Dialysis Access Interventions: What Was and What's Flowing Next

A summary of this past year's most important papers, top headlines in dialysis access, and what to expect for the future of the field.

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Although much of the endovascular world experienced seismic shifts over the past decade, one could argue that dialysis access interventions had largely been left without a rumble. If so, the past 18 months have provided enough quaking in the dialysis access field to burst a noncompliant balloon. This article reviews what we consider this year's most important articles and headlines and prognosticates what will be shaking up the field in years to come.

Clinical and Economic Benefits of Stent Grafts in Dysfunctional and Thrombosed Hemodialysis Access Graft Circuits in the REVISE Randomized Trial

Mohr BA, Sheen AL, Roy-Chaudhury P, et al. J Vasc Interv Radiol. 2019;30:203–211.e4.

The improved patency outcomes of stent grafts versus percutaneous transluminal angioplasty (PTA) alone for arteriovenous graft (AVG) circuit stenosis has been reported by multiple studies, but no studies have directly evaluated whether the higher up-front costs of stent grafts are sufficiently offset by decreased downstream reintervention costs. Mohr et al compared the total cost of initial and subsequent reinterventions within a 24-month follow-up period for patients in the REVISE randomized controlled trial (RCT).[1]

The REVISE trial randomized patients with AVG dysfunction from venous anastomotic stenoses, including patent and thrombosed circuits, to the Viabahn stent graft (Gore & Associates) or PTA. In the 24-month follow-up period, the number and types of interventions were assessed and associated costs were calculated from publicly available Medicare data.

Patients in the stent graft group had significantly fewer reinterventions (27% less) than the PTA group (P = .005), but there was no significant difference in associated costs ($27,483 vs $28,664), reflecting the up-front stent graft cost. In a subgroup analysis of thrombosed grafts, the stent graft arm had a significant decrease in number of reinterventions and total cost (18% savings; $30,329 vs $37,206; P = .022). In nonthrombosed grafts, there was no significant difference in the number of reinterventions or costs. The initial $5,139 mean cost savings from primary PTA versus stent grafting was eventually offset by the $5,221 mean cost expenditure for subsequent interventions in the PTA group.

The study results support the primary use of stent grafts for venous anastomotic AVG stenosis, particularly in the setting of AVG thrombosis, where stent grafts provide overall cost savings by decreasing the number and cost of reinterventions. This analysis is particularly relevant in our current health care environment, where cost-efficiency is an increasingly important consideration.

The Lutonix AV Randomized Trial of Paclitaxel-Coated Balloons in Arteriovenous Fistula Stenosis: 2-Year Results and Subgroup Analysis

Trerotola SO, Saad TF, Roy-Chaudhury P, et al. J Vasc Interv Radiol. 2020;31:1–14.e5.

The Lutonix AV randomized trial was designed to compare the efficacy and safety of drug-coated balloons (DCBs) versus conventional balloon angioplasty in a large, multicenter RCT in patients with dysfunctional arteriovenous fistulas (AVFs).[2] The 6-month results demonstrated no significant difference in target lesion primary patency (TLPP) but did show that fewer interventions were needed to maintain target lesion patency in the DCB group.[3] This article by Trerotola et al is a follow-up to that 6-month publication and presents the 2-year results of the Lutonix AV trial.

The Lutonix AV RCT included 285 patients from 23 sites who were randomized 1:1 to treatment of the dialysis fistula stenosis with the Lutonix DCB (BD Interventional) versus conventional balloon angioplasty. In both groups, a single target lesion was first prepared by predilation with a high-pressure balloon, followed by treatment with a DCB or a similar non–drug-coated conventional balloon. Endpoints included TLPP and access circuit primary and secondary patency. Subgroup analyses were performed to assess differences between patient and anatomic characteristics, including age of the fistula and location of the target stenosis. A safety and mortality analysis was also conducted.

At 9-month follow-up, there was significantly higher TLPP in the DCB group versus the conventional balloon group (58% vs 46%; $P = .02$) and significantly fewer interventions were needed to maintain TLPP in the DCB group (mean, 0.53 per patient) compared with the conventional balloon group (mean, 0.71 per patient) ($P = .02$). At 12-, 18-, and 24-month time points, there was no significant difference in TLPP or interventions needed to maintain patency. There were no significant differences in access circuit primary and secondary patency at any time point. Complication rates were not significantly different at any time point. The 2-year mortality rate was also not significantly different, at 23% in the DCB group and 18% in the conventional balloon group ($P = .27$).

This study has the most robust design to date for evaluating DCB outcomes in dialysis access maintenance and will serve as an important foundation for future investigation. The positive 9-month outcomes can be viewed as supporting DCB use, particularly when considering the modest survival times of most dialysis patients. However, the lack of improved patency outcomes at all other study time points suggests that DCBs do not provide an exponential leap over conventional balloon outcomes.

Given the substantial cost difference compared with conventional balloons, the DCB value proposition requires further investigation. Importantly, the mortality analysis demonstrated no association between paclitaxel DCBs and increased mortality risk in patients with AVFs, which should help assuage concerns inferred from the peripheral artery disease (PAD) literature.[4]

Mortality After Paclitaxel-Coated Device Use in Dialysis Access: A Systematic Review and Meta-Analysis

Dinh K, Limmer AM, Paravastu SCV, et al. J Endovasc Ther. 2019;26:600–612.

The association of paclitaxel-coated devices in PAD with increased mortality risk reported by Katsanos et al[4] has raised concern for a possible elevated mortality risk with DCB use in the dialysis population. Dinh et al performed a systematic review and meta-analysis of available RCTs to compare all-cause mortality rates between patients treated with DCBs versus plain old balloon angioplasty (POBA).[5]

The analysis included eight RCTs evaluating 327 DCB patients and 331 POBA patients with dysfunctional dialysis access. All-cause mortality rates were pooled using a random effects model. There was no significant difference in overall all-cause mortality between the DCB and POBA groups (13.8% vs 11.2%, respectively; $P = .25$). Specific time point analysis also demonstrated no significant difference in mortality rate at 6 months (5.2% for DCB vs 4.8% for POBA) and 12 months (6.3% for DCB vs 6 % for POBA).

This meta-analysis of the highest-quality data available from DCB studies in dialysis access intervention demonstrated no significant difference in all-cause mortality versus POBA.

Drug-Coated Balloon Angioplasty in Hemodialysis Circuits: A Systematic Review and Meta-Analysis

Kennedy SA, Mafeld S, Baerlocher MO, et al. J Vasc Interv Radiol. 2019;30:483–494.e1.

Data on DCBs for dialysis access interventions continue to mature, but the available studies remain relatively heterogeneous in their designs and endpoints. Kennedy et al performed a meta-analysis of existing RCT and cohort study results to assess DCB patency outcomes in dialysis circuits.[6]

The meta-analysis included 12 studies and a total of 908 patients. The majority of the included studies were RCTs evaluating DCB outcomes in AVFs. GRADE (Grading of Recommendations, Assessment, Development and Evaluations) assessment of the analyzed RCTs demonstrated low evidence quality, with substantial heterogeneity and imprecision among studies. Angioplasty technique varied between studies, with some using high-pressure or cutting balloon angioplasty before or after DCB use, while others did not. One RCT met inclusion criteria for AVGs, and two RCTs met inclusion criteria for central venous stenosis. The primary outcome was target lesion patency at 3, 6, 12, and 24 months. The safety profile and 12-month mortality were also evaluated.

In AVFs, DCBs demonstrated improved patency rates compared with POBA at 3, 6, 12, and 24 months when including all studies and at 3, 6, and 12 months when including only RCTs. The pooled patency rate at 6 months was 73.7% for DCB versus 55.2% for POBA from the RCT data. In AVGs, the single study that met criteria for analysis demonstrated improved DCB arm patency at 12 months (100% vs 62% patency; $P = .003$). For central venous stenosis, there was no significant difference between DCB and POBA patency rates at 3, 6, or 12 months. Procedural complications occurred in < 1% of patients, and pooled 12-month mortality rates demonstrated no significant difference between DCB (7.6%) and POBA (5.8%) groups.

This meta-analysis of existing DCB studies demonstrates significantly improved AVF target lesion patency rates at 3, 6, and 12 months compared with POBA, but the quality of existing literature remains low, with significant heterogeneity between studies. Notably, this analysis did not include the Lutonix AV trial's 2-year results by Trerotola et al.[2] Nonetheless, the results of this meta-analysis support the current use of DCBs for AVF maintenance, with the caveat that data from recent, large, multicenter RCTs were not included. Regarding central venous stenosis, current evidence is limited but does not show any significant improvement in patency rates with the use of DCBs. In AVGs, the DCB data are even more sparse, with one study showing patency improvement, but it is difficult to derive any practice recommendations from this alone, particularly given the efficacy of stent grafts in AVGs.

Assessment of Use of Arteriovenous Graft vs Arteriovenous Fistula for First-Time Permanent Hemodialysis Access

Hicks CW, Wang P, Kernodle A, et al. JAMA Surg. Published online June 12, 2019.

The Fistula First Breakthrough Initiative (FFBI) is driven by the superior clinical results from AVFs compared with AVGs. As such, the Centers for Medicare & Medicaid Services (CMS) proposed a national goal of 66% AVF use in hemodialysis patients. This target has been in place for a decade, and this article by Hicks et al characterizes the practice patterns and characteristics of vascular access surgeons as they relate to the FFBI.[7]

Medicare fee-for-service carrier claims for first-time hemodialysis access procedures were analyzed in 2016 and 2017. Procedures were characterized as either AVG or AVF based on CPT codes. Patients with a previous AVF or AVG were excluded, but those who had undergone dialysis via a catheter were included. Patient and physician characteristics were analyzed using a logistic regression model.

For first-time permanent hemodialysis access, 66,489 (77.9%) patients received an AVF and 18,831 (22.1%) received an AVG. The patient factors associated with AVG use were age, female sex, nonwhite race other than North American native, and lack of preoperative vein mapping. Surgery in a nonhospital setting was protective against AVG use. Of the 2,397 physicians included in the study, 498 (20.8%) had AVG use rates > 34% and 168 (7%) had AVG rates > 50%.

Although most physicians creating surgical hemodialysis access successfully reach the AVF target as proposed by CMS, one in five use AVGs in > 34% of first-time hemodialysis patients. The authors suggest an initiative to identify and educate surgeons practicing outside the targeted boundaries in a nonpunitive, peer-to-peer feedback mechanism via the Improving Wisely Campaign.

This article focuses on surgical hemodialysis access placement, but its message on improving high-value care by sharing performance data—albeit potentially controversial—may be readily extended to the endovascular space as well.

TOP HEADLINES IN DIALYSIS ACCESS

- **More Data Needed on Efficacy of DCBs for AV Access; No Mortality Link Seen**

  Those involved in the treatment of PAD are keenly aware of the meta-analysis findings from Katsanos et al suggesting increased mortality in patients treated with paclitaxel-coated devices.[4] Physicians using DCBs in hemodialysis access were understandably concerned about whether these findings translate to the dialysis patient population. Thus far, studies have demonstrated no increased mortality risk for AV paclitaxel use. However, the efficacy of DCBs in hemodialysis access remains less certain. The Lutonix AV trial 2-year results[2] and the meta-analysis by Kennedy et al[6] demonstrated disparate results, with the meta-analysis suggesting patency benefit from DCBs in AVFs at multiple time points, while the Lutonix AV trial only showed a benefit at 9 months. The In.Pact Admiral AV DCB (Medtronic) was recently approved by the FDA based on results of the IN.PACT AV Access trial (NCT03041467), which demonstrated maintained patency and fewer reinterventions through 6 months in DCB-treated patients compared with those treated with standard PTA. Interventionalists need to stay tuned for additional data on the role of paclitaxel in hemodialysis access.

- **Percutaneous Endovascular AVF Creation Is Promising, But Real-World Data Are Needed**

  The recent advent and initial adoption of percutaneous endovascular AVF (endoAVF) creation devices has generated a lot of excitement as a potentially disruptive technology in hemodialysis access. The Ellipsys (Avenu Medical) and WavelinQ (BD Interventional) devices have distinct mechanisms and target vessels for fistula creation but have both demonstrated promising results in early trials.[8,9] In these studies, fistulas meeting criteria for dialysis were achieved in 86% and 87% of patients, with cumulative 1-year patency rates of 87% and 84% for the Ellipsys and WavelinQ devices, respectively.[8,9] The endoAVF reintervention rates were lower than for surgical AVFs, which may translate to lower access maintenance costs.[10] However, current endoAVFs may require multiple additional procedures to promote fistula maturation, and the complex outflow anatomy of endoAVFs creates unique challenges for fistula cannulation and subsequent revision. Furthermore, the nascent evidence base has been derived from carefully selected clinical trial patients, so outcomes in a real-world population remain to be seen. Additional evidence and experience in the next years will be essential to determine the optimal role of endoAVFs. Whether it evolves into the new gold standard, serves merely as a backfill for underserved patients, or is remembered as a fad, it is incumbent on the interventionalist to evaluate and implement this new technology judiciously.

- **Disparities in Hemodialysis Access Persist**

  Multiple headlines this year serve to remind us that although we may strive to care for each of our patients equally, much work remains to be done. Despite a larger number of women affected by chronic kidney disease, one recent study indicates that fewer women are receiving renal replacement therapy.[11] Additionally, women had lower odds of receiving AV access than men at initiation of hemodialysis; this was similarly true for Hispanic patients compared to white patients.[12] Not surprisingly, disparities adversely affect our patients without insurance, who more commonly initiate dialysis with suboptimal access, thus increasing risks of hospitalization and vascular access infection.[13] Although health care disparities will certainly persist throughout our careers, physician education and public advocacy may help mitigate ill effects and promote more balanced health care delivery for our most vulnerable patients.

WHERE IS DIALYSIS ACCESS HEADED?

The future of the dialysis access field is predicated on continued development and maintenance of the best renal replacement therapy for our patients. Although we've witnessed tremendous advances in the past 18 months, there is a need for continued innovation and vigilant assessment of existing approaches. The FFBI drew attention to the comparative effectiveness between AVFs and AVGs, but its scope was narrowly focused. Beyond the nascent appraisal of surgical versus percutaneous access creation, other forms of renal replacement therapy will continue to evolve; hemodialysis, peritoneal dialysis, or any novel future dialysis approach must aim to improve not only traditional dialysis outcomes but also safety and quality of life. It is an exciting and optimistic time to be involved in the care of patients with chronic kidney disease, and we should all look forward to and help advance the technologies that benefit our patients. ■

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