Impact of Infection on Outcomes after revascularization for chronic limb threatening ischemia and what can be done about it

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Demography is Destiny

- Fontaine and Rutherford are pure ischemia models; the concept of CLI was never intended to be applied to diabetics
- Global epidemic of diabetes; emerging evidence that etiology of foot ulcers in these patients has changed over the last 2 decades from primarily neuropathic to neuroischemic and purely ischemic
- Neuropathy, wound characteristics and infection complicate management
- Eurodialte: PAD + infection TRIPLES amputation risk
- Our patients have changed but our classification system has not

The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk stratification based on Wound, Ischemia, and foot Infection (WIF)

Joseph L. Mills, Sr, MD; Michael S. C��, MD; David G. Armstrong, DPM, MD, PhD; Prakash B. Penumatcha, MD; Andrea Schuman, MD; Norman N. Salley, MD, ATC; and George Arnaud, MD, on behalf of the Society for Vascular Surgery Lower Extremity Guidelines Committee, Tucson, Ariz; San Francisco and Van Nuys, Calif; Philadelphia and Worcester, Mass; and Minneapolis, Minn.

Critical limb ischemia, also defined as CLI, was intended to delineate a subgroup of patients with a threatened lower extremity primarily because of severe ischemia. It was the intent of the original authors that patients with diabetes be excluded in any way. Several factors can cause patients with CLI to have a higher risk of amputation and bloodstream infection. The current classification system has been updated to allow the clinician to use the same risk stratification and treatment decisions for all patients, regardless of etiology. The current system is based on four risk factors: wound, ischemia, and infection, and incorporates a comprehensive approach to the decision-making process. The Society for Vascular Surgery Lower Extremity Guidelines Committee has developed a new classification system that reflects these important considerations. We were the first to frame, for Society for Vascular Surgery Lower Extremity, this as a new risk stratification system. Risk stratification is based on these four factors that define risk: wound, ischemia, infection, and presence of amputation. Our primary risk stratification system is intended to permit more meaningful analysis of outcomes for various forms of therapy in this challenging, heterogeneous population. (J Vasc Surg. 2016;63:229-243.)
**SVS Lower Extremity Threatened Limb Classification**

**WIfI Index**

- **Wound:**
  - extent and depth
- **Ischemia:**
  - perfusion/flow
- **Foot Infection:**
  - presence and extent

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**Hypothesis**

Foot infection in patients with limb threatening ischemia adversely impacts limb salvage in patients who undergo infrainguinal bypass

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**Wound Classification**

1. Wound:
   - extent and depth
2. Ischemia:
   - perfusion/flow
3. Foot Infection:
   - presence and extent

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**Before the SVS WIfI Threatened limb classification, prior classification systems (Fontaine/Rutherford) failed to consider infection as risk factor for amputation**

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**What is the effect of foot infection on outcomes after infra-inguinal bypass?**

- Before the SVS WIfI Threatened limb classification, prior classification systems (Fontaine/Rutherford) failed to consider infection as risk factor for amputation.

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**Foot Infection in patients with limb threatening ischemia adversely impacts limb salvage in patients who undergo infrainguinal bypass**

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**The need for improved risk stratification in chronic critical limb ischemia; Chung et al., J Vasc Surg, 2014 Dec;60(6):1677-85.**
Study Design and Study Base

- Retrospective review of a prospectively maintained database of patients with limb threatening ischemia who underwent infrainguinal bypass in a single VAMC
- Inclusion criteria: Ischemic rest pain and/or tissue loss who underwent infrainguinal bypass
- Exclusion criteria: Acute limb ischemia, vasculitis, trauma
- We analyzed 454 bypasses performed between 2006-2015

- Infection: 215 (47%)
- No infection: 239 (53%)

Methods and Statistical Analysis

- Primary outcome
  - Major amputation
- Secondary outcomes
  - Readmission, postoperative length of stay, wound healing time
- Cox proportional hazards regression for time to event analyses (amputation and wound healing)
- Logistic regression for analysis of readmission rates
- Quantile regression for analysis of length of stay

### Outcome: Amputation

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>2.13</td>
<td>1.41, 3.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statin</td>
<td>1.92</td>
<td>1.06, 3.01</td>
<td>0.028</td>
</tr>
<tr>
<td>Age</td>
<td>0.96</td>
<td>0.93, 0.99</td>
<td>0.013</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.94</td>
<td>0.90, 0.98</td>
<td>0.007</td>
</tr>
<tr>
<td>Vein conduit</td>
<td>0.36</td>
<td>0.17, 0.70</td>
<td>0.003</td>
</tr>
</tbody>
</table>

### Outcome: Time to wound healing

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>1.57</td>
<td>1.01, 2.48</td>
<td>0.05</td>
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<tr>
<td>Infection</td>
<td>0.73</td>
<td>0.58, 1.42</td>
<td>0.36</td>
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</table>

### Outcome: Postoperative length of stay

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Median (days)</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex conduit</td>
<td>1.90</td>
<td>0.14, 3.26</td>
<td>0.004</td>
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<tr>
<td>Infection</td>
<td>1.54</td>
<td>0.62, 2.50</td>
<td>0.001</td>
</tr>
<tr>
<td>Re-operation</td>
<td>1.41</td>
<td>0.52, 2.31</td>
<td>0.002</td>
</tr>
<tr>
<td>Intraoperative blood loss</td>
<td>0.003</td>
<td>0.001, 0.004</td>
<td>0.005</td>
</tr>
<tr>
<td>Glomerular filtration rate</td>
<td>-0.03</td>
<td>-0.04, -0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aspirin</td>
<td>-1.13</td>
<td>-2.14, -0.12</td>
<td>0.028</td>
</tr>
<tr>
<td>Albumin</td>
<td>-1.30</td>
<td>-2.10, -0.53</td>
<td>0.001</td>
</tr>
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</table>
Study conclusions

- Despite revascularization, infection was a significant predictor of major amputation and prolonged length of stay in patients requiring infrainguinal bypass.
- Infection had no effect on time to wound healing or readmission rates
- Vein graft conduit was strongly associated with freedom from major limb amputation

CONCLUSIONS

- Venn diagram rubric of Wound, Ischemia and foot infection (WIf) is a logical construct for evaluating and treating threatened limbs
- INFECTION must be aggressively identified and treated EARLY, followed by prompt revascularization as soon as practical. Vein grafts and endovascular approach preferred over prosthetic in this setting
- Limb disease burden, especially infection, has a significant impact on outcome despite aggressive revascularization and needs to be considered up front when designing and comparing therapeutic approaches