Recent Publications in Vascular Access Maintenance

Robert Lookstein, MD, MHCDL
Icahn School of Medicine at Mount Sinai
New York City, NY
Disclosures:
In the past 12 months, my spouse or myself have engaged in financial relationships as follows:

- **Advisory Board**: Boston Scientific, Medtronic
- **Consultant**: Penumbra, Neptune Medical, Bard Vascular, Cordis, Biosense Webster, Abbott Vascular, Becton Dickinson, Surmodics
- **Speakers Bureau**: Abbott Vascular
- **Research Support**
  - Philips Healthcare, Spectranetics, Terumo, Boston Scientific, INARI, Penumbra, Ethicon, Walk Vascular, Vesper, Black Swan
- **Equity Shareholder**: Imperative Vascular, Summa Vascular, Innova Vascular, Thrombolex
# Vascular Access Maintenance

## Endovascular Devices

<table>
<thead>
<tr>
<th>Angioplasty Balloons</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTA</td>
</tr>
<tr>
<td>High-pressure PTA</td>
</tr>
<tr>
<td>Drug-coated Balloons</td>
</tr>
<tr>
<td>Cutting / specialty</td>
</tr>
<tr>
<td>balloons</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bare metal stents</td>
</tr>
<tr>
<td>Covered stents</td>
</tr>
<tr>
<td>Drug-eluting stents</td>
</tr>
</tbody>
</table>

Today's talk will not include:
- balloon-assisted maturation
- surgical revision
- use of other devices like the HeRO, Surfacer, etc

Today's talk will include:
- Key maintenance publications
AV Maintenance - Endovascular

New Publications of Interest – Review Articles

Choosing the right treatment for the right lesion, part I: a narrative review of the role of plain balloon angioplasty in dialysis access maintenance

Daniel M. DePietro, Scott O. Trenotola

Department of Interventional Radiology, Department of Radiology, Perelman School of Medicine at the University of Pennsylvania, PA, USA

Correspondence: (D) Conceptual design: Both authors; (E) Administrative support: Both authors; (F) Provision of study materials or patients: Both authors; (G) Collection and assembly of data: Both authors; (H) Data analysis and interpretation: Both authors; (I) Manuscript writing: Both authors; (J) Final approval of manuscript: Both authors.

Correspondence to: Daniel M. DePietro, MD, Department of Radiology, University of Pennsylvania, 3400 Spruce Street, 3 Schwartz/Residency Administration, Suite 110, Philadelphia, PA 19104, USA. Email: Daniel.dep@uphs.upenn.edu

Conclusions: High-quality plain balloon angioplasty, performed utilizing the available evidence-based regarding techniques and considerations for specific lesion locations, is successful in treating the large majority of AV access stenoses. While initially successful, patency rates remain non-durable. Part two of this review will discuss the evolving role of DCBs, which seek to improve angioplasty outcomes.

Choosing the right treatment for the right lesion, Part II: a narrative review of drug-coated balloon angioplasty and its evolving role in dialysis access maintenance

Daniel M. DePietro, Scott O. Trottola

Division of Interventional Radiology, Department of Radiology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA

Correspondence: (D.M.D.) Division of Interventional Radiology, Department of Radiology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA 19104, USA. Email: daniel.depietro@pennmedicine.upenn.edu.

Conclusions: DCB implementation has been tempered by the lack of clear signal regarding the benefits of DCB use. As further evidence is obtained, it is possible that a precision-based approach to DCBs may shed light onto which patients will truly benefit from DCBs. Until that time, the evidence reviewed herein may serve to guide interventionalists in their decision making, knowing that DCBs appear safe when used in AV access and may provide some benefit in certain patients.
AV Maintenance - Endovascular
New Publications of Interest – Review Articles

Table 1: Paclitaxel-coated balloons available in the market that have been used in published studies

<table>
<thead>
<tr>
<th>Device</th>
<th>Company</th>
<th>Dose (µg/mm²)</th>
<th>Excipient</th>
<th>Diameter (mm)</th>
<th>Number of studies</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ixlia</td>
<td>Becton Dickinson, Franklin Lakes, New Jersey</td>
<td>2</td>
<td>Polysorbate/Sorbitol</td>
<td>4-12 mm</td>
<td>9</td>
<td>825</td>
</tr>
<tr>
<td>IN.PACT</td>
<td>Medtronic, Dublin, Ireland</td>
<td>3.5</td>
<td>Urea</td>
<td>4-12 mm</td>
<td>19</td>
<td>701</td>
</tr>
<tr>
<td>Aperto</td>
<td>Cardiovum, Bonn, Germany</td>
<td>3.0</td>
<td>Ammonium salt</td>
<td></td>
<td>3</td>
<td>329</td>
</tr>
<tr>
<td>Passeo-18 Lux</td>
<td>Bionorik SE &amp; Co KG, Berlin, Germany</td>
<td>3.0</td>
<td>Hydrophobic butyltriethyloxirane citrate (BTiC)</td>
<td>2-7 mm</td>
<td>1</td>
<td>60</td>
</tr>
<tr>
<td>Elutax-SV</td>
<td>Aachen Resonance, Aachen, Germany</td>
<td>2.2</td>
<td>No excipient/ dextran coating</td>
<td>4-7 mm</td>
<td>3</td>
<td>31</td>
</tr>
<tr>
<td>Freeway</td>
<td>Eurocor GmbH, Bonn, Germany</td>
<td>3</td>
<td>Shellac</td>
<td>4-8 mm</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>SQuent Plea</td>
<td>B Braun, Berlin, Germany</td>
<td>3.55</td>
<td>Iogromide</td>
<td>4-8 mm</td>
<td>1</td>
<td>10</td>
</tr>
</tbody>
</table>

*One study may include more than one device.
*Patients may have been included in more than one study.

PCBs, although described as a single entity/category due to the common drug used, have specific differences when it comes to dose or excipient. Studies on PCBs apart from having different designs whether from retrospective cohorts, with or without a longitudinal comparative group, to big multicenter randomized trials have fundamental qualitative differences. Different endpoints, different ways of measuring the same outcome, different target lesions with different characteristics (e.g., de novo/restenotic and in-stent) exist between trials. Even the prior presence of thrombosis within a vascular circuit makes any attempt to pool data with an aim to draw a conclusion regarding PCBs efficacy, challenging if not impossible.35 If one adds the different geographies of the subjects included, system’s entropy is further increased (► Fig. 4). This explains the fact that different meta-analyses come to different conclusions regarding PCBs’ effectiveness, although the majority of those are favoring their use.36-49

Drug-Coated Balloons for the Dysfunctional Vascular Access: An Evidence-Based Roadmap to Treatment and the Existing Obstacles
Panagiotis Kritou, MD, MSc, PhD, EBR, FCRSE1, Konstantinos Katsanos, MD, MSc, PhD, EBR1, Georgia Andriana Georgopoulou, MD2, Dimitrios Karnabatidis, MD, PhD, EBR, FCRSE1

1 Department of Interventional Radiology, Patras University Hospital, Patras, Greece
2 Department of Nephrology, Patras University Hospital, Patras, Greece

Address for correspondence: Panagiotis Kritou, MD, Department of Interventional Radiology, Patras University Hospital, Patras 26100, Greece (e-mail: panos.kritou@gmail.com)

Table 1: Paclitaxel-coated balloons available in the market that have been used in published studies

<table>
<thead>
<tr>
<th>Device</th>
<th>Company</th>
<th>Dose (µg/mm²)</th>
<th>Excipient</th>
<th>Diameter (mm)</th>
<th>Number of studies</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ixlia</td>
<td>Becton Dickinson, Franklin Lakes, New Jersey</td>
<td>2</td>
<td>Polysorbate/Sorbitol</td>
<td>4-12 mm</td>
<td>9</td>
<td>825</td>
</tr>
<tr>
<td>IN.PACT</td>
<td>Medtronic, Dublin, Ireland</td>
<td>3.5</td>
<td>Urea</td>
<td>4-12 mm</td>
<td>19</td>
<td>701</td>
</tr>
<tr>
<td>Aperto</td>
<td>Cardiovum, Bonn, Germany</td>
<td>3.0</td>
<td>Ammonium salt</td>
<td></td>
<td>3</td>
<td>329</td>
</tr>
<tr>
<td>Passeo-18 Lux</td>
<td>Bionorik SE &amp; Co KG, Berlin, Germany</td>
<td>3.0</td>
<td>Hydrophobic butyltriethyloxirane citrate (BTiC)</td>
<td>2-7 mm</td>
<td>1</td>
<td>60</td>
</tr>
<tr>
<td>Elutax-SV</td>
<td>Aachen Resonance, Aachen, Germany</td>
<td>2.2</td>
<td>No excipient/ dextran coating</td>
<td>4-7 mm</td>
<td>3</td>
<td>31</td>
</tr>
<tr>
<td>Freeway</td>
<td>Eurocor GmbH, Bonn, Germany</td>
<td>3</td>
<td>Shellac</td>
<td>4-8 mm</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>SQuent Plea</td>
<td>B Braun, Berlin, Germany</td>
<td>3.55</td>
<td>Iogromide</td>
<td>4-8 mm</td>
<td>1</td>
<td>10</td>
</tr>
</tbody>
</table>

*One study may include more than one device.
*Patients may have been included in more than one study.

PCBs, although described as a single entity/category due to the common drug used, have specific differences when it comes to dose or excipient. Studies on PCBs apart from having different designs whether from retrospective cohorts, with or without a longitudinal comparative group, to big multicenter randomized trials have fundamental qualitative differences. Different endpoints, different ways of measuring the same outcome, different target lesions with different characteristics (e.g., de novo/restenotic and in-stent) exist between trials. Even the prior presence of thrombosis within a vascular circuit makes any attempt to pool data with an aim to draw a conclusion regarding PCBs efficacy, challenging if not impossible.35 If one adds the different geographies of the subjects included, system’s entropy is further increased (► Fig. 4). This explains the fact that different meta-analyses come to different conclusions regarding PCBs’ effectiveness, although the majority of those are favoring their use.36-49

Conclusion:
Compared with balloon angioplasty alone, published clinical trial results have shown stent grafts to significantly improve primary patency of failing dialysis access grafts. Stent grafts have also been shown to significantly reduce the rates of reintervention compared with balloon angioplasty alone. Studies have shown the value of stent graft placement for treatment of in-stent restenosis within the dialysis circuit. For more specific indications, such as BAT stenoses, initial studies have shown that grafts outperform balloon angioplasty on primary and assisted patency of the circuit. Future research should investigate stent graft performance in dialysis circuits on narrower subsets of conditions and prioritize study designs that analyze the effects of stent grafts on lifetime hemodialysis access as a primary endpoint.
AV Maintenance - Endovascular
New Publications of Interest – Review Articles

Table 1: TRIALS EVALUATING THE USE OF COVERED STENTS IN AVGs AND

<table>
<thead>
<tr>
<th>Sponsor</th>
<th>FLAIR Pivotal</th>
<th>RENOVA</th>
<th>REVISE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device</td>
<td>BD Interventional</td>
<td>BD Interventional</td>
<td>W.L. Gore &amp; Associates</td>
</tr>
<tr>
<td>ACCESS</td>
<td>AVG</td>
<td>AVG</td>
<td>AVG</td>
</tr>
<tr>
<td>Study design</td>
<td>Prospective randomized to PTA</td>
<td>Prospective randomized to PTA</td>
<td>Prospective randomized to PTA</td>
</tr>
</tbody>
</table>

In summary, eTPFE stent grafts provide undisputed and definitive advantages in prolonging access patency and function in the tested areas [20–22]. The multiplicity of controlled trials emphasizes their recommended and perhaps obligate use in when treating patients who match those trial participants. Useful, limited, or salvage uses such as treating pseudoaneurysms, ruptures, cannulation, or arterial anastomotic zone lesions have been reported but will likely remain one-off applications unsupported by larger trials and regulatory approvals (Figs. 4,5) [23–30]. Future trials will likely focus upon future replicative trials in AV fistula patients, potential comparisons of DCBs or future technologies, as well as medication and “tuning” of stent designs and coverings to best match vessel compliance, sizes, and elastic modulus.
Abstract conclusion: “TLPP was statistically significantly higher with DCBs than with standard PTA at 12 months, demonstrating the sustained and superior effectiveness of this device for the treatment of dysfunctional arteriovenous dialysis fistulae.”
Abstract conclusion: “Thus, our multicenter, prospective, randomized study of a covered stent used to treat AVF stenosis demonstrated noninferior safety with better TLPP and fewer target-lesion reinterventions than PTA alone through 24 months.”
Abstract conclusion: “In this post hoc analysis of Japanese participants from the IN.PACT AV Access trial, participants treated with DCB had higher TLPP through 6 and 12 months compared with PTA.”
Abstract conclusion: “We conclude that PTA with the paclitaxel resveratrol drug-coated SeQuent® Please OTW balloon in patients with de novo or recurrent stenosis in dialysis arteriovenous fistulas or grafts prolongs the time needed for target lesion reintervention and improves primary patency rates in the first year after the index procedure.”

Figure 3. Comparison of primary patency rates after index procedure between patients with conventional angioplasty (POBA) and drug-coated balloon (DCB) on a Kaplan–Meier plot.

Abstract conclusion:
“This clinical trial did not demonstrate any significant differences between DEB angioplasty and standard balloon angioplasty when treating dysfunctional haemodialysis access.”

DCB used: Advance 18 PTX Drug-Eluting PTA Balloon

Abstract conclusion:
“With AVF/AVG abandonment considered, DCB may be weakly cost-effective compared with cPTA in treating AVF/AVG flow dysfunction. AV access creation and maturation costs could have important explanatory value in assessing DCB cost-effectiveness.”

DCB efficacy data obtained from DEBAPTA trial (IN.PACT DCB)
- All-comer trial on 119 Singaporean patients (mean age, 59.2 years; 79 men, 40 women) with failing AVFs or AVGs, who were randomized to treat only 1 lesion with either DCB or cPTA during the index angioplasty Mortality from Singapore 2018 Life Table

Abstract conclusion:
“Endovascular therapy for arteriovenous access stenosis with the IN.PACT AV DCB can be expected to be cost-saving if longer follow-up data confirm its clinical effectiveness..”

Abstract conclusion: “When modeled from a payer’s perspective over 2 years, the cost utility of DCB versus POBA varies with mortality outcomes. POBA is cost-effective if 2-year all-cause mortality after DCB is greater than 3.4% higher than after POBA. If 2-year mortality after DCB is less than 3.4% higher than after POBA, DCB is cost-effective until its additional cost per procedure exceeds $4213 more than POBA.”
Abstract conclusion: “Treatment of arteriovenous fistulas with the IN.PACT AV drug-coated balloon, based on preliminary data, may lead to meaningful reductions in reintervention costs that would render it cost-saving at timeframes of around 1 year in Korea and between 3 and 5 years in Japan.”

Abstract conclusion:
“In failing AVF and AVG stenosis, HBA might be a preferential option as it is related to a lower risk of complications and has numerically higher primary patency than DcBA and CBA. Further studies are needed to confirm these findings.”

Recent Publications in Vascular Access Maintenance

Summary

• Generally reasonable to use therapies like stent grafts and DCBs for treatment of dysfunctional vascular access

• Clinical evidence needed:
  • Better understanding of where technologies work best (geography, lesion location, AVF type, lesion type, etc)
  • Longitudinal patient outcomes