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Improving Cost-Effectiveness: How Stent-Grafts Change the Natural History of the Dialysis Access Circuit

Advancing the paradigm for the treatment options of hemodialysis access grafts.

BY JOHN E. ARUNY, MD, AND BELINDA A. MOHR, PHD

After its initial clinical success as graft material for femoropopliteal artery bypass, expanded polytetrafluoroethylene (ePTFE) was proposed as a vascular access conduit for chronic hemodialysis.[1] ePTFE was believed to have similar complication rates when compared to widely used bovine heterografts with improved availability, ease of handling, and decreased cost. After slightly more than a year, complications leading to graft failure were identified. Venous anastomotic stenoses were found to be a leading cause of the majority of these graft failures.[2]

Longitudinal reporting of ePTFE patency revealed a primary patency rate of 41% and a secondary patency rate of 59% at 1 year.[3] Cumulative patency was maintained by surgical revisions that often included jump grafts that shortened the length of available vein for future access placement. Importantly, the interval patency after each revision was shorter than previously reported rates, with 1-year patency rates of 23%, 16%, and 17% after the first, second, and third revisions, respectively. The number of surgical revisions needed to maintain 1-year cumulative patency was not disclosed, making the costs difficult to determine.

Thus, the natural history of ePTFE access grafts, from their earliest days of hemodialysis access use, was defined by poor primary patency, followed by a need to maintain secondary patency through subsequent interventions that were less effective, eventually culminating in graft abandonment.

BALLOON ANGIOPLASTY

In 1982, the application of balloon angioplasty expanded the treatment options with emphasis on the nonsurgical preservation of dialysis access.[4] Today, despite the development of high-pressure balloons and smaller delivery systems, the patency results remain disappointing. Reports from the percutaneous transluminal angioplasty (PTA) arm of several comparative trials, including the FLAIR trial, the GORE REVISE clinical study, and a peripheral cutting balloon study showed a 6-month primary patency rate between 23% and 36% at the treatment site.[5-7] The 6-month primary patency at the dialysis access circuit was between 20% and 36% (weighted average, 30%). Elastic recoil of the treatment site, development of intimal hyperplasia, and occasional rupture of the native vein are the limiting factors of PTA alone. Thus, PTA alone failed to meaningfully alter the natural history of failing synthetic grafts.

BARE-METAL STENTS

After gaining experience in the treatment of these difficult lesions, it became apparent that PTA alone would not solve the recurrent problems of venous outflow stenoses from ePTFE dialysis conduits. The feasibility and safety of using self-expanding metal stents was demonstrated in 1989 with the clinical use of the WALLSTENT™ Endoprosthesis (Boston Scientific Corporation) to treat lesions that responded poorly to PTA alone.[8] Bare-metal stents (BMS) solved the problem of technically failed PTA secondary to elastic recoil, but were disappointing in significantly prolonging patency. Ingrowth of intimal hyperplasia remained unchecked. No multicenter, prospective, randomized trial comparing BMS to PTA has ever been conducted. Retrospective analysis of access circuit 6-month primary patency in studies reported between 2004 and 2013 using a variety of BMS varied between 19% and 67% (weighted average, 33%).[9-16] Disappointingly, the results are not significantly different from PTA alone,

TABLE 1. PATENCY RESULTS OF THE GORE REVISE CLINICAL STUDY FOR THE TARGET LESIONS AND THE ENTIRE DIALYSIS ACCESS CIRCUIT[7]

Outcomes Effectiveness-per-protocol group	GORE® VIABAHN® Endoprosthesis (N = 131)	Angioplasty (N = 138)	*P* Value
Target lesion primary patency (TLPP)			.008
Month 6	52.9%	35.5%	—
Month 12	30.2%	18.2%	—
Month 24	15.7%	9.9%	—
Median days to loss of TLPP	203	108	—
Vascular access circuit primary patency (CPP)			.035
Month 6	43.4%	29.4%	—
Month 12	21.4%	15.2%	—
Month 24	9.6%	6.8%	—
Median days to loss of CPP	126	91	—

suggesting an inability of BMS to reliably alter the natural history of a failing synthetic graft.

STENT-GRAFTS

Like BMS, ePTFE-covered stents address elastic recoil—one of the major failings of PTA. However, unlike BMS and PTA, the ePTFE covering can also more effectively address a second failure mode of restenotic lesions at the graft venous anastomosis—exuberant tissue hyperplasia. The ePTFE covering adds a physical barrier through which tissue cannot penetrate. Covered stents alter the natural history of a failing graft with this dual effect of limiting tissue ingrowth and resisting elastic recoil.

Two large, multicenter, randomized trials comparing the results of PTA alone with PTA plus stent-grafts have been conducted to investigate this line of thinking. The first study, the FLAIR trial, randomized 190 patients at 13 sites with dialysis access graft venous anastomotic stenosis to PTA alone or PTA with placement of a self-expanding nitinol stent covered in carbon-impregnated ePTFE (FLAIR® Endovascular Stent-Graft, Bard Peripheral Vascular, Inc.).[5] The results showed statistically better primary patency of both the site target lesion (51% vs 23%; $P < .001$) and the access circuit at 6 months (38% vs 20%; $P = .008$). In addition, freedom from subsequent interventions at 6 months was lower in the stent-graft group (78% vs 28%; $P < .001$).

The GORE REVISE clinical study is a multicenter trial that randomized 293 patients with significant stenosis at the venous anastomosis of an ePTFE graft to PTA alone or PTA plus placement of the GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface.[7] The GORE REVISE clinical study allowed the inclusion of thrombosed grafts as well as those that were failing. Patients were followed for 2 years, and the primary patency results are presented in Table 1.

Because of differences in follow-up methods and inclusion/exclusion criteria, it is difficult to directly compare the results of the two trials. However, it is clear that both trials showed superiority of stent-grafts in prolonging primary patency, thereby altering the natural history of the access in some way.

The 24-month results of the GORE REVISE clinical study further support that stent-grafts alter the natural history of a failing synthetic graft. Indeed, the clinical superiority of prolonged primary patency translated into fewer interventions to maintain secondary patency of the circuit (3.7 vs 5.1 over 24 months) and pointed to a potential economic benefit of this treatment modality.

Figure 1 demonstrates cost-effective results of improved primary patency and fewer interventions to maintain secondary patency realized when patients were treated with PTA plus the GORE VIABAHN Endoprosthesis. The average total cost at 24 months for the PTA plus GORE VIABAHN Endoprosthesis group was $23,001 compared to $24,882 for the PTA alone group, representing a cost savings of $1,881.[17]

Figure 2 shows the crossing point at 13 months of the cost curves. At this point, the initial increased cost of implanting a covered stent is exceeded by the more

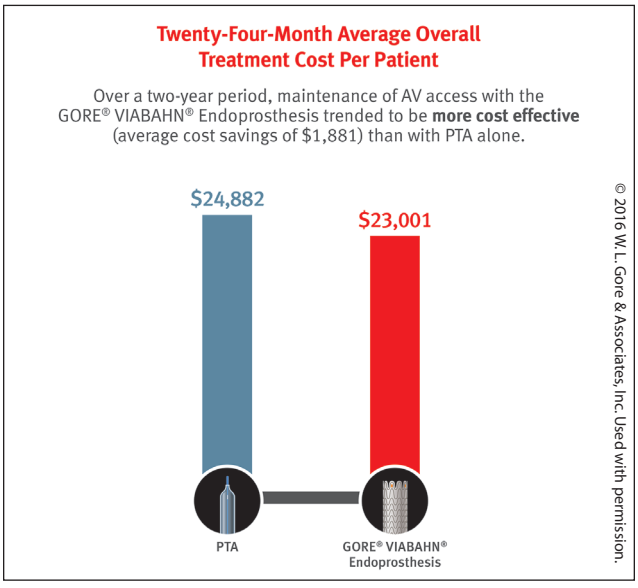

Figure 1. Average total costs at 24 months for PTA versus the GORE® VIABAHN® Device in the GORE REVISE clinical study.

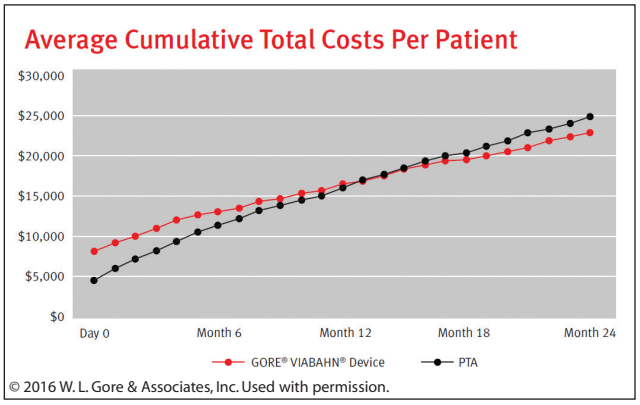

Figure 2. Cost curves for the GORE REVISE clinical study showing average total cumulative costs per patient. Note the curves cross at 13 months, where the increased costs of maintaining the grafts treated with PTA alone surpass the costs of the cohort treated initially with the stent-graft.

frequent, costly procedures in the PTA alone cohort to maintain secondary patency at 2 years. In the entire PTA alone group, repeat interventions cost $20,632. Although repeat interventions were $14,939 in the PTA plus the GORE VIABAHN Endoprosthesis group, there was a savings of $5,693 over 2 years ($P < .001$).[17]

In the GORE REVISE clinical study, when grafts presented thrombosed, the cost-effectiveness was amplified as compared to the entire group. The average total cost at 24 months in the PTA alone cohort was $31,717. This included an initial index procedure cost of $5,202 and subsequent cost of $26,514 for repeat interventions over 2 years. In the covered stent cohort, the larger initial index procedure cost of $9,074 was neutralized over 2 years by significantly decreased repeat intervention costs of $15,989 ($P < .001$).[17]

STENT-GRAFTS AS PRIMARY THERAPY?

Given the complexities and uniqueness of each patient's access, many physicians find it difficult to believe that every stenosis at the venous anastomosis of a synthetic graft should receive a stent-graft at first pass. Thus, although there is level 1 evidence that clearly demonstrates the clinical and economic advantages of stent-grafts over PTA alone, it remains to be seen if this is the right choice for treating de novo lesions for every patient. More studies are needed to better clarify which patients should be treated with a stent-graft as a first-line therapy.

SUMMARY

Clinical superiority of stent-grafts over PTA alone to treat lesions at the venous anastomosis has been demonstrated by two large, multicenter, randomized trials that demonstrated how to change the natural history of failing synthetic grafts in ways that alternative therapies have not. The GORE REVISE clinical study showed that altering the natural history of the dialysis graft with stent-grafts has economic benefits. Integrating patency data with cost data from the GORE REVISE clinical study shows economic value of stent-grafts as a primary treatment for dysfunctional and especially thrombosed grafts. Further research efforts should focus on clarifying when and for what patients a stent-graft is the optimal choice. ■

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John E. Aruny, MD
Interventional Radiologist
Yale New Haven Hospital
New Haven, Connecticut
john.aruny@yale.edu
Disclosures: Consultant for Gore & Associates.

Belinda A. Mohr, PhD
Health Economist
W.L. Gore & Associates, Inc.
Flagstaff, Arizona
Disclosures: Employee of Gore & Associates.