Drug Coated Balloons: Are they the Holy Grail for Dysfunctional Dialysis Arteriovenous Fistulas?

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The recent publication of 6-month results of the IN.PACT AV Access study has brought the use of drug coated balloons (DCB) in the treatment of dysfunctional dialysis arteriovenous fistulas (AVFs) into the spotlight [1].

This global prospective trial randomized 330 patients to either DCB or standard balloon angioplasty (sPTA) following lesion preparation using a high-pressure balloon (HPB). The primary end point was target lesion primary patency (TLPP) based on clinically driven target lesion revascularization (TLR) and safety data for major adverse event at 30 days. The trial was conducted with independent events committee and core lab adjudication. The study achieved its primary end points. The 6-month TLPP was superior in the DCB arm (82.2% (DCB) vs 59.5% (sPTA); $p < 0.001$), and these results held true for sensitivity analysis. The primary safety end point showed DCB to be non-inferior to sPTA (4.2% vs 4.4% respectively; $p = 0.002$).

Thus, have we found the Holy Grail for treating dysfunctional AVFs? The results of this study are very similar to those reported in an earlier randomized trial [2] where both TLPP and access circuit primary patency (ACPP) were statistically improved in the DCB cohort at 6 months (TLPP 81% vs 61% $p = 0.03$; ACPP 76% vs 56% $p = 0.048$). While these results are very promising for DCBs, there are several points that we should reflect on.

We note that the TLPP in the IN.PACT AV Access trial was based on clinically driven need for reintervention and 6-month ultrasound rather than angiography which is the gold standard. Also, the operators were not blinded to the study device because of the difference in balloon construct. These two factors could have introduced bias into the study.

A similarly constructed randomized FDA device exemption trial using another brand of DCB [3] did not reach its primary end point of improved TLPP at 6 months, although it did show significance in favor of DCB at 210 days. Complete 2-year data analysis showed DCB improved TLPP only at 9 months and not at any other pre-determined time period [4]. This raises the question of whether all DCBs are equally effective and highlights the need for head-to-head comparison between different DCBs.

The above 3 trials only treated a single severe clinically relevant lesion or two tandem focal lesions within 3 cm of each other over a 100 mm consecutive length. This does not reflect real-world practice, wherein most AVFs have multiple lesions. Hence, trials where all lesions are treated with DCB to see their impact on ACPP as well as cost-effectiveness should be undertaken.

HPB angioplasty may also not be the most effective preparation for DCB, as cutting balloon was proven to be superior to HPB angioplasty in prolonging TLPP in resistant lesions [5]. The combination of cutting or scoring balloons with the use of DCB should be explored, to study whether these are more effective in delivering the drug to the medial smooth muscle cells.

All the data so far have shown that paclitaxel DCBs are safe in treating dialysis access lesions with no increase in mortality at 1 and 2 years, and we await the longer-term

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results of ongoing trials. One should not forget the effectiveness of other limus drugs, and studies involving sir-olimus DCBs should be performed.

In conclusion, the IN.PACT AV access trial proves the clinical effectiveness of DCB in the treatment of dysfunctional AVFs at 6 months. However, more investigator-initiated trials looking at safety and longer-term clinical and cost-effectiveness of treating all lesions within the access circuit are needed before we proclaim DCBs as the Holy Grail.

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Compliance with Ethical Standards

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