BTK Interventions in 2025: What is going to help make BTK procedures more effective?

William A. Gray MD FACC FSCAI
Co-director, Lankenau Heart Institute
System Chief of Cardiovascular Services, Main Line Health
Wynnewood, PA
2025 is not that far in the future!

• Realistically...only devices either already approved/available, or currently in or soon to be starting clinical trials are relevant for inclusion in this discussion
• In the US today, only PTA, atherectomy, lithoplasty and Tack system are approved for BTK intervention. No ani-proliferative therapy is available
• So there is much to look forward to...
What are some of the incompletely addressed issues?

• Maintenance of vessel patency
  • Acute recoil
  • “Classic” restenosis (intimal hyperplasia consisting of fibroblast proliferation and extracellular matrix production resulting in vessel contraction and lumen loss)

• Assessment of tissue perfusion deficits pre-procedure, intra-procedural effectiveness of intervention, and post-procedure surveillance

• Better understanding and treatment of the “no option” patient
Maintenance of vessel patency

- Acute recoil
  - Since PTA is currently the primary modality used today, we must reconcile its well-known shortcomings: dissection, recoil, late vessel contraction, and neointimal hyperplasia.
  - Specialty balloons and atherectomy have been designed to address some of these issues.
  - Intravascular Lithoplasty (IVL) has shown significant promise in the most heavily calcified lesions.
  - The Tack system, in non-heavy calcified vessels, achieves high-rates of long-term patency likely in part due to resolution of dissection and in part due to anti-recoil action, all while seemingly without provoking excessive hyperplasia with 6 month primary patency of 87% and freedom from TLR of 92%.
Maintenance of vessel patency

• Restenosis avoidance
  • Paclitaxel DCB has been underwhelming
  • Current data is strongest for sirolimus analogue DES in the proximal vessels, but not well-tested/suited to more distal locations

• SAVAL PTX coated self-expanding stent trial in progress

• Adventitial injection of temsirolimus using the Mercator Bullfrog device in a small Phase 2 trial showed marked reductions in TVAL (19% vs. 38%)

• Bioabsorbable scaffolds are currently in testing: Abbott LIFE-BTK study
Real-time assessment of tissue perfusion

• The adequacy of an interventional result is generally perfusion of the affected angiosome

• Currently judged primarily by angiogram-determined flow of the macroscopic vessel, but this may not reflect the tissue-level perfusion
Angiosome-driven BTK is helpful, but...
...only if the metric for success is clear

• By comparison, the ability to assess completeness of procedural revascularization in the coronary artery beyond angiography is reasonably established
  • Anatomic
    • IVUS
    • OCT (ILLUMIEN)
  • Physiologic
    • FFR/iFR
In infrapopliteal intervention...

- ...the challenge is even greater
  - Longer segments of disease
  - Calcification
  - Bony background interference
  - Outflow/pedal circulation is smaller than coronaries
  - There are 3 of them!
What are the options?

- Improve the ascertainment of procedural adequate/optimal distal perfusion (physiologic)

- Once determined, would guide not only intra-procedural decisions but also augment pre- and post- decision clinical assessment
# Assessment of global perfusion

<table>
<thead>
<tr>
<th>Modality</th>
<th>Description</th>
<th>Benefits</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler (physiological)</td>
<td>Continuous wave Doppler transmits and receives sound waves to evaluate rate of blood flow in vessels</td>
<td>Fast, noninvasive, cost effective Office/clinic application</td>
<td>Limited by user skill and patient body habitus Cannot localize location of obstruction</td>
</tr>
<tr>
<td>ABV/segmental pressure (physiological)</td>
<td>Measuring the difference in blood pressure between the brachial and ankle arteries with Segment pressures displaying a gradient if there is PAD</td>
<td>Fast, noninvasive, cost effective Office/clinic application</td>
<td>Can be false elevated secondary to arterial calcinosis in DM and renal disease</td>
</tr>
<tr>
<td>Plethysmography/ PVR (physiological)</td>
<td>Evaluates and records variations in the volume or blood flow through an extremity as well as arterial pulsatility</td>
<td>Fast, noninvasive, cost effective Office/clinic application</td>
<td>Must be combined with PVR and Segmental pressures to provide a relevant and significant clinical information</td>
</tr>
<tr>
<td>Ultrasound (anatomical)</td>
<td>Sonography to visualize vessel caliber, obstruction, flow, and characterize plaque lesions</td>
<td>Fast, noninvasive, cost effective Office/clinic application</td>
<td>Limited by user skill Difficulty assessing perfusion in distal and smaller size vessels in lower leg and foot Liddened contrast is nephrotoxic Imaging obscured by vessel calcification</td>
</tr>
<tr>
<td>CTA (anatomical)</td>
<td>CT-cross-sectional imaging to provide 360 reconstruction of vasculature</td>
<td>Fast and noninvasive More cost effective vs traditional angiography</td>
<td>Length and cost of study Gadolinium is nephrotoxic Imaging obscured by venous artifact</td>
</tr>
<tr>
<td>MRA (anatomical)</td>
<td>MR-cross-sectional imaging to provide 360 reconstruction of vasculature</td>
<td>Noninvasive Not obscured by vessel calcification</td>
<td></td>
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</tbody>
</table>
Assessment of regional perfusion

<table>
<thead>
<tr>
<th>Modality</th>
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<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>TcPO₂</td>
<td>Physiologic testing to evaluate potential wound healing by measuring the partial pressure of O₂ in tissue</td>
<td>Fast, noninvasive, cost effective</td>
<td>The accepted level of TcPO₂ that indicates tissue healing remains controversial.</td>
</tr>
<tr>
<td>his</td>
<td>Scanning spectroscopy to display tissue perfusion on a microvascular level. Measures oxyhemoglobin and deoxyhemoglobin, along with surface temperature.</td>
<td>Office/clinic application</td>
<td>No large-scale studies have been undertaken to verify the reliability of measurements in patient with PAD</td>
</tr>
<tr>
<td>ICGA</td>
<td>Traditional angiography with injection of intravascular contrast agents to visualize the vasculature and areas of tissue perfusion.</td>
<td>Can be used to monitor perfusion closely.</td>
<td>Nephrotoxic contrast agents. Costly and time consuming. Invasive study requiring direct arterial puncture for access.</td>
</tr>
<tr>
<td>SPECT</td>
<td>Employ small amounts of radioactive substances that are injected into a vein and used with special cameras to produce images of the lower-extremity vasculature and angiogenesis.</td>
<td>Noninvasive Can be used for surveillance imaging post revascularization procedure.</td>
<td>No large-scale studies have been undertaken to verify the reliability of measurements in patient with PAD.</td>
</tr>
<tr>
<td>Laser Doppler</td>
<td>Uses light penetration and absorption to evaluate microcirculatory perfusion.</td>
<td>Fast, noninvasive, cost effective</td>
<td>Cannot provide absolute perfusion values, must combine with other modalities.</td>
</tr>
</tbody>
</table>

HSI, hyperspectral imaging; ICGA, indocyanine green angiography; PAD, peripheral arterial disease; SPECT, single photon emission tomography; TcPO₂, transcutaneous partial pressure of oxygen.
Better understanding and treatment for the no-option patient

A Review and Proposed Classification System for the No-Option Patient With Chronic Limb-Threatening Ischemia

Tanner I. Kim, MD¹, Shant S. Vartanian, MD², and Peter A. Schneider, MD²

Table 3. Classification of the No-Option and Poor-Option Patient.

<table>
<thead>
<tr>
<th>Type</th>
<th>Category</th>
<th>Conventional Revascularization Options</th>
<th>No or Poor Option</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I: Desert foot pedal anatomy</td>
<td>Anatomic</td>
<td>No</td>
<td>No option</td>
<td>• No patent pedal vessels or desert foot anatomy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Should be staged with the Wiff and GLASS staging classifications (including pedal modifier)</td>
</tr>
<tr>
<td>II: Inadequate venous conduit</td>
<td>Anatomic</td>
<td>No</td>
<td>No option</td>
<td>• Patent pedal target without adequate venous conduit for bypass</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• No endovascular options</td>
</tr>
<tr>
<td>III: Extensive tissue loss</td>
<td>Anatomic</td>
<td>Yes</td>
<td>Poor option</td>
<td>• Tissue loss with exposure of vital structures precluding limb salvage of a functional foot</td>
</tr>
<tr>
<td>IV: Prohibitive risk for procedure</td>
<td>Medical-comorbid</td>
<td>Yes</td>
<td>Poor option</td>
<td>• Excessive or prohibitive risk for revascularization due to advanced medical comorbid conditions</td>
</tr>
<tr>
<td>V: Nonfunctional limb</td>
<td>Medical-comorbid</td>
<td>Yes</td>
<td>Poor option</td>
<td>• Nonfunctional limb due to conditions, such as contractures, paralysis, or chronic nonambulatory status</td>
</tr>
</tbody>
</table>

Abbreviations: GLASS, Global Limb Anatomic Staging System; Wiff, wound, ischemia, and foot infection.
High SAD (small artery disease) and MAC (medial artery calcification) score patients

Ferraresi R et al. JEVT 2020
Deep venous arterialization (DVA) LimFlow

**PROMISE I**
- 32 No-Option Patients
- 70% AFS
- 75% Wound Healing

**ALPS Registry**
- 32 No-Option Patients
- 71% AFS
- 86% Wound Healing

**Demographics**
- 87% Rutherford 5
- 13% Rutherford 6
- 69% Diabetes
- 34% Renal insufficiency
- 72% Rutherford 5
- 28% Rutherford 6
- 66% Diabetes
- 16% Dialysis dependent
Summary

• 2025 is just around the corner

• Anticipated BTK interventional strategies intended to augment our current approaches will address, and hopefully improve:
  • Maintenance of vessel patency
  • Real-time, and reliable, assessment of tissue perfusion
  • Therapy for the no-option patient