Current meta-analysis comparison between DCB and POBA in below-the-knee therapy

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

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<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tr>
<td>Consulting Fees/Honoraria</td>
<td>Abbott Vascular</td>
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<td>Bard Peripheral Vascular</td>
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Infrapopliteal or “Below the knee” Arterial Disease

- Risk factors include diabetes, chronic kidney disease, and advanced age (all on the rise)
- Progresses to critical limb ischemia (CLI)
- Disease may be multi-level
- Higher risk for amputation with shorter amputation-free survival
- Goal: Re-establish direct flow through at least one infrapopliteal artery to reduce pain and promote wound healing.

Notice, no mention of preventing Amp

Types Vascular Smooth Muscle cells (VSMC)

- The two ends of a spectrum of VSMC:
  1. Proliferative, synthetic VSMCs
  2. Quiescent, contractile VSMCs
  3. Intermediate phenotypes exist

  - Differentiation and proliferation of VSMCs are not mutually exclusive. Depending on the signals present in their local environment, contractile VSMCs can acquire distinct phenotypes with the ability to:
    - migrate
    - proliferate
    - promote ECM production
    - elicit inflammatory signals
    - and/or calcification
Types Vascular Smooth Muscle cells (VSMC)

• The phenotypic modulation of VSMCs is determined by the environmental signals:
  – mechanical forces
  – endocytosis of specific molecules
  – growth factors that influence expression of a panel of VSMC-specific genes
  – inflammatory cytokines
  – calcium-phosphate homeostasis
  – oxidized phospholipids, retinoic acid
  – involves multiple signaling pathways including MAPK kinases, Rho, Notch, BMP
  – and β-catenin signaling
<table>
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<tr>
<th>Location and Features</th>
<th>Associated Condition(s)</th>
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<tr>
<td>Calcific atherosclerosis</td>
<td>Intimal; ossification</td>
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<tr>
<td>Calcific medial vasculopathy (Mönckeberg’s medial calcific sclerosis)</td>
<td>Tunica media</td>
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<tr>
<td>Elastocalcinosis</td>
<td>Internal elastic lamina/interna External elastic Externa</td>
</tr>
<tr>
<td>Calcific uremic arteriolopathy</td>
<td>Microvessels; amorphous</td>
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Infrapopliteal Treatment Trials – Disappointing Results for 20 Years

- Distal Bypass
- POBA
- BMS
- DES (for mid and distal tibials)
- DCB
- Other


Bypass Graft

- Option for good surgical candidates
- Comorbidities, inadequate conduit, lack of good distal target limit eligibility for many CLI patients
- Index limb re-operation within 3 months, hospital re-admission, and > 3 month wound healing time have been reported in the 50% range
- High morbidity/mortality rates & cost


POBA

Meta-analysis (1990-2006):
- Limb salvage rate was high
- Primary and secondary patency were low
- PTA had inferior primary and secondary patency but comparable limb salvage to open surgical procedures

Meta-analysis estimates of primary patency (black line), secondary patency (gray line), limb salvage (red line).

Kaplan-Meier life-table analysis of outcomes after angioplasty for CLI. *Dashed line* – portion of plot where the SE is greater than 10%.

- Limb salvage rate was high
- Primary and secondary patency were low
- Purpose of treatment in this population is symptom relief rather than long-term patency
- Risk factor analysis showed hypertension, multiple segment lesions, more distal lesions, and TASC D lesions were predictors of worse long-term outcomes

BMS

- Good limb salvage rates
- 12-month freedom from TLR 54.3%
- Rate of AEs 63.3%, largely due to high rate of TLR

12-Month amputation-free survival and limb salvage curves.

DES

ACHILLES TRIAL

- SES group superior to PTA with freedom from death, TLR, bypass, amputation, and RC ≥4.
- 12 month vessel patency higher in SES vs. PTA (75% vs. 57.1%)

META-ANALYSIS

- DES reduces risk of TLR, restenosis and amputation compared to PTA or BMS
- DES had no significant difference on mortality or RC improvement at 1 year


DES

- DES trials limited to primarily focal lesions
- Stent deformation limits use in distal vessels

A: Overall distribution and rates of stent fractures and compressions in various infrapopliteal anatomical levels
B: Anatomical relationship of distal anterior tibial artery may render the vessel more prone to stent fatigue


DCB

Multiple randomized trials comparing DCB to POBA with varied results:

- **DEBATE-BTK**: DCB associated with significant reduction in binary restenosis, TLR and vessel occlusion at 12 months
- **DEBELLEUM**: DCB demonstrated reduction in restenosis at 6 months
- **IN.PACT DEEP**: DCB had comparable efficacy, increased major amputation rates.
- **BIOLUX**: DCB outcomes comparable to PTA


DCB

**DEBATE BTK**
- Binary restenosis 27% (DCB) vs. 74.3% (PTA)
- Freedom from TLR significantly higher with DCB

**IN.PACT DEEP**
- Binary restenosis 41% (DCB) vs. 35.5% (PTA)
- Clinically driven TLR comparable, 11.9% (DCB) vs. 13.5% (PTA)
- 12 month major amputation 8.8% (DCB) vs. 3.6% (PTA)

- No major amputations in DCB group


### Potential Reasons for Success:

- Average DEBATE DCB balloon size was 0.56 larger than IN.PACT
- DEBATE pre-dilatation size ratio closer to 1:1 versus 0.9:1 with IN.PACT
- DEBATE acute luminal gain higher
Other Treatments

• Cryoplasty – No long term benefit
• Cutting balloon – No long term benefit
• Scoring balloon – No long term benefit

Based on comparative analysis
Is POBA the best option?

- Optimal infrapopliteal treatment modality remains controversial and PTA remains standard of care
- Contemporary meta-analysis performed (2005-2015) to assess current PTA outcomes
- 1-year outcomes from contemporary meta-analysis comparable to Romiti meta-analysis:
  - Technical success: 91% vs. 89%
  - Primary patency: 63% vs. 58%
  - Major amputation: 15% vs. 14%
  - All-cause mortality: 15% vs. 13%
- Infrapopliteal PTA outcomes have not changed over last decade despite advanced knowledge and techniques

The real problem is NOT what we think is the problem

- It is ALL in the WALL

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<th>Tunica media</th>
<th>Type 2 diabetes mellitus; end-stage renal disease; hyperphosphatemia; amputation</th>
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<td>Pseudoxanthoma elasticum; Marfan syndrome (concentric tibial calcification)</td>
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Thank you

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