The present status of self-expanding and balloon-expandable tibial BMS and DES for CLI: Why and when to use

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Disclosure

Speaker name: Sean Lyden, MD

I have the following potential conflicts of interest to report:

- [x] Consulting: Spectranetics, Biomet, Endologix, TVA Medical
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [x] Other(s): VIVA Physicians Board Member

- [ ] I do not have any potential conflict of interest
DES/BMS vs DCB/PTA

Comparing Apples to Oranges
In-hospital and 30-day outcomes after tibioperoneal interventions US Medicare population with CLI

• 13,258 in-patients underwent tibioperoneal angioplasty (54.2% men; 75.7% white, 17.1% African American; 42.8% gangrene, 46.7% rest pain, 10.5% claudication) and 29.3% had a stent, 47.3% had femoral-popliteal angioplasty, and 20.1% had atherectomy during their initial procedure

• Initial hospital complications included renal complications (8.1%), respiratory complications and pneumonia (5.1%), and cardiac complications with acute myocardial infarction (3.2%)

• Mortality in-hospital was 2.8% and at 30 days was 6.7%

• Thirty-day rehospitalization rate was 29.6%

• Thirty-day reinterventions included repeat angiogram (8.5%), repeat tibioperoneal angioplasty (3.2%), open bypass (2.1%), and lower extremity amputations (23.8%)

• Gangrene was the most frequent diagnosis at rehospitalization (13.5%)

• About one-quarter of patients (23.8%) within 30 days after their initial procedure underwent amputation at any level of the lower limb.

DESTINY
Drug Eluting STents IN the critically ischemic lower leg

- Everolimus DES vs BMS (Xience V vs Multilink Vision by ABBOTT) in the treatment of below the knee lesions

- 140 patients
  - Lesion length < 40mm
    - 15.9mm in DES group, 18.9mm in BMS group
    - Max 2 over 50% stenosis, max 2 stents.

- End point: primary patency at 12 months
DESTINY
Drug Eluting STents IN the critically ischemic lower leg

- 6 month F/U with Duplex
- Trend in favor of DES for short below the knee lesions

6 moths results
DESTINY
Drug Eluting STents IN the critically ischemic lower leg

- 12 month data
- Angiography with quantitative vessel analysis

<table>
<thead>
<tr>
<th></th>
<th>Primary patency</th>
<th>Limb salvage</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>DES</td>
<td>85.2%</td>
<td>98.7%</td>
<td>81.9</td>
</tr>
<tr>
<td>BMS</td>
<td>54.4%</td>
<td>97.1%</td>
<td>84.2</td>
</tr>
</tbody>
</table>
DES for revascularization of infrapopliteal arteries: updated meta-analysis of randomized trial

- 611 patients from 5 trials were randomly assigned to DESs (n = 294) versus control therapy (plain balloon angioplasty/BMS implantation, n = 307)
- Overall, the median lesion length was 26.8 mm (interquartile range [IQR]: 18.2 to 30.0 mm)
- Reference vessel diameter of 2.86 mm (IQR: 2.68 to 3.00 mm)

JACC Cardiovasc Interv. 2013 Dec;6(12):1284-93
<table>
<thead>
<tr>
<th>Trial/First Author (Ref. #)</th>
<th>No. of Patients</th>
<th>Age, yrs</th>
<th>Males, %</th>
<th>Diabetes, %</th>
<th>CLI, %</th>
<th>Occlusion %</th>
<th>Lesion length, mm</th>
<th>Vessel Diameter, mm</th>
<th>DAPT, mo</th>
<th>Longest FU, months</th>
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<tbody>
<tr>
<td>ACHILLES (7)</td>
<td>200</td>
<td>73.4</td>
<td>71</td>
<td>65</td>
<td>N/A</td>
<td>78.3</td>
<td>26.9</td>
<td>2.60</td>
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<td>12</td>
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<td>BELOW (25)</td>
<td>60</td>
<td>72.4</td>
<td>64</td>
<td>68</td>
<td>100</td>
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<td>2.90</td>
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<tr>
<td>DESTINY (8)</td>
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<td>75.5</td>
<td>64</td>
<td>55</td>
<td>100</td>
<td>16.0</td>
<td>15.9</td>
<td>3.00</td>
<td>12</td>
<td>12</td>
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<tr>
<td>Falkowski et al. (24)</td>
<td>50</td>
<td>69.4</td>
<td>58</td>
<td>66</td>
<td>32</td>
<td>N/A</td>
<td>17.8</td>
<td>2.69</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>YUKON-BTK (6)</td>
<td>161</td>
<td>72.9</td>
<td>67</td>
<td>54</td>
<td>47</td>
<td>22.4</td>
<td>30.0</td>
<td>3.00</td>
<td>6</td>
<td>50</td>
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Overall mean values are reported.
Trial acronyms as in Table 1.
A  Target lesion revascularization

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>DES</th>
<th></th>
<th>Control</th>
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<th>Odds Ratio</th>
<th>Odds Ratio</th>
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<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
<td>M-H, Random, 95% CI</td>
<td>M-H, Random, 95% CI</td>
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<td>8</td>
<td>80</td>
<td>14</td>
<td>85</td>
<td>27.6%</td>
<td>0.56 [0.22, 1.43]</td>
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<tr>
<td>BELOW</td>
<td>1</td>
<td>10</td>
<td>6</td>
<td>28</td>
<td>5.6%</td>
<td>0.41 [0.04, 3.88]</td>
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<td>DESTINY</td>
<td>7</td>
<td>74</td>
<td>22</td>
<td>66</td>
<td>27.4%</td>
<td>0.21 [0.08, 0.53]</td>
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<tr>
<td>Falkowski et al.</td>
<td>3</td>
<td>25</td>
<td>14</td>
<td>25</td>
<td>13.0%</td>
<td>0.11 [0.03, 0.45]</td>
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<tr>
<td>YUKON-BTK</td>
<td>7</td>
<td>82</td>
<td>15</td>
<td>79</td>
<td>26.3%</td>
<td>0.40 [0.15, 1.04]</td>
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</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td></td>
<td>271</td>
<td>283</td>
<td>100.0%</td>
<td></td>
<td>0.31 [0.18, 0.54]</td>
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</tr>
<tr>
<td><strong>Total events</strong></td>
<td></td>
<td>26</td>
<td>71</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Heterogeneity: \( \tau^2 = 0.06; \chi^2 = 4.69, df = 4 (P = 0.32); I^2 = 15\%
Test for overall effect: \( Z = 4.19 (P < 0.0001) \)

B  Restenosis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>DES</th>
<th></th>
<th>Control</th>
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<tr>
<td></td>
<td>Events</td>
<td>Total</td>
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<td>Total</td>
<td>Weight</td>
<td>M-H, Random, 95% CI</td>
<td>M-H, Random, 95% CI</td>
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<tr>
<td>ACHILLES</td>
<td>15</td>
<td>67</td>
<td>31</td>
<td>74</td>
<td>27.1%</td>
<td>0.40 [0.19, 0.84]</td>
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<tr>
<td>BELOW</td>
<td>2</td>
<td>10</td>
<td>19</td>
<td>28</td>
<td>8.2%</td>
<td>0.12 [0.02, 0.68]</td>
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<tr>
<td>DESTINY</td>
<td>17</td>
<td>75</td>
<td>36</td>
<td>73</td>
<td>28.2%</td>
<td>0.39 [0.15, 0.61]</td>
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<tr>
<td>Falkowski et al.</td>
<td>4</td>
<td>25</td>
<td>19</td>
<td>25</td>
<td>11.6%</td>
<td>0.06 [0.01, 0.25]</td>
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<tr>
<td>YUKON-BTK</td>
<td>12</td>
<td>62</td>
<td>28</td>
<td>63</td>
<td>24.8%</td>
<td>0.30 [0.13, 0.67]</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td></td>
<td>239</td>
<td>263</td>
<td>100.0%</td>
<td></td>
<td>0.25 [0.15, 0.43]</td>
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<tr>
<td><strong>Total events</strong></td>
<td></td>
<td>50</td>
<td>133</td>
<td></td>
<td></td>
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</table>

Heterogeneity: \( \tau^2 = 0.14; \chi^2 = 6.48, df = 4 (P = 0.17); I^2 = 38\%
Test for overall effect: \( Z = 5.02 (P < 0.00001) \)

C  Amputation

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
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<th>Control</th>
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<th>Odds Ratio</th>
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<td>Events</td>
<td>Total</td>
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<td>Total</td>
<td>Weight</td>
<td>M-H, Random, 95% CI</td>
<td>M-H, Random, 95% CI</td>
</tr>
<tr>
<td>ACHILLES</td>
<td>11</td>
<td>80</td>
<td>17</td>
<td>85</td>
<td>61.7%</td>
<td>0.64 [0.28, 1.46]</td>
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<tr>
<td>BELOW</td>
<td>2</td>
<td>10</td>
<td>8</td>
<td>28</td>
<td>13.8%</td>
<td>0.63 [0.11, 3.61]</td>
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</tr>
<tr>
<td>DESTINY</td>
<td>1</td>
<td>74</td>
<td>2</td>
<td>66</td>
<td>7.2%</td>
<td>0.44 [0.04, 4.95]</td>
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<tr>
<td>YUKON-BTK</td>
<td>2</td>
<td>82</td>
<td>9</td>
<td>79</td>
<td>17.3%</td>
<td>0.19 [0.04, 0.93]</td>
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</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td></td>
<td>246</td>
<td>258</td>
<td>100.0%</td>
<td></td>
<td>0.50 [0.26, 0.97]</td>
<td></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td></td>
<td>16</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: \( \tau^2 = 0.00; \chi^2 = 1.82, df = 3 (P = 0.61); I^2 = 0\%
Test for overall effect: \( Z = 2.06 (P = 0.04) \)
DES for revascularization of infrapopliteal arteries: updated meta-analysis of randomized trial

- Median follow-up of 12 months (IQR: 12 to 36 months)
- DESs reduced the risk of
  - TLR (odds ratio [OR]: 0.31; 95% confidence interval [CI]: 0.18 to 0.54; p < 0.001)
  - Restenosis (OR: 0.25; 95% CI: 0.15 to 0.43; p < 0.001)
  - Amputation (OR: 0.50; 95% CI: 0.26 to 0.97; p = 0.04)
  - Without a significant difference in terms of death (OR: 0.81; 95% CI: 0.45 to 1.49; p = 0.50) and Rutherford class improvement (OR: 1.36; 95% CI: 0.91 to 2.04; p = 0.13) versus control therapy.

JACC Cardiovasc Interv. 2013 Dec;6(12):1284-93
Incidence, anatomical location, and clinical significance of compressions & fractures in tibial bare metal stents

- 63 CLI patients (45 men; mean age 71.3+/−9.5 years) who had been treated with infrapopliteal angioplasty and stent placement for 191 lesions in 84 limbs.
- 369 stents (296 stainless steel and 73 cobalt-chromium alloy) were implanted; 239 were placed overlapping in tandem lesions.
- Mean length of the overall stented segment was 4.4+/−6.3 cm (range 1.6-14.0). Stents were located in the tibioperoneal (n = 34), anterior tibial (n = 195), posterior tibial (n = 63), and peroneal (n = 77) arteries.
- Follow-up consisted of digital subtraction angiography and infrapopliteal radiography imaging at 2 different angles.
- Mean follow-up was 15+/−11 months (range 6-60). Image analysis detected 1 (0.3%) severe stent fracture (complete separation and misalignment of stent struts) and 11 (3.0%) stent compressions.
- Infrapopliteal stent fracture and compressions were associated with increased artery restenosis [100% (12/12) versus 47.3% (169/357), p<0.001] and an increased rate of clinical deterioration and clinically-driven reinterventions [41.7% (5/12 limbs) versus 19.4% (14/72 limbs), p = 0.04].
- The single fracture and most of the compressions were located in the distal third of the anterior tibial artery.

J Endovasc Ther. 2009 Feb;16(1):15-22
Durability and Efficacy of Tibial Stent for CLI

- January 2005 to June 2012, 168 limbs (155 patients) were Rx (PTA)/stent placement for de novo tibial disease
  - 92.9% were classified with Rutherford category 5/6
  - Concomitant interventions were performed in 58%
  - Bare metal (84%) and drug-eluting (16%) stents were used.
- Technical success rate was 99%.
- Mean follow-up was 33 months (range, 1-96 mo).
- Symptomatic intrastent restenosis occurred in 20 limbs (12%) at a mean of 10.3 months ± 11.27; this was identified as a prognostic factor for limb loss (P = .045).
- TLR was necessary in 10.8% of limbs, for a limb salvage rate of 89.2%.
- Survival was influenced by age (> 75 y; P < .001), diabetes (P = .048), and renal insufficiency and/or dialysis (P < .001)
- Estimated survival rate was 63% at 36 months (hazard ratio, 1.63; 95% CI, 54%-70%).

J Vasc Interv Radiol. 2015 Apr;26(4):475-83
Absorb Rx focal tibial and distal popliteal lesions

- 38 limbs/ 33 patients
  - CLI (68.4%) or severe claudication (31.6%)
  - 50 stents for 43 lesions, mean length of 19.2 ± 11.6 mm
  - During a mean follow-up period of 12.0 ± 3.9 months, 5 patients died
  - Clinical improvement was present in 30 (79%)
  - Binary restenosis was detected in 3 of 50 scaffolds (6%).
  - Kaplan-Meier primary patency 96% and 84.6% at 12 and 24 months
  - CD-TLR 96% and 96% at 12 and 24 months
  - Complete wound healing occurred in 64% of those treated for tissue loss, with no major amputation and a limb-salvage rate of 100%.

JACC Cardiovasc Interv. 2016 Aug 22;9(16):1721-8
Everolimus-Eluting Stent for Patients With CLI & Infrapopliteal PAD

- Xience-Prime Everolimus-Eluting Stent (EES), in Rutherford-Becker category 4/5 with distal popliteal and proximal tibial arteries long occlusive lesions up to 10 cm, between June 2011 - April 2014
- 122 patients angiographic documented segment P3 of popliteal artery and proximal tibial arteries stenosis >70%, and mean lesion length of 52.7 mm (range: 20-100 mm)
- End points 1 & 3 year primary patency, major amputation-free survival, TLR and wound healing rates.
- 1- and 3-year primary patency rates were 88.9% and 80.1%,
  - Survival 88.1% and 70.4%
  - Major amp free survival 93% and 89.3%
  - TLR 91.5% and 85.1%
- Primary patency influenced major amputation rate, which was 60% in patients with no target artery patency versus 5.4% in patients with patency (P = .022).
- At 1-year follow-up, 78 (88.6%) of 88 patients improved 1 or more of their Rutherford-Becker category, and 48(80%) of 69 patients had wound healing.

Vasc Endovascular Surg. 2017 Jan 1:1538574416689429
Conclusions

• Current data is not comparable between therapies
• DES seems to improve therapy over BMS for short lesions
• Compressions and fractures may be a late concern
• Time for DAPT is unknown
The present status of self-expanding and balloon-expandable tibial BMS and DES for CLI: Why and when to use

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