Unfortunately, PTA of AVG stenosis is not durable. Recoil and neointimal proliferation at the PTA site frequently lead to recurrent stenosis within several months following PTA. Based upon many reports, the 2000 National Kidney Foundation’s Dialysis Outcome Quality Initiative (K-DOQI) Vascular Access Clinical Practice Guideline #19 recommended a target goal of “50% unassisted patency at 6 months” after successful PTA of an AVG stenosis (4). Clearly, the expectation for PTA durability in AV access is much lower than that for PTA used almost anywhere else in the body, where post-PTA failure in half the patients at 6 months would not be acceptable.

Stents were once believed to hold promise in prolonging PTA patency. It is now accepted that stents offer no advantage over technically successful angioplasty (5-8), largely due to neointimal proliferation leading to in-stent stenosis. Contemporary use of stents in AV access intervention is best summarized in the 2000 K-DOQI Vascular Access Clinical Practice Guideline #19, “Stents are useful in selected instances (e.g., limited residual access sites, surgically inaccessible lesions, contraindication to surgery) when PTA fails.” Simply stated, stents are used as a PTA bailout.

Hopes that the peripheral cutting balloon (Boston Scientific, Natick, MA, USA) would provide better patency than PTA for AVG stenoses were dashed by the Cutting Edge trial. This study was randomized, prospective, and multi-center. It showed that there was no patency advantage for the peripheral cutting balloon compared to PTA for treating stenotic AVGs (9). This trial also afforded some
of the best data on plain old balloon angioplasty. Primary patency at 6 months following conventional PTA of stenotic AVGs was only 41%, below the K-DOQI recommended threshold of 50% 6-month primary patency following PTA of AVGs!

Therefore, neither stents nor the peripheral cutting balloon has improved patency after percutaneous intervention in AVGs. So, we have had to settle for relatively poor results from PTA...until the Haskal study. The hypothesis of this trial was that in-stent restenosis due to neointimal ingrowth could be prevented by a barrier of graft material on a stent. The barrier selected for this stent-graft was expanded polytetrafluoroethylene (ePTFE), the same material used to create synthetic AVG circuits.

It seems intuitive that a barrier could prevent in-stent restenosis, however, there were many steps to reach this goal. Early modeling of stent grafts for “medium sized” blood vessels, 5 to 12 millimeters in diameter, began with laboratory study of handmade devices that coupled stents with either ePTFE or Dacron-type (Polyethylene terephthalate, PET) bypass graft materials. Ultimately, collaboration with device manufacturers led to the PET-covered Wallstent (Boston Scientific, Natick, MA, USA), the ePTFE-covered Hemobahn (now called the Viabahn; W.L. Gore and Associates, Flagstaff, AZ, USA), the ePTFE-covered Fluency (Bard Peripheral Vascular Inc., Tempe, AZ, USA), and the device used by Haskal et al – the ePTFE Flair (Bard Peripheral Vascular Inc., Tempe, AZ, USA).

All of these stent grafts were tested in vivo, characterized by histopathologic methods, quantified by angiographic and morphometric analysis, and in some cases studied in vivo with intravascular ultrasound. A variety of materials, modification of these materials, and different composite designs were studied (10-12), and data from much of this work ultimately accompanied clinical trial data when the devices were submitted for FDA approval.

When it came time for human clinical trial, there were several notable departures from the design of most prior stent studies. For example, unlike many other stent trials where stents were only used when PTA failed, this stent graft trial called for primary stent-graft placement irrespective of PTA result. The purpose was not to improve upon PTA technical results (although in fact, the stent-graft did improve the technical result). The quest was to study patency.

Another study design was mandatory angiography at 2 and 6 months. During the study planning phase it was recognized that if the stent-graft group patency was no better, or worse than PTA, there would be no explanation if angiograms were not obtained. Not only was angiographic study of the treatment site performed, but the entire circuit from inflow artery to right atrium was imaged and angiograms were independently measured by a quantitative core lab. Angiographic data, along with clinical signs of AVG dysfunction, were ultimately coupled into the definition of treatment site patency and also access circuit patency. For example, if a 50% stenosis was found at 2 months but there was no clinical dysfunction, primary circuit patency would end. If that stenosis was at the treatment site, treatment area primary patency would also end. Conversely, if there was a measure of dysfunction, but no stenosis was seen anywhere, primary access circuit patency was lost. By using both angiographic findings and/or clinical findings, the hurdle was set high, making it more likely that patency would be lost for both the PTA group and the stent-graft group. However, since the study was a randomized trial, the real outcome is evaluation of the difference between the two groups under similar endpoint definitions.

Finally, sample size for this study was calculated to show “non-inferiority” when the stent graft was compared to PTA. This was a cautious approach, and speaks to the uncertainty regarding use of a stent graft in arteriovenous access. It was believed that many more patients would be needed in the trial to show a difference in patency between the two groups, using the best information available at the outset.

At the end of the day, trial data clearly showed statistically superior patency benefit when a stent graft was placed immediately after PTA. Both 6-month primary treatment site patency, as well as primary access circuit patency, were doubled. It also showed that when the treatment site is actually measured by an independent quantitative lab, the technical (angiographic) result after PTA in this trial did not come close to 98% success, as reported in Beatard’s series (3). In fact, PTA success was only 73%, using the widely accepted definition of residual angiographic stenosis <30% after PTA.

Putting all this together, the stent-graft, now called the Flair (Bard Peripheral Vascular, Tempe, AZ, USA), has shown benefit for extending the patency of AVGs at 6 months. With publication of this article, the long-awaited multicenter, randomized, prospective clinical stent-graft data has been vetted through the peer-review process.

There are now many more steps to be taken. First, the FDA has required a larger (270 patients) and longer (24-month) post-market approval trial of the Flair stent graft in AVGs. Similar to the pivotal trial, this clinical study (RENOVA), now under way, will randomize patients between PTA and PTA with stent graft. Beyond this, there is an ongoing clinical trial of the Viabahn ePTFE stent graft (W.L. Gore and Associates, Flagstaff, AZ, USA) in AVGs (REVISE), as well as other clinical studies of stent grafts in AVGs and arteriovenous fistulae that are planned for the upcoming years. All of this is good news for physicians who care for hemodialysis patients, and great news for these patients, who return so frequently for ongoing maintenance of their hemodialysis access.
Conflict of interest: Bart Dolmatch, MD, is Professor of Radiology and Director of Vascular and Interventional Radiology at the University of Texas Southwestern Medical Center in Dallas, Texas. He has disclosed that he is a paid consultant and speaker for Bard Peripheral Vascular, Inc., and receives royalties from Bard Peripheral Vascular, Inc. He receives stock options for participating on the advisory board of the Endovascular Forum. He is a consultant for Merit Medical Systems, Inc., receives stock for his participation on the Vital Access Inc. medical advisory board, and stock options for serving on the medical advisory board of the Endovascular Forum. He is co-course director of Controversies in Dialysis Access, for which he receives an honorarium.

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