Medical Affairs Corner

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Drug-Coated Balloon Angioplasty in Failing AVFs: Where Are We?

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In this article, Drs. Holden and Gallo discuss current clinical evidence on drug-coated balloons (DCBs) for treatment of dysfunctional dialysis arteriovenous fistulas (AVFs) and improving outcomes for end-stage kidney disease (ESKD) patients. Dr. Gallo shares a case example of how he used IN.PACT™ AV drug-coated balloon (Medtronic) to treat a high-grade cephalic stenosis.

DISCUSSION WITH DRS. HOLDEN AND GALLO

IN.PACT AV Access trial data have been reported through 3 years, with mortality reported through 4 years. What are the most clinically meaningful outcomes from this data set?

Dr. Holden: There are four key parts of this study that I keep returning to as an interventionalist treating ESKD patients. The first is safety in terms of mortality—after the paclitaxel safety concerns, it's important to note that through 4 years, there is no difference in mortality between DCB and percutaneous transluminal angioplasty (PTA) arms in this trial. The second is the sustained superior patency through 3 years that you see when a participant was treated with DCB: 52.1% compared to 36.7% with PTA.[1] Third, beyond the raw patency data is the median time to reintervention between the DCB group and the PTA group; there was a 14.7-month delay if a participant was treated with DCB. When I think of my patients, this increase in time spent without a reintervention is critical. It's one less interruption in dialysis, one less intervention. That matters.

Finally, especially long term, AV access thrombosis is an important factor. Thrombosis significantly impacts a patient's ability to undergo timely and adequate hemodialysis and puts the access at risk for failure and abandonment. Through 3 years, AV circuit thrombosis was significantly lower with DCB (8.2%) compared to plain balloon (18.3%).

Does this mean we have sufficient evidence to support DCBs as the standard of care for ESKD patients?

Dr. Holden: Let's start with what guidelines say are standard of care. Per the Kidney Disease Outcomes Quality Initiative, a given AVF should have ≤ 3 interventions per year.[2] Plain balloon, with high pressure as needed, is considered the "reasonable" primary treatment for dysfunction. Expectations here are set: We know that it's not *if* an AVF will experience dysfunction, it's *when*. Because frequent short-term interventions are required to maintain AV access patency, there aren't much long-term data. The IN.PACT AV Access study is the first of its kind—large, prospective, multicenter, randomized, and adjudicated to report outcomes through 3 years in patients with dysfunctional access. The primary effectiveness endpoint was target lesion primary patency through 6 months and adverse events involving the access circuit through 30 days. Both outcomes were met, as reported in the *New England Journal of Medicine* publication.[3]

Twelve-month outcomes further demonstrated safety, with statistically significant improved outcomes in target lesion primary patency and access circuit primary patency.[4,5] Now, we have

data that demonstrate durability through 24 and 36 months, with no difference in mortality through 48 months and sustained benefit seen in several subgroups.[1] Furthermore, there was a statistically significant advantage of DCB over plain balloon through 3 years, whether the fistula was located in the forearm or upper arm, was a de novo or restenotic lesion, and/or the lesion was located in the perianastomotic location, with other subgroups showing directionality supporting the use of DCB.

Looking at this recent evidence, it is reasonable to suggest that IN.PACT AV DCB should be incorporated as part of our standard of care. We also have information that indicates this would be a highly cost-effective approach. It's important to note that there were differences between this trial and both the Lutonix AV[6] and PAVE[7] randomized controlled trials, which used a different DCB technology and had some differences in enrollment criteria and geographies. These trials have not demonstrated superior effectiveness of DCB compared to plain balloon as that seen in the IN.PACT AV Access trial.

If someone was new to using DCBs to treat AVF lesions, where would you recommend they begin?

Dr. Gallo: I would recommend that the endovascular specialist use the DCB in a very similar fashion to how it was studied in IN.PACT AV Access trial, which included de novo or restenotic lesions up to 100 mm in length in autogenous AVFs. Adequate vessel prep is also very important. I use high-pressure balloons covering the entirety of the lesion, with 1-cm extension on each side. If successful, I then treat it with a DCB of the same diameter.

Any practical considerations and technical tips?

Dr. Gallo: Vessel preparation is imperative to having the best results. Predilate with a high-pressure balloon for > 90 seconds. If there is an adequate treatment response (< 30% residual stenosis) on repeat AV fistulography, without evidence of flow-limiting dissection (grade > B) or perforation, consider using the DCB. The DCB should also cover the entirety of the lesion, with 1-cm extension on each side and inflation maintained for at least 180 seconds.

Dr. Holden: For de novo or restenotic access circuit stenosis, we now use the term "optimized vessel preparation," which includes using a high-pressure balloon to treat the entire stenotic lesion and appropriate balloon sizing for the target lesion. We use a combination of transcutaneous ultrasound, angiography, intravascular ultrasound, and image overlay of the fistula at the time of intervention for real-time balloon sizing, and then we predilate with a high-pressure balloon for at least 2 minutes. After the optimal vessel preparation, we continue with a DCB. The preferred DCB is the IN.PACT AV DCB because it's the only DCB that has shown long-term efficacy.*

DR. GALLO'S PATIENT CASE

A man in his late 70s with a history of ESKD on maintenance hemodialysis had a right upper extremity, percutaneous, endovascular, proximal radial artery–to–antecubital perforator vein fistula, with cephalic dominant outflow. He presented with low venous flow volumes within the targeted cannulation vein. Duplex ultrasound flow volume measurement demonstrated inadequate flow volumes within the cephalic vein (Figure 1A). A transradial right upper extremity AV fistulogram demonstrated a patent proximal radial artery–to–antecubital vein fistula with a high-grade, short-segment stenosis (92% stenosis, 2-cm lesion length) involving the juxtaanastomotic segment (Figure 1B and 1C). The reference vessel diameter of the target fistula was approximately 6 mm. The cephalic vein was otherwise unremarkable.

The vessel preparation was performed with high-pressure balloon angioplasty inflated for 2 minutes. There was no angiographic evidence of perforation or flow-limiting dissection at this point. I proceeded to treat the patient with a 6- X 40-mm IN.PACT AV DCB (Figure 2A). The final angiogram after DCB

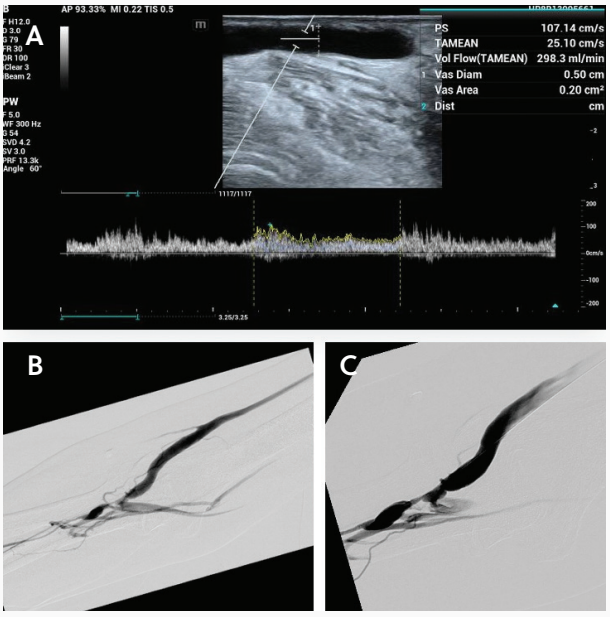

Figure 1. Duplex ultrasound flow volume measurement of the cephalic vein (A). A transradial AV fistulogram showed a high-grade, short-segment stenosis (B, C)

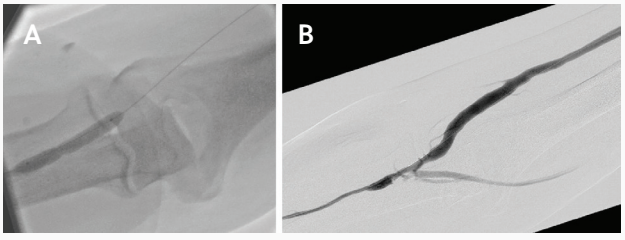

Figure 2. IN.PACT AV DCB angioplasty (A) and the final angiogram (B).

*IN.PACT AV DCB is available for sales in US, Canada and Japan

angioplasty demonstrated a patent right cephalic vein (Figure 2B) with adequate flow volume. At the time of this article, it has been > 3 months since his last intervention and no clinically significant issues with hemodialysis have been reported. ■

Disclosures

Dr. Holden: Medical advisory board member for Boston Scientific Corporation, Gore & Associates, Medtronic, and Phillips; clinical investigator for Abbott, Bard/BD, Boston Scientific Corporation, Biotronik, Cagent Medical, Cook Medical, Efemoral, Endologix, Endospan, Gore Medical, Intact Vascular, Medtronic, Nectero, Reflow Medical, Philips, Reflow Medical, Shape Memory, Shockwave Medical, Terumo, and TriReme Medical.

Dr. Gallo: Consultant to Medtronic.

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