous anastomosis with the GORE VIABAHN Device seems to affect the successful outcomes for these patients. For the described patient, the only intervention in 33 months was for thrombosis due to dysfunction at the arterial anastomosis. The GORE VIABAHN Device was unremarkable at the time of that intervention (Figure 3C). Only a minimal stenosis was found at 33 months and 39 months (Figure 4).

My single-center experience was validated by the effectiveness outcomes of the REVISE Study. The GORE VIABAHN Device group included 25 patients who required a device to be placed across the antecubital fossa. Of those patients, three were protocol deviations, and 22 were analyzed for effectiveness. The outcomes for those patients were 72% for target lesion primary patency at 6 months and 83% for access secondary patency at 24 months.[2] These outcomes compare favorably to the overall outcomes reported in the REVISE Study and support the use of the device across the antecubital fossa.

Choosing the correct intervention for access preservation for failed AV accesses in patients undergoing hemodialysis has been difficult in the past. The use of stent-grafts has increased our ability to improve on the previous standard of care—angioplasty. However, the need for flexibility and durability is essential to the long-term benefit of therapy with an implantable device, especially in difficult anatomical locations. The mechanical properties of the GORE VIABAHN Device have been attractive for AV access applications across flexion points and have now been validated by the outcomes of the REVISE Study in areas where other devices have failed. ■

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(Continued from page 8)

the axillary vein. Access of the graft was within 24 hours after placement, and removal of the temporary catheter was 12 hours after the first cannulation of the GORE ACUSEAL Graft. The graft has been functioning without any problems.

Case 2

A 58-year-old man with tunneled dialysis catheter placement for hemodialysis presented after venous mapping demonstrated no adequate veins for fistula creation. The patient had a catheter for 70 days and already experienced one infection. He underwent a left arm GORE ACUSEAL Graft placement with removal of the catheter 8 days after graft placement. The graft is functioning in this patient with no evidence of infection.

Case 3

This patient is a 68-year-old woman with patent ePTFE forearm loop graft of 3 year duration. She presented with a large pseudoaneurysm along the entire length of the graft. The patient underwent a jump graft around the pseudoaneurysm with a GORE ACUSEAL Graft. The graft was accessed 24 hours after placement, and no catheter was utilized in this patient.

SUMMARY

The GORE ACUSEAL Graft is a new trilayer graft that has been cleared by the US Food and Drug Administration for vascular access and has the claim of early cannulation. The use of this graft has the potential to shift the paradigm of catheter usage. This may be done by either early access of the graft after implantation and removal of the present catheter or with catheter avoidance by cannulating the graft immediately after placement. Education of the dialysis facility is imperative in order to achieve excellent results with this new graft. Continued experience with this graft allows for a more aggressive approach to these very complex patients. ■

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Flow Disturbances of Upper Arm Graft Outflow Uncovered by Positional Studies

Stent-graft flexibility must be considered when stenting upper arm access dysfunction.

BY MARC WEBB, MD, FACS

One of the advantages of the current paradigm of dialysis access maintenance and rescue by percutaneous means is the ability to diagnose, treat, and restore access functionality quickly, at a lower cost, and more conveniently without interval catheter placement, hospitalization, or incisional surgery. In our area, a clotted access is most often restored by one of a dozen interventional practices within 24 hours of patient presentation. The benefit to the patients is obvious. Less obvious is the truth that an array of practitioners—interventional radiologists, vascular surgeons, interventional nephrologists, and even cardiologists—are becoming more expert, adept, and successful in managing access problems percutaneously with a variety of tools, including the placement of stent-grafts. In 2010, a seminal paper was published in *The New England Journal of Medicine* on FDA approval of primary stenting for arteriovenous graft venous anastomotic stenosis.[1] Finally, there was evidence suggesting that stent-grafts need not be reserved for failure of venoplasty, but could perhaps be used as a primary treatment option.

I had my doubts. As early as 2005, I experienced an unwanted effect of a venous anastomotic stent, leading me to believe that stents were not totally benign in the axilla. A rigid stent was placed in the venous anastomosis and outflow vein of an arm graft. Repeated thrombosis of the graft was experienced in the ensuing 6 months. Finally, when the freshly declotted graft thrombosed in the recovery room, and was reopened the same evening with no signal finding, it occurred to me to reimage the functioning graft with the arm at the side, rather than in the 90° abducted position. Angulation of the vein at the trailing end of the stent suggested a compliance mismatch. Unfortunately, I did not immediately realize the importance of what I was seeing and did not have the presence of mind to capture this image. My solution was to extend the stent further, hoping to find a more central zone of the vein where movement of the arm would not lead to a kink at the trailing end of the stent. The graft experienced further events and was replaced within the year.

Later, I ran into a similar situation with a left arm graft placed 10 months earlier. In this case, I observed a similar phenomenon where the compliance mismatch of a rigid body stent led to kinking of the vein at the trailing end. This time I extended the rigid stent with a more flexible device that could better match the vessel compliance. That case report is described subsequently.

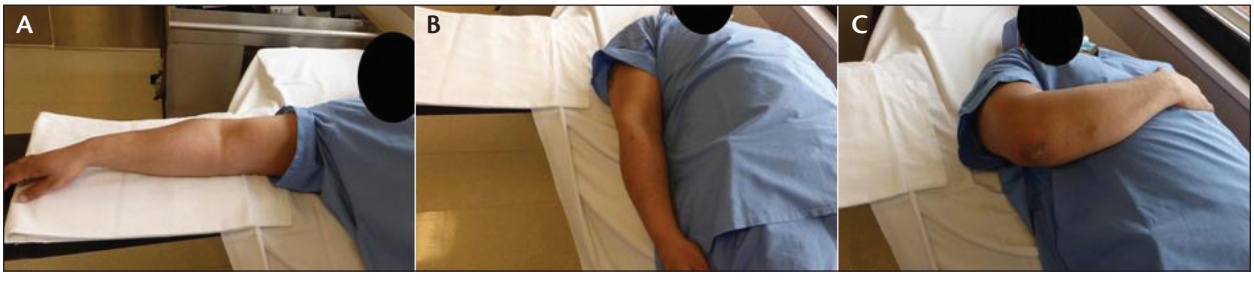

Figure 1. Placement of the arm extended out 90° from the body (A), lying at the side (B), and across the chest (C).

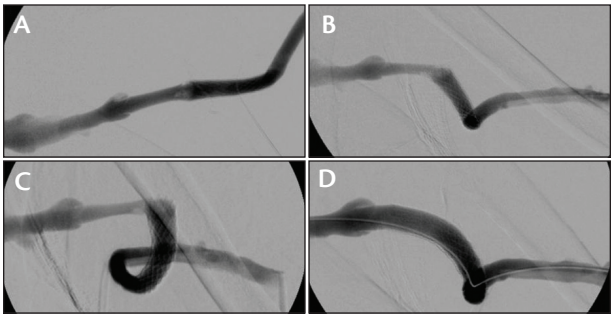

Figure 2. Angiographic images represent the kinking that can occur in the upper arm graft with a rigid stent-graft in response to the placement of the arm extended out 90° from the body (A), lying at the side (B), and across the chest (C). Correction of the kinking with a more flexible stent-graft (D).

CASE REPORT

The patient underwent one fistulagram for dysfunction and two percutaneous thrombectomies, with a BARD FLAIR® Stent-Graft (Bard Peripheral Vascular) placed in the venous anastomosis during the second thrombolysis. However, the patient experienced clotting a third time.

After successfully declotting the graft with the arm positioned out over the arm board (as represented in Figure 1A), I placed the patient's arm in two anatomically normal positions—at the side (Figure 1B) and with the arm folded over the chest (Figure 1C). Contrast injection images obtained in these positions demonstrate progressive angulation of the outflow vein at the central end of the stent, as the arm is brought in toward the body, as shown in Figure 2A through C. Access blood flow measurements obtained in these same positions demonstrated changes in flow commensurate with the angulation of the outflow vein: arm straight out from body, 1,365 ± 151 mL/min flow; arm on chest, 775 ± 170 mL/min flow. In general, flow was reduced as the arm was adducted.

My conclusion was that a hemodynamically significant compliance mismatch existed, and that it was unreasonable to expect the patient to live her life keeping her arm extended to 90° for the sake of a well-functioning dialysis graft. My solution was to extend the stent, but this time with a more compliant and flexible stent (Figure 2D).

DISCUSSION

The axilla is a soft tissue component of the shoulder girdle/upper extremity, and the vessels traversing this space are subject to angulation, torsion, and foreshortening as a result of abduction or adduction of the arm at the shoulder,[2] medial or lateral rotation of the arm, and pronation or supination of the forearm. Noncompliant foreign bodies in the vessels may constrain these vessels unnaturally, as in the previous example. In another example with an arm loop graft, it is apparent that in bringing the arm to the side, one adducts and rotates the arm from a supinated palm up to a neutral hand position (Figure 3A and B), distorting the outflow. In placing the forearm on the chest, one further adducts and medially rotates the arm (Figure 3C), torsing the vessels in the upper arm and making the arm graft look complicated. In this case, where a drop in access flow was measured with the arm on the chest, the outflow was restented with a more flexible stent-graft (Figure 3D).

In Figure 4, adduction and internal rotation of the arm placed on the chest "uncovers" a stenosis at the trailing end of the outflow stent—or does it? It is just as likely that the long outflow stent-graft prevents the vein from making a gentle twist over several inches, forcing it to accommodate the turn in the short distance between the end of the stent and fixation points of the vein (branches). More subtle than outright angulation, this is a torsion effect. In this case, flow measurements did not demonstrate a significant change in access flow when the arm was adducted and internally rotated, and an intervention was not indicated.

Like most practitioners confronted with multiple problems of access dysfunction on a daily basis, I have placed a large number of stents (more than 2,000 noted in an accounting performed several years ago). Through my experience, I have become aware of several benefits and also various limitations of stenting. The immediate outcome can be gratifying, but the long-term consequences are more difficult to predict. For that reason, and for reasons of economy and wise stewardship of resources, I am deeply hesitant to embrace fuzzy or questionable indications for axillary stenting. When axillary stenting is truly indicated, a flexible stent-graft such as the GORE VIABAHN Device is my device of choice.

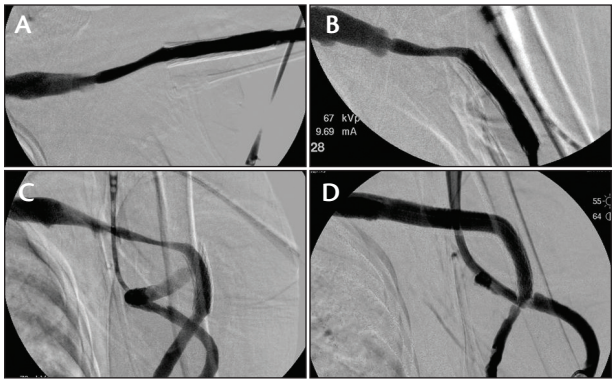

Figure 3. Angiographic images represent the torsion that can occur of the upper arm graft with a rigid stent-graft in response to the placement of the arm extended out 90° from the body (A), lying at the side (B), and across the chest (C). Correction of the torsion with a more flexible stent-graft (D).

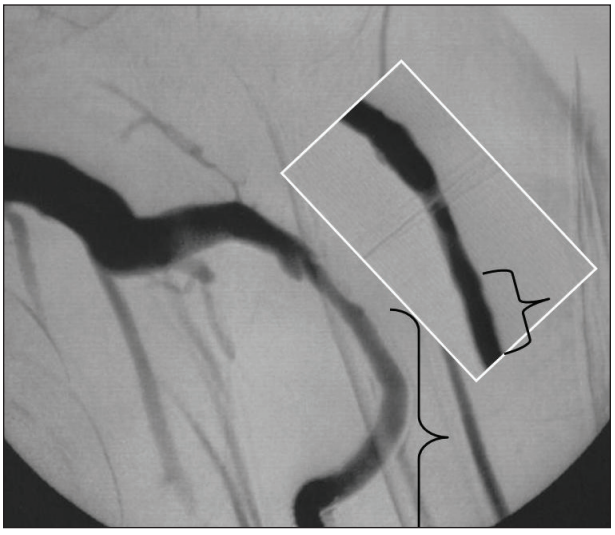

Figure 4. Angiographic image represents the ability of the GORE VIABAHN Device (bracket) to conform to the changing orientation of the upper arm graft when the arm is laid across the chest. Some torsion was observed when compared to the arm extended 90° from the body (inset), but was not determined to be clinically significant.

CONCLUSION

Although we typically examine accesses in the arm in an abducted position, the arm is normally at the side, and there can be significant changes in the length and course of the vein in different arm positions. These changes can be hemodynamically significant. Stents or stent-grafts should be used with caution in the axilla, as there is a downside to stiff foreign bodies in the veins. Stents and stent-grafts can solve many problems in dialysis access management, but they can also cause problems that might not be immediately obvious. Positional studies can uncover these complications, and flow measurements can confirm their significance. ■

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Successful Outcomes With the GORE VIABAHN Endoprosthesis

Experts share their experience with this device for AV access.

PARAMJIT "ROMI" CHOPRA, MD
The Midwest Institute of Minimally Invasive Therapies
Melrose Park, Illinois
Dr. Chopra has disclosed that he has served as paid consultant to Covidien; Cardiovascular Systems, Inc.; and W. L. Gore & Associates, Inc.

STEPHEN SETTLE, MD
Cardiothoracic and Vascular Surgeons
Austin, Texas
Dr. Settle has disclosed that he has received paid honorarium from W. L. Gore & Associates, Inc. for speaking engagements.

TOUFIC SAFA, MD, FACS
Medical Director, AAA Vascular Care PLLC
Great Neck, New York
Dr. Safa has stated that he has no financial interests to disclose.

Please share with us the impact the GORE VIABAHN Endoprosthesis has on the outcomes for your patients.

Dr. Chopra: The VIABAHN Device has been very effective in long-segment stenosis of the venous outflow. I use the VIABAHN Device as an extension of the graft, rather than placing a bare stent in the elbow joint or across the shoulder. Almost 4 or 5 years ago, I stopped using bare stents altogether in venous outflow. I have patients who have been on dialysis with patent VIABAHN Devices for 6 or 7 years. I have one patient, in fact, in whom we have done a lot of interventions, and he literally has a graft from one wrist up to the cephalic arch right to the subclavian. He's been patent for many years. The VIABAHN Device has been very good for long term outcomes and avoiding surgery.

Dr. Settle: The VIABAHN Device has allowed me to offer a less invasive method for a more complete resolution of access dysfunction secondary to venous outflow problems. This especially applies to situations in which surgical revisions are not possible due to inaccessible lesions and prevents the abandonment of the access. The VIABAHN Device is the best option for revising AV access grafts because I am able to treat only the diseased segment of vein, allowing for greater vein preservation. It creates a more physiologic repair with laminar flow into the outflow vein than would occur with a typical end-to-side surgical revision. In addition, there is a lower morbidity and wound complication rate. I believe it is the best treatment when you have an obvious outflow abnormality with increased pulse pressure on exam but a marginal radiographic stenosis. This minimally invasive approach diminishes the need for anesthesia and decreases the risk of serious metabolic and electrolyte imbalances. In addition, it also comes with higher patient satisfaction due to a decrease in the pain and scarring that come with surgical revisions. The VIABAHN Device is always my first choice for revisions, when technically feasible.

Dr. Safa: The VIABAHN Device has transformed the way I practice vascular surgery in recent years. Ever since it became available for clinical use in the United States, I started implanting it in the SFA. Shortly, thereafter, I started using it for AV access management. In my opinion, when this stent-graft is used appropriately and selectively, it stands to significantly improve outcomes with the least amount of postprocedure morbidity.

What characteristics unique to VIABAHN provide you a distinct advantage over other stent-graft offerings when treating dysfunctional dialysis access grafts?

Dr. Chopra: First, the length is great. It is flexible. It is trackable.

Dr. Safa: The VIABAHN Device is very flexible and has an excellent radial support. Not only does it maintain good patency in resistant occlusive lesions after implantation, it can handle tortuosities, curves, and bends like no other stent-graft. This makes it suitable for lesions across joints and in a curve of a graft. Stent fracture, collapse, and kink are extremely rare and almost nonexistent.

Dr. Settle: The unique characteristics that make the GORE VIABAHN Device my choice of stent-graft for the treatment of dysfunctional dialysis access are its simple deployment mechanism with precise placement; smaller sheath size; flexibility of the stent across joint space with more durability and no stent fracture; and heparin bonding to provide decreased thrombogenic surface.

Can you articulate the value of the GORE VIABAHN Device over BMS in AV graft revisions?

Dr. Chopra: I don't think of the VIABAHN Device as a stent; I think of it as a graft with a little exoskeleton of wires (so technically, they may define it as a stent). I don't see restenosis in the middle of the graft; all the bare stents have progressive restenosis. If a problem develops, it is typically at the edges and easily revised. I am able to keep it patent for a long time.

Dr. Safa: The VIABAHN Device has been shown, without any doubt, to extend the life of a failing AV graft when used instead of balloon angioplasty alone at the venous anastomosis. In my experience, I have also noticed that the patency of AV grafts can be extended by using VIABAHN Devices instead of BMS. On long-term follow-up, recurrent occlusive lesions seem to develop more rapidly and in a more diffuse fashion in a BMS patient as compared to a VIABAHN Device patient. A recurrent lesion in a VIABAHN Device tends to be more focal and much easier to manage and deal with.

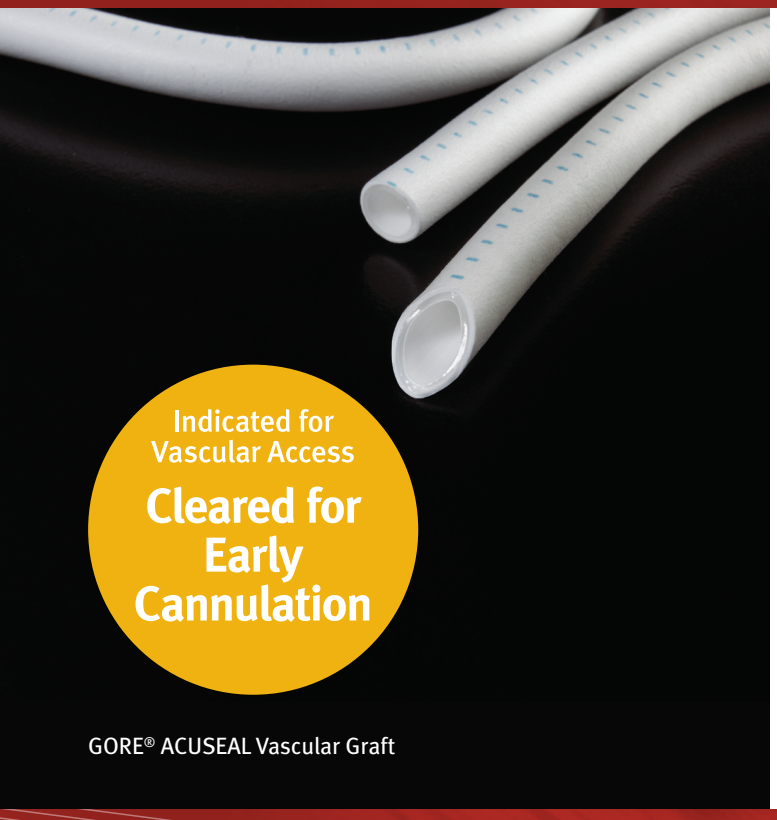
At what point in your treatment algorithm do you implant a GORE VIABAHN Device rather than continued PTA revisions? Why?

Dr. Chopra: Sometimes, even if I get good technical results, I still look for clinical success, which is getting a thrill. Often, I will wait a good 5 or 7 minutes, sometimes even 10 minutes, to see if there is a rebound. I will do an angioplasty, and if there is any doubt of irregularity, I will place a VIABAHN Device, because it costs more to bring the patient back later—not just in terms of dollars, but also for the patient, both in terms of diminishing health due to missing dialysis and the overall cost of the additional revision. You must see what works for the patient. I will do a declot and obtain the angiogram. If I see a stenosis, I perform angioplasty and test to see if there is clinical success. If there is a great thrill, and I have waited 10 minutes, the patient doesn't need a device. If there is any doubt or some irregularity, I cover it with the device. I can keep that open for a long time.

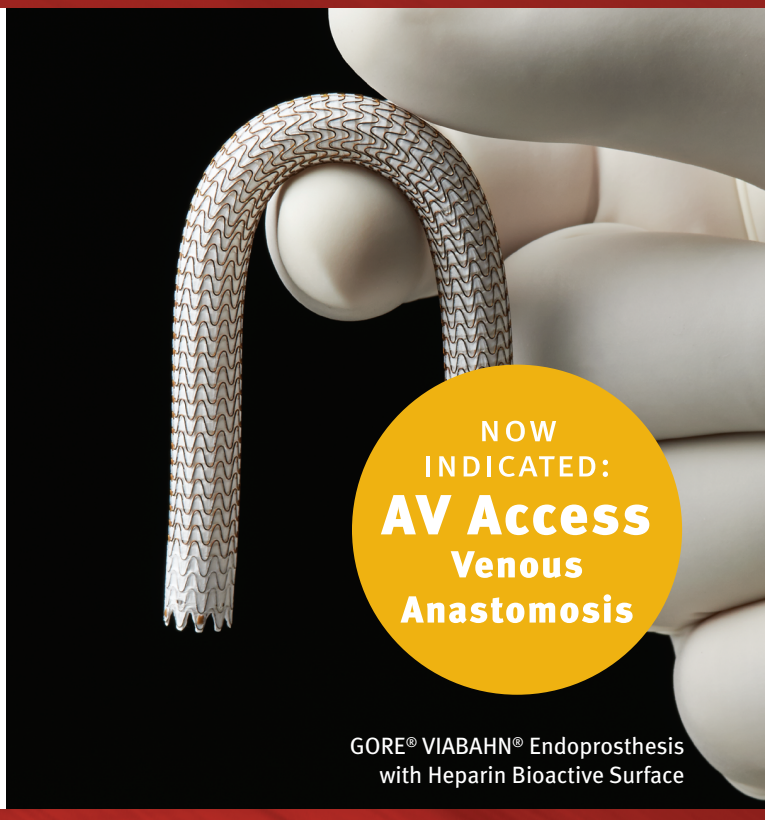
Dr. Settle: I think the 2006 KDOQI guidelines stated that if the same lesion requires angioplasty within a 3-month period, then a surgical revision was indicated. Treatment with a VIABAHN Endoprosthesis is now an appropriate substitution and a good place to start. If I see a patient with a quick recurrence or thrombosis in the same lesion within a 30-day period, I believe these lesions should also be treated with a stent-graft. In addition, any lesion that does not give a satisfactory result, either radiographically or on physical examination, should be treated.

Dr. Safa: After an over 7-year experience with the VIABAHN Device in the AV access field, I have come to realize that it should be the first choice in the management of occlusive lesions at the venous anastomosis of an AV graft. This would provide much better patency and freedom from reinterventions over a 6 to 12 month period when compared to other treatment modalities. ■

Data-driven Solutions, Patient-focused Outcomes



GORE® ACUSEAL Vascular Graft



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INTENDED USE / INDICATIONS: The GORE® VIABAHN® Endoprosthesis is indicated for improving blood flow in patients with symptomatic peripheral arterial disease in superficial femoral artery lesions up to 230 mm in length with reference vessel diameters ranging from 4.0 – 7.5 mm. The GORE® VIABAHN® Endoprosthesis is indicated for improving blood flow in patients with symptomatic peripheral arterial disease in iliac artery lesions up to 80 mm in length with reference vessel diameters ranging from 4.0 – 12 mm. The GORE® VIABAHN® Endoprosthesis is also indicated for the treatment of stenosis or thrombotic occlusion at the venous anastomosis of synthetic arteriovenous (AV) access grafts. Refer to *Instructions for Use* at goremedical.com for a complete description of all contraindications, warnings, precautions and adverse events. ℞ Only

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