Differing Patterns of Restenosis with Various Endovascular Treatments: What are the Implications for Determining the Best Treatment?

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• Intellectual Property Rights
• Other Financial Benefit
  - None

The Challenge of Femoropopliteal Artery Disease

• No single endovascular therapy has emerged as a "gold standard"
• All devices have primary patency, CD-TLR rates that on average seem similar from device to device
• However, to date we still do not understand the failure mode and restenotic pattern on any one device
• Benefits and limitations of existing scoring systems
  - Mehrotra, et al. and Tosoia, et al., developed a pragmatic and easily-applied system for stent-based restenosis classification
  - Both systems have demonstrated associations of restenosis type of class to outcomes
  - Limited to in-stent restenosis (ISR) classification, thus not applicable to TTA, UCG- and Atherectomy-based approaches
• Therefore, characterizing "the restenotic pattern" remains a critical component in advancing PAD standard of care and device specific treatment choices and may impact healthcare economics

Results: Scoring System

Type 1: Focal lesions <20% ITL
  - Edge proximal >2cm of proximal ITL margin
  - Edge distal >2cm of distal ITL margin

Type 2: Multifocal lesions
  - Multiple lesions combining to <50% ITL but with 3cm separation
  - Edge bilateral within 2cm of both ITL margins

Type 3: Moderate lesions
  - Lesions ≥20% but <50% of the ITL
  - Multiple lesions with <3cm separation

Type 4: Diffuse lesions
  - Lesions ≥50% ITL regardless of separation

Type 5: Occlusive lesions

Methods: Study Scope

• Inclusion Criteria
  - Medtronic Peripheral trials and registries
  - First TLRs ≤12mo of index procedure
• Exclusion Criteria
  - Unrevaluable or absent angiographic studies
  - Below-knee TLRs (as part of DEFINITIVE LE)

Analysis of Potential

Analytical Potential

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment Cohort</th>
<th>Total Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>IN.PACT SFA PTA</td>
<td>111</td>
<td>22</td>
</tr>
<tr>
<td>IN.PACT SFA DCB</td>
<td>220</td>
<td>6</td>
</tr>
<tr>
<td>IN.PACT Global - Interim Analysis DCB</td>
<td>655</td>
<td>54</td>
</tr>
<tr>
<td>DEFINITIVE LE - Above-knee Atherectomy</td>
<td>655</td>
<td>139</td>
</tr>
<tr>
<td>DEFINITIVE AR Atherectomy+DCB</td>
<td>121</td>
<td>22</td>
</tr>
<tr>
<td>DURABILITY II BMS</td>
<td>287</td>
<td>33</td>
</tr>
<tr>
<td>Complete SE SFA BMS</td>
<td>196</td>
<td>18</td>
</tr>
<tr>
<td>IN.PACT Global ISR - Baseline ISR BMS</td>
<td>131</td>
<td>169</td>
</tr>
<tr>
<td>IN.PACT Global ISR - DCB treatment BMS+DCB</td>
<td>2376</td>
<td>486</td>
</tr>
</tbody>
</table>

Original study scope expanded to include 47 additional subjects as part of IN.PACT SFA continued follow-up through 4 years (Total 533 subjects)
Restenosis with Respect to Baseline Stenosis

- 256 TLRs analyzed
  - 457 total TLRs less 145 unevaluable and 56 disqualified as BTK lesions or restenoses <50%
- Focal lesions exhibited tendency to fail in a focal restenosis pattern
- Diffuse and occlusive lesions tended to fail in diffuse and occlusive patterns

Restenosis Pattern at TLR

<table>
<thead>
<tr>
<th>Baseline Pattern</th>
<th>Treatment Modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal</td>
<td>PTA and Atherectomy+DCB tended to fail more focally than the others</td>
</tr>
<tr>
<td>Diffuse and Occlusive</td>
<td>However, this perspective does not account for differing baselines among cohorts</td>
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Restenosis with Respect to Treatment Modality

- 455 TLRs analyzed
  - 531 total TLRs less 8 unevaluable and 68 disqualified as BTK lesions or restenoses <50%
- PTA and Atherectomy+DCB tended to fail more focally than the others
- However, this perspective does not account for differing baselines among cohorts

Restenosis Pattern at TLR

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<thead>
<tr>
<th>Treatment Modality</th>
<th>Restenosis Pattern</th>
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<tr>
<td>PTA</td>
<td>Often more diffuse-occlusive</td>
</tr>
<tr>
<td>Atherectomy+DCB</td>
<td>More focal</td>
</tr>
<tr>
<td>DCB</td>
<td>More diffuse</td>
</tr>
</tbody>
</table>

Restenosis with Respect to Treatment Modality and Baseline Stenosis

- Patterns Classification Tool enables accounting for baseline angiographic patterns
- PTA and Atherectomy+DCB tended to fail more focally than the others
- DCB cohort began with most occlusions

Progression of Restenosis: All Modalities

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Baseline Pattern</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Focal</td>
</tr>
<tr>
<td>2</td>
<td>Diffuse and Occlusive</td>
</tr>
<tr>
<td>3</td>
<td>Diffuse and Occlusive</td>
</tr>
<tr>
<td>4</td>
<td>Occlusive</td>
</tr>
<tr>
<td>5</td>
<td>Occlusive</td>
</tr>
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</table>

Restenosis with Respect to Time

- While DCB restenosis patterns appear evenly distributed from 1- to 4-years
- PTA patterns split between focal and diffuse-occlusive; concentrated in first ~12-months

Alternative method of analysis

- Working backwards from restenotic pattern to index stenosis

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Restenosis failure reflects baseline stenosis pattern
Summary

- Existing restenosis scoring systems lack descriptive value for non-stent treatments and long, complex FPA lesions
- Proposed system provides all-inclusive nomenclature with more description of failure morphologies
  - These may provide for more information regarding subsequent therapy (ies)
- Potential determinant for index procedural technology
- The proposed “patterns of restenosis” may unify previous and future device trials regardless of technology
- Initial scoring “patterns” is effective and consistent among all modalities
- Upcoming analysis will incorporate subject specific data as to entry pattern and their failure mode and vice versa
- Additionally, we will evaluate time to TLR and device specific analysis to time to TLR