Maintenance of Hemodialysis Access With Stents and Covered Stents

Hemodialysis access maintenance advances beyond angioplasty.

BY BART L. DOLMATCH, MD

The recent United States Renal Data System report[1] shows an ongoing increase in the number of patients undergoing hemodialysis. In 2006, more than 350,000 Americans with end-stage renal disease required hemodialysis for renal failure. Hemodialysis is best performed using a permanent vascular circuit with either a direct arteriovenous anastomosis (arteriovenous fistula [AVF]) or an interposed conduit between the artery and vein (arteriovenous graft [AVG]).

The Fistula First Initiative has substantially increased the prevalence of AVFs in the United States. Current data from the Fistula First Web site[2] cite AVF prevalence to be at 54.9%. The "best guess" estimate of AVG prevalence places it around 20%, while the remaining 25% of patients undergo hemodialysis with a catheter.

Both AVFs and AVGs are prone to failure, often on the basis of stenosis and subsequent thrombosis. Regarding AVFs, Huber's meta-analysis of AVFs and AVGs[3] found that the primary patency rate of more than 1,800 AVFs was 51% at 18 months, but that does not include AVFs that cannot be used, often related to inflow stenosis. Historical data report that early AVF failure occurs in one-third to one-half of all AVFs in the United States. However, a recent Dialysis Access Consortium multicenter prospective study of 877 AVFs[4] found that early failure was seen in 60% of all AVFs, and half of these AVFs were abandoned without expectation of future use. Therefore, when one looks at primary patency of an AVF based on the intention to use it for hemodialysis, the combined effect of early failure and attrition due to late stenosis and thrombosis would probably result in fewer than half of the AVFs remaining primarily patent and functional at 1 year.

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For patients who cannot receive an AVF, an AVG is often the next best form of hemodialysis access. Additionally, there may be some benefit of an AVG over an AVF in select patient populations, such as in the very elderly, in which benefits from early use of an AVG may supercede the conceptual benefits of an AVF. Unlike AVFs, in which early failure is a formidable problem, AVGs suffer from ongoing loss of primary patency due to venous anastomotic stenosis that often leads to thrombosis. In another Dialysis Access Consortium study,[5] the primary patency rate in a series of 649 AVGs placed at 13 different centers was only 25% at 1 year.

AV ACCESS ANGIOPLASTY: WORKS WELL BUT IS NOT DURABLE

Although there are different reasons that many AVFs and AVGs are not primarily patent at 1 year, the reality is that loss of primary patency is often due to stenosis. Both surgical and percutaneous options can be used to maintain AV access patency. Percutaneous transluminal angio-

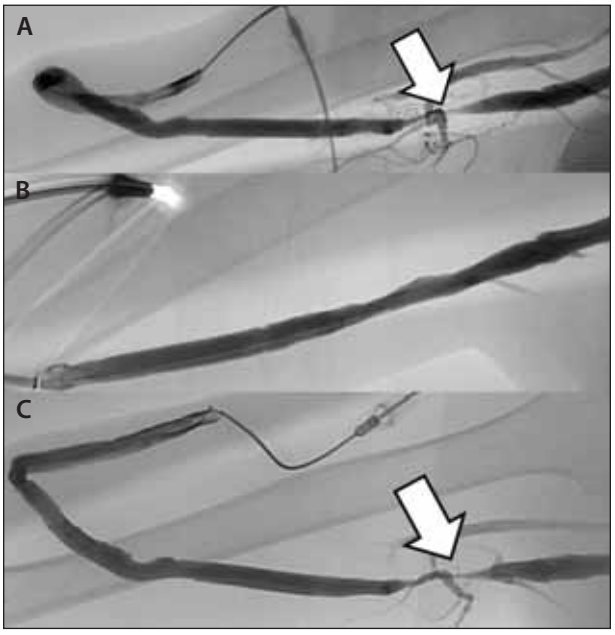

Figure 1. Early recurrent stenosis after PTA of an AVG venous anastomotic stenosis. Venous anastomotic stenosis (arrow) in an upper arm AVG (A). Postangioplasty result (8-mm PTA) (B). Recurrent stenosis at 3 months (arrow) (C).

plasty (PTA) has been widely adopted as a first-line therapy because, when compared to surgical revision, it is less invasive and can be readily scheduled and performed.

PTA is also technically successful and safe. The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines[6] have defined post-PTA anatomic success as a reduction of the original stenosis (50% diameter or greater) to a final diameter of < 30% of the nonstenosed reference circuit diameter. Beathard et al[7] reported a 97% anatomic success rate in 1,561 AVF PTA procedures and a 98% success rate in 3,560 AVG procedures. The major complication rates were only 0.19% and 0.11%, respectively, for AVF and AVG angioplasties. AV access PTA is widely seen as a terrific technique that effectively treats stenosis, maintains access function, and has few associated major complications.

The problem with AV access PTA is that it is not very durable (Figure 1). Recoil and neointimal proliferation at the PTA site frequently lead to recurrent AV access dysfunction within several months after PTA. Based on many reports, KDOQI's Vascular Access Clinical Practice Guideline 19 recommends a target goal of "50% unassisted patency at 6 months" after successful PTA of an AVG stenosis.[6] Since that recommendation was published, Vesely et al prospectively followed a control group of 94 patients with AVG stenoses who underwent PTA and noted 6-month circuit patency of only 40.9%.[8] The reality is that approximately half of the patients who undergo PTA will return with recurrent AV access dysfunction within 6 months.

AV ACCESS STENTS: RECENT STUDIES CONFIRM THE ESTABLISHED RECOMMENDATIONS FOR LIMITED STENT USE

Various reports from the 1990s demonstrated that stents offered no advantage over successful AV access angioplasty.[9-11] More recently, Vogel and Parise[12] studied the use of nitinol self-expanding stents for post-PTA bailout in AVGs and found 51% 6-month patency—not much different from previous reports in which PTA was successful. Kariya et al[13] compared the Wallstent (Boston Scientific Corporation, Natick, MA) for salvage of failed PTA and compared the results with successful PTA. At 6 months, the Wallstent's 39% primary patency was statistically inferior to the 73% primary patency rate in the successful PTA group (P = .028).

Failure of stents to provide better post-PTA patency is largely due to the development of in-stent stenosis (Figure 2). Contemporary use of stents in AV access intervention is best summarized in the KDOQI Vascular Access Clinical Practice Guideline 19,[6] which states that "stents are useful in selected instances (eg, limited residual access sites, surgically inaccessible lesions, contraindication to surgery) when PTA fails." Simply stated, stents are used as a PTA bailout.

COVERED STENTS FOR AVG STENOSIS: THE TIME HAS COME

A multicenter, randomized clinical trial of the Flair covered stent (Bard Peripheral Vascular, Inc., Tempe, AZ) was recently reported by Haskal et al.[14] This covered stent, composed of a self-expanding nitinol stent embedded within expanded polytetrafluoroethylene (ePTFE) graft material, was studied in a prospective, randomized human clinical trial.

The Flair trial study design randomized patients with AVG venous anastomotic stenosis to either conventional PTA or PTA with covered stent placement. Primary patency was met only if both angiographic and clinical criteria were fulfilled. For example, if the access was functional without any clinical problem but a 50% stenosis was seen at the treatment site, circuit primary patency was lost. Or if there was any report of AV access dysfunction (based on KDOQI parameters and defined in the clinical protocol) but no stenosis was found anywhere in the AVG, circuit primary patency was lost. Treatment of any stenosis was considered loss of primary patency, even if the interventionist decided to treat a 30% stenosis during one of the scheduled fol-

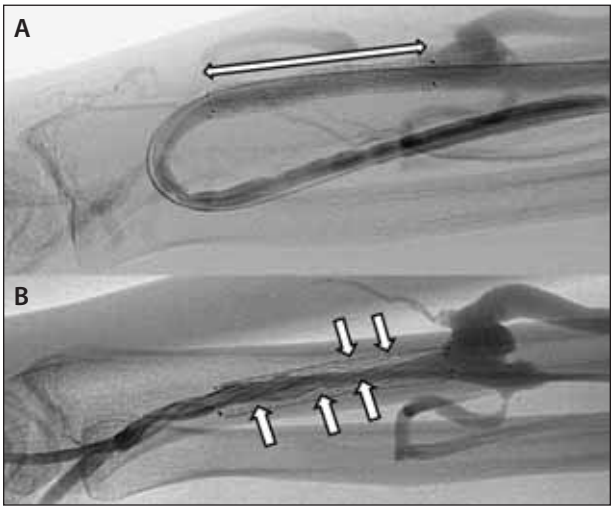

Figure 2. In-stent stenosis within a stent placed in the juxtaanastomotic venous segment of a radiocephalic AVF. Self-expanding stent (double arrow) placed at PTA site in a radiocephalic AVF because of residual stenosis (A). Three-month angiographic study shows in-stent restenosis (arrows) (B).

low-up studies. Given this very high bar that each AVG had to clear to remain primarily patent, and noting that in both groups there were also bona fide stenoses in dysfunctional AVGs at the follow-up studies, the patency rates for both treatment groups were much lower than most other studies where such rigid criteria were not applied. However, the strength of a randomized study is not in the absolute patency rates but rather the comparison of two groups under the same definitions and criteria.

When PTA was compared to PTA/Flair, the primary patency rate for AVGs in patients who received the Flair covered stent was nearly twice as good as for patients who were treated with PTA alone (38% vs 19.8%; $P = .008$), and patency at the treatment site was more than doubled for the PTA/Flair group (50.6% vs 23.3%; $P < .001$). There were also some remarkable follow-up angiographic studies long after the clinical trial had concluded, with widely patent Flair covered stents well beyond a year (Figure 3).

The Flair demonstrated a safety profile and patency advantage that garnered US Food and Drug Administration approval for primary use when performing PTA of AVG venous anastomotic stenosis, even when PTA was technically successful. A larger, randomized postapproval clinical study of the Flair, RENOVA (Postapproval Study of the FLAIR Endovascular Stent Graft), is underway and will collect data to 24 months for 270 patients who will be randomized between PTA and PTA/Flair.

Concurrently, there is an ongoing 280-patient, multicenter, randomized clinical trial of the Viabahn endoprosthesis (W. L. Gore & Associates, Flagstaff, AZ) for treating AVG venous anastomotic stenosis. This trial, called REVISE (Vascular Access Revision With Viabahn Endoprosthesis vs Percutaneous Transluminal Angioplasty), has not announced midterm results yet.

Not only have the RENOVA and REVISE trials shown that it is possible to create acronyms by a nearly random selection of letters, but it is hoped that these studies will give us a comprehensive understanding of the role of ePTFE-covered stents in AVGs as well as a better understanding of many other factors that relate to maintenance of AVG patency.

COVERED STENTS FOR AVF STENOSIS: THE NEXT FRONTIER

Although clinical trials are being done to explore the role of covered stents in AVGs, today there are fewer AVGs than AVFs, largely due to the success of the Fistula First program. How do covered stents fare when used to treat stenoses in AVFs? We are now beginning to see early clinical reports. A recent retrospective, single-center report describes use of the Fluency ePTFE-covered stent

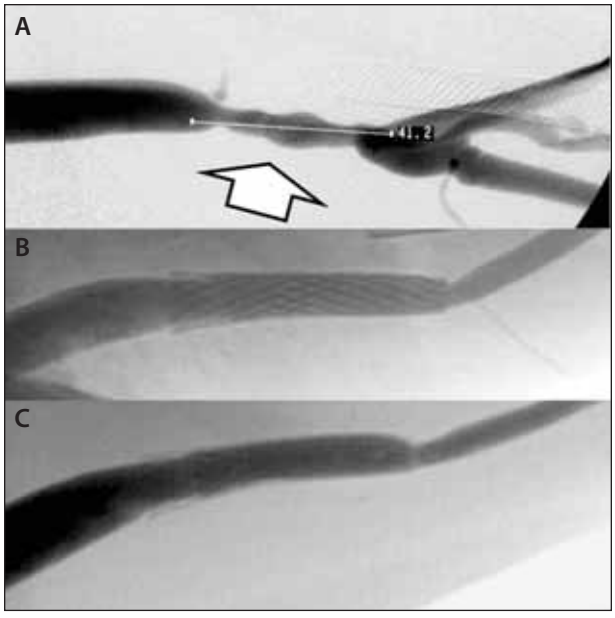

Figure 3. Long-term follow-up of the treatment site in a patient who was randomized to receive the Flair covered stent in the original prospective clinical trial. Stenosis at the venous anastomosis of an AVG before treatment (arrow) (A). PTA and Flair covered stent placement 10 months earlier remain patent (B). Thirty-five-month patency at the treatment site (C). Patient returned due to intragraft stenosis (not shown).

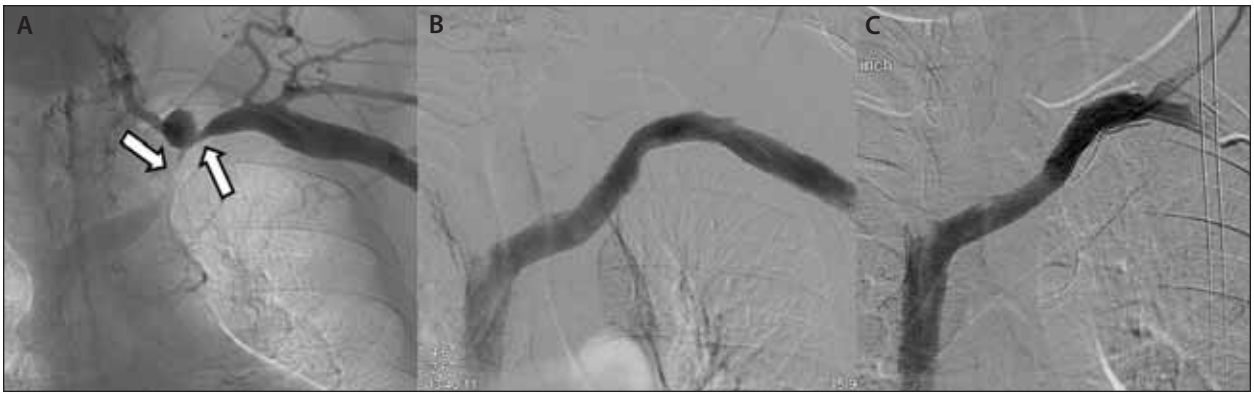

Figure 4. Patency of a central vein covered stent. Left subclavian and brachiocephalic vein stenoses before treatment (arrows) (A). After angioplasty and Viabahn covered stent placement (B). Six-month venogram of Viabahn during declotting of peripheral AVG (C).

(Bard Peripheral Vascular, Inc.) to treat five stenotic AVFs with an 80% 9-month patency rate.[15] More recently, this group described the use of the Fluency covered stent in 17 patients with an 88.2% primary access patency rate at 6 and 12 months.[16]

BEYOND AVF STENOSIS: OTHER COVERED STENT APPLICATIONS IN AV ACCESS

A few other potential applications of covered-stent technology in hemodialysis access should be mentioned, such as treatment of PTA-induced rupture, pseudoaneurysm repair, and as an adjunct to PTA during the treatment of central vein stenosis and occlusion.

We reported the use of the Fluency covered stent to treat immediate PTA-induced rupture in both AVGs and AVFs[17] with excellent technical success, although 6-month AV access patency was not very different from previous reports in which bare stents were used to treat rupture. Nevertheless, covered stent placement was technically successful and avoided late pseudoaneurysms, hospital admission, and the need for urgent surgery. Although it is not clear why patency was not improved with a covered stent, these access circuits may fail for many reasons, often related to very diseased AV access circuits and the development of new stenoses elsewhere in the circuit.

There may also be a role for covered stents in treating AV access aneurysms and pseudoaneurysms. The Viabahn covered stent has been successfully used to treat AVG pseudoaneurysms, as reported by Vesely.[18] These pseudoaneurysms form at the AVG cannulation sites from repeated puncture of the graft material during cannulation. Treating these pseudoaneurysms with the Viabahn necessitated its placement at a cannulation site where it would be repeatedly punctured, so the development of Viabahn stent fractures over time was not surprising.

Finally, both Fluency and Viabahn covered stents have been used to treat central venous stenosis in hemodialysis circuits with anecdotal success (Figure 4). Presently, however, peer-reviewed reports to support this practice are lacking. Furthermore, neither the Fluency nor the Viabahn were specifically designed for use in central veins, where covered stent length, diameter, design, and delivery system requirements are very different from requirements in the AV access circuit, and the tracheobronchial and peripheral arterial systems. So, although these devices may work better than PTA in central veins (although we do not know that for sure), they have not been optimized for this application.

CONCLUSION

Angioplasty has been used to maintain failing AVGs and AVFs for more than 2 decades, and although safe and technically successful, primary patency is poor. Stents do not improve on PTA results and are now recommended only for PTA bailout. Covered stents show early promise, with particular reference to the Flair covered stent trial results in AVGs, where this covered stent nearly doubled access circuit patency compared to PTA alone. Both the RENOVA and REVISE clinical trials will likely add a great deal to our understanding of covered stent use in AVGs. Meanwhile, challenges and opportunities lie ahead for the use of covered stents in AVFs, AV access pseudoaneurysms, and central venous obstructions. ■

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1. National Institute of Diabetes and Digestive and Kidney Diseases. US Renal Data System. 2008 annual data report: atlas of chronic kidney disease and end-stage renal disease in the United States. http://www.usrds.org/2008/view/esrd_04.asp. Accessed January 13, 2009.
2. Fistula First National Vascular Access Improvement Initiative. http://www.fistulafirst.org/. Accessed April 27, 2010.
3. Huber TS, Carter JW, Carter RL, et al. Patency of autogenous and polytetrafluoroethylene upper extremity arteriovenous hemodialysis accesses: a systematic review. J Vasc Surg. 2003;38:1005-1011.
4. Dember LM, Beck GJ, Allon M, et al. Effect of clopidogrel on early failure of arteriovenous fistulas for hemodialysis: a randomized controlled trial. JAMA. 2008;299:2164-2171.
5. Dixon BS, Beck GJ, Vazquez MA, Greenberg A, et al. Effect of dipyridamole plus aspirin on hemodialysis graft patency. N Engl J Med. 2009;360:2191-2201.
6. NKF-K/DOQI Clinical Practice Guidelines for Vascular Access: update 2000. Am J Kidney Dis. 2001;7:S137-S181.
7. Beathard GA. Percutaneous transvenous angioplasty in the treatment of vascular access stenosis. Kidney International. 1992;42:1390-1397.
8. Vesely TM, Siegel JB. Use of the peripheral cutting balloon to treat hemodialysis-related stenoses. J Vasc Interv Radiol. 2005;1593-1603.
9. Hoffer EK, Sultan S, Herskowitz MM, et al. Prospective randomized trial of a metallic intravascular stent in hemodialysis graft maintenance. J Vasc Interv Radiol. 1997;8:965-973.
10. Gray RH, Horton KM, Dolmatch BL, et al. Use of Wallstents for hemodialysis access-related venous stenoses and occlusions untreatable with balloon angioplasty. Radiology. 1995;195:479-484.
11. Patel IR, Peck SH, Cooper SG, et al. Patency of Wallstents placed across the venous anastomosis of hemodialysis grafts after percutaneous recanalization. Radiology. 1998;209:365-370.
12. Vogel PM, Parise C. SMART stent for salvage of hemodialysis access grafts. J Vasc Interv Radiol. 2004;15:1051-1060.
13. Kariya J, Tanigawa N, Kojima H, et al. Peripheral stent placement in hemodialysis grafts. Cardiovasc Intervent Radiol. 2009;32:960-966.
14. Haskal ZJ, Trerotola S, Dolmatch B, et al. Stent graft versus balloon angioplasty for failing dialysis-access grafts. N Engl J Med. 2010;362:494-503.
15. Gupta M, Rajan DK, Tan KT, et al. Use of expanded polytetrafluoroethylene-covered nitinol stents for the salvage of dysfunctional autogenous hemodialysis fistulas. J Vasc Interv Radiol. 2008;19:950-954.
16. Bent CL, Rahan DK, Tan K, et al. Effectiveness of stent-graft placement for salvage of dysfunctional arteriovenous hemodialysis fistulas J Vasc Interv Radiol 2010;21:496-502.
17. Dale JD, Dolmatch BL, Duch JM, et al. Expanded polytetrafluoroethylene-covered stent treatment of angioplasty-related extravasation during hemodialysis access intervention: technical and 180-day patency. J Vasc Interv Radiol. 2010;21:322-326.
18. Vesely TM. Use of stent grafts to repair hemodialysis graft-related pseudoaneurysms. J Vasc Interv Radiol. 2005;16:1301-1307.