Critical Limb Ischemia:
A Selective Approach to Revascularization Works Best

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Case Discussion

- 58 yo M, DM, CAD, HTN
- Presents with >1 week R foot rest pain and erythema, gangrenous changes 3rd, 4th toes. Absent pedal pulses
- Stable CAD, prior PCI
- No prior vascular interventions; intact GSV
- Angiogram
- Drainage amputation toes 3-5

Disclosures

None
Revascularization Strategy?

A. Attempt recanalization of popliteal and TP trunk using transluminal or subintimal PTA

B. Atherectomy of popliteal and TP trunk

C. Femoral-tibial bypass using GSV
CLI: Treatment Goals

- Relief of pain
- Healing of wounds
- Preservation of a functional limb

**EFFECTIVE REVASCULARIZATION**

- Minimize risk of other major CV events

**EFFECTIVE LIFESTYLE MODIFICATION AND MEDICAL THERAPIES**

Revascularization Options in CLI

The Increase in Endovascular Interventions has outpaced the Decline in Bypass Surgery by More Than 3:1

**Revascularization Strategies in CLI: Key Factors in Decision-Making**

- General health of the patient
  - Age, comorbidities, ambulatory status
- Foot: likelihood of functional salvage
- Severity of limb ischemia
- Anatomic distribution of disease
- Prior vascular interventions
- Availability of autogenous vein for LEB
  - Ipsilateral GSV > contralateral GSV > alternative veins
  - Prosthetics and other non-autogenous conduits inferior
Circulase I: N= 379 No Option pts
“Natural History”
Limb Salvage 87% at 1 year

Sustained hemodynamic improvement is the most direct measure of effective revascularization therapy

Infrainguinal Bypass Surgery for CLI

- Bypass with autogenous vein is the “gold standard”
- Results well documented in hundreds of reports: anecdotal > retrospective > randomized trials
- Versatile: results in complex situations (anatomic, patient related) well established
- Low mortality, good durability
- BUT—there are limitations and risks:
  - Wound and other complications
  - Prolonged recovery
  - Vein quality and availability
  - Surveillance and reintervention
  - Technically demanding procedures

PREVENT III: N=1,404 LEB with Vein for CLI; 83 Centers; Perioperative (30 day) complications

<table>
<thead>
<tr>
<th></th>
<th>Edifoligide</th>
<th>Placebo</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total major morbidity</td>
<td>124 (17.3%)</td>
<td>125 (17.9%)</td>
<td>249 (17.6%)</td>
</tr>
<tr>
<td>Cardiac or resp arrest</td>
<td>12 (1.7%)</td>
<td>9 (1.3%)</td>
<td>21 (1.5%)</td>
</tr>
<tr>
<td>DVT</td>
<td>6 (&lt;1.0%)</td>
<td>8 (1.1%)</td>
<td>14 (&lt;1.0%)</td>
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<tr>
<td>Death</td>
<td>20 (2.8%)</td>
<td>16 (2.6%)</td>
<td>36 (2.7%)</td>
</tr>
<tr>
<td>Graft occlusion</td>
<td>30 (4.2%)</td>
<td>43 (6.2%)</td>
<td>73 (5.2%)</td>
</tr>
</tbody>
</table>

PIII Cohort: 75% tissue loss, 24% high risk conduits, 66% infrapopliteal bypass targets

<table>
<thead>
<tr>
<th></th>
<th>Edifoligide</th>
<th>Placebo</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Dehiscence</td>
<td>3 (&lt;1.0%)</td>
<td>9 (1.3%)</td>
<td>12 (&lt;1.0%)</td>
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<tr>
<td>Infection</td>
<td>25 (3.5%)</td>
<td>15 (2.1%)</td>
<td>40 (2.8%)</td>
</tr>
<tr>
<td>Necrosis</td>
<td>9 (1.3%)</td>
<td>6 (&lt;1.0%)</td>
<td>15 (1.1%)</td>
</tr>
<tr>
<td>Graft hemorrhage</td>
<td>3 (0.4%)</td>
<td>4 (0.6%)</td>
<td>7 (0.5%)</td>
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</table>

PREVENT III: One Year Outcomes

<table>
<thead>
<tr>
<th>One Year Outcome</th>
<th>Edifoligide</th>
<th>Placebo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary patency</td>
<td>61.5</td>
<td>59.3</td>
<td>0.33</td>
</tr>
<tr>
<td>Primary assisted patency</td>
<td>78.6</td>
<td>74.6</td>
<td>0.09</td>
</tr>
<tr>
<td>Secondary patency</td>
<td>80.9</td>
<td>76.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Limb salvage</td>
<td>87.7</td>
<td>89.2</td>
<td>0.37</td>
</tr>
<tr>
<td>Survival</td>
<td>83.2</td>
<td>84.4</td>
<td>0.55</td>
</tr>
</tbody>
</table>

PREVENT III: Performance of Good Quality Vein

- N = 604 bypasses (43% of study population) completed with a single segment GSV, diameter > 3.5 mm
- 30 day failure 1.7%
- One year results:
  - PP 72%
  - SP 87%
  - Limb salvage 91%

Importance of conduit assessment and quality

SSGSV ≥ 3.5 mm

Level of distal anastomosis is not an important limitation for a good quality vein

Risk Stratification: the PIII CLI Risk Score

<table>
<thead>
<tr>
<th>COVARIATES</th>
<th>DF</th>
<th>β coefficient</th>
<th>Integer score</th>
<th>HR (95% CI)</th>
<th>P-Value</th>
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</thead>
<tbody>
<tr>
<td>Age ≥ 75 years</td>
<td>1</td>
<td>0.50</td>
<td>2</td>
<td>1.64 (1.21, 2.22)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hematocrit &lt; 30</td>
<td>1</td>
<td>0.48</td>
<td>2</td>
<td>1.85 (1.11, 3.04)</td>
<td>0.012</td>
</tr>
<tr>
<td>History of advanced CAD</td>
<td>1</td>
<td>0.34</td>
<td>1</td>
<td>1.81 (1.05, 3.18)</td>
<td>0.021</td>
</tr>
<tr>
<td>Dialysis</td>
<td>1</td>
<td>1.03</td>
<td>4</td>
<td>2.81 (1.97, 3.99)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CLI criterion</td>
<td>1</td>
<td>0.80</td>
<td>3</td>
<td>2.22 (1.43, 3.44)</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

Endovascular Therapy for Limb Salvage

- Relatively new and continually evolving technology
- Recent advances: DES, DCB hold promise
- Potential advantages
  - Less invasive; ↓mortality and morbidity (?)
  - Fast recovery
- Potential disadvantages
  - Reduced efficacy: hemodynamics, durability
  - Risk of limb deterioration
  - May affect surgical options
  - Cost: repeated treatments, ↓symptom-free intervals

Techniques are not standardized

Results not well documented: mostly small single center observational series with heterogeneous cohorts, variable f/u quality and time

Factors Associated with Inferior Results Of Infrainguinal Endovascular Therapy

- Claudication vs limb salvage
- Stenosis vs occlusion
- TASC C/D SFA/pop disease
- Multi-level disease
- Poor runoff
- Diabetes
- Creatinine > 1.3

This encompasses the majority of CLI patients

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Reckless Fallacy

- Concerns about:
  - Increasing use of stents
    - May compromise inflow and outflow targets
    - May influence runoff of subsequent bypass
  - Embolization:
    - Loss of a tibial or pedal vessel
    - Trash to forefoot/roles
    - Growing enthusiasm for embolic protection?

- Additional tissue loss, procedures, pain, etc secondary to failures of revascularization are common

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In-hospital and 30-day outcomes after tibioperoneal interventions in the US Medicare population with critical limb ischemia

- N=13,258 from 2005-2007; >40% octogenarians
- 30-days: mortality 6.7%, complications 14%, rehospitalization 29.6%
- 30-day reinterventions: angiogram 8.5%, repeat PCI 12%, bypass 2.1%
- 30-day amputations: 23.8% any level; 17.3% major amp in Rutherford 6 pts

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Meta-analysis of infrapopliteal angioplasty for chronic critical limb ischemia

Marcello Romiti, MD,* Maximiano Albers, MD,* Francisco Cardoso Breachado-Neto, MD,* Anis Espinelli S. Durazzo, MD,* Carlos Alberto Bragaçu Penteado, PhD,* and Nelson De Lucena, MD,*/umo and Sao Paulo, Sao Paulo, Brazil

Table II. Meta-analysis results of renal percutaneous transluminal angioplasty and percutaneous-to-renal bypass

<table>
<thead>
<tr>
<th></th>
<th>1 month</th>
<th>6 months</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
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</thead>
<tbody>
<tr>
<td>Primary revascularization</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTA</td>
<td>77.4 ± 4.1</td>
<td>65.0 ± 7.0</td>
<td>58.1 ± 4.6</td>
<td>51.3 ± 6.6</td>
<td>48.6 ± 8.0</td>
</tr>
<tr>
<td>Bypass</td>
<td>98.3 ± 1.1</td>
<td>98.8 ± 2.1</td>
<td>98.1 ± 2.0</td>
<td>76.8 ± 2.3</td>
<td>72.3 ± 2.7</td>
</tr>
<tr>
<td>Secondary revascularization</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTA</td>
<td>81.3 ± 1.4</td>
<td>73.8 ± 2.7</td>
<td>64.2 ± 5.9</td>
<td>66.3 ± 6.1</td>
<td>62.0 ± 6.0</td>
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<tr>
<td>Bypass</td>
<td>94.9 ± 1.0</td>
<td>99.3 ± 1.6</td>
<td>95.9 ± 1.9</td>
<td>91.6 ± 2.3</td>
<td>76.7 ± 2.9</td>
</tr>
<tr>
<td>Limb salvage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTA</td>
<td>93.4 ± 2.3</td>
<td>88.2 ± 4.4</td>
<td>83.0 ± 2.7</td>
<td>83.8 ± 3.5</td>
<td>82.4 ± 3.4</td>
</tr>
<tr>
<td>Bypass</td>
<td>96.1 ± 1.2</td>
<td>96.9 ± 1.9</td>
<td>88.5 ± 2.2</td>
<td>85.2 ± 2.8</td>
<td>82.3 ± 4.0</td>
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<tr>
<td>Patient survival</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTA</td>
<td>98.8 ± 0.7</td>
<td>92.3 ± 5.5</td>
<td>87.0 ± 2.1</td>
<td>74.3 ± 3.7</td>
<td>68.4 ± 5.5</td>
</tr>
<tr>
<td>Bypass</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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Large datasets suggest early amputation rates appear high after endovascular interventions in patients with significant tissue loss.

**BASIL Trial:** Bypass vs Angioplasty in Severe Ischemia of the Limb
- Only RCT to date: surgery-first vs angioplasty-first for limb threatening ischemia (1999-2004)
- 452 patients with ischemia; 27 centers in UK
- Patients pre-selected as candidates for both PTA and surgery: 29% of all-comers on audit
  - 34% deemed “unreconstructable”
  - 70% with ankle pressure >50 mm Hg
  - 42% diabetics
- Primary endpoint: amputation free survival
- Secondary endpoints: survival, M&M, LOS, cost, QOL.

BASIL: Results diverge at two years

>70% of limb salvage patients treated with revascularization lived beyond two years.

AND THIS IN A SETTING WHERE THERE WAS NO ATERECTOMY AND NO METAL LEFT BEHIND.....

“BAP was associated with a significantly higher failure rate than BSX. Most BAP patients ultimately required surgery. BSX outcomes after failed BAP are significantly worse than for BSX performed as a first revascularization attempt. BSX with vein offers the best long term AFS and OS and, overall BAP appears superior to prosthetic BSX.”


This is what results will look like if all LEB are performed only after ENDO has failed!

Is BASIL Relevant to Practice in 2011?

- YES - because:
  - It's the only level I evidence in the field
  - POBA still a dominant treatment in below-knee vessels
  - The potential negative effects of failed endoluminal treatment, first identified in BASIL, appear to be a real issue
  - It confirms that durability is an important consideration for a significant proportion of CLI patients, and life expectancy must be carefully considered in selecting the approach

- However...
  - Results of both bypass surgery (vein) and endovascular treatments observed in BASIL may not accurately reflect outcomes in current practice
  - Hard to interpret because the cohort was highly selected

CLI: A Selective Revascularization Strategy

Revascularization Strategy?

A. Attempt recanalization of popliteal and TP trunk using transluminal or subintimal PTA
B. Atherectomy of popliteal and TP trunk
C. Femoral-tibial bypass using GSV