Critical Limb Ischemia: Optimal care, an interdisciplinary challenge

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Landesklinikum Baden-Mödling
Austria
Disclosure

Speaker name:

Markus Haumer, MD

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

✔ I do not have any potential conflict of interest
Critical Limb Ischemia
An interdisciplinary approach

Interdisciplinary Core
- Vascular medicine physicians
- Interventional cardiologists
- Interventional radiologists
- Vascular surgeons

Attendees @ LINC 2015 (n ~ 5,000)
Critical Limb Ischemia
An interdisciplinary approach

Interdisciplinary Core
- Vascular medicine physicians
- Interventional cardiologists
- Interventional radiologists
- Vascular surgeons

~80% of 120 (140) sites enrolling in BEST-CLI Trial have multidisciplinary CLI Teams [Endovascular Today 11/2015]

Teamwork matters!

Complementary Disciplines
- Podiatrist, wound manager, diabetologist; microbiologist,
Critical Limb Ischemia
An interdisciplinary approach

Critical Limb Ischemia still poorly outcomes and lack of guideline adherence

44% "Too late or too sick?"

49% Critical Limb Ischemia

10% Amputations (n=20.685)

11% Critical Limb Ischemia

10% Amputations (n=4.298)

Revascularisation in 11% technically not feasible? Still poor outcomes and lack of guideline adherence

Primary Amputations

Revascularisation in 44% "Too late or too sick?"
Critical Limb Ischemia
Still poor outcomes and lack of guideline adherence

**A** Death

<table>
<thead>
<tr>
<th>Rutherford Category</th>
<th>Patients</th>
<th>Deaths</th>
<th>Cumulative Risk</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF 1-3</td>
<td>21,197</td>
<td>2,954</td>
<td>0.526</td>
<td>4</td>
</tr>
<tr>
<td>RF 4</td>
<td>5,353</td>
<td>4,487</td>
<td>0.392</td>
<td>4</td>
</tr>
<tr>
<td>RF 5</td>
<td>5,916</td>
<td>5,261</td>
<td>0.284</td>
<td>4</td>
</tr>
<tr>
<td>RF 6</td>
<td>8,416</td>
<td>8,605</td>
<td>0.264</td>
<td>4</td>
</tr>
</tbody>
</table>

**B** Amputation

<table>
<thead>
<tr>
<th>Rutherford Category</th>
<th>Patients</th>
<th>Amputations</th>
<th>Cumulative Risk</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF 1-3</td>
<td>21,197</td>
<td>3,304</td>
<td>0.296</td>
<td>4</td>
</tr>
<tr>
<td>RF 4</td>
<td>5,353</td>
<td>4,237</td>
<td>0.264</td>
<td>4</td>
</tr>
<tr>
<td>RF 5</td>
<td>5,916</td>
<td>4,125</td>
<td>0.264</td>
<td>4</td>
</tr>
<tr>
<td>RF 6</td>
<td>8,416</td>
<td>2,497</td>
<td>0.236</td>
<td>4</td>
</tr>
</tbody>
</table>

**C** Death or Amputation

<table>
<thead>
<tr>
<th>Rutherford Category</th>
<th>Patients</th>
<th>Deaths or Amputations</th>
<th>Cumulative Risk</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF 1-3</td>
<td>21,197</td>
<td>5,304</td>
<td>0.296</td>
<td>4</td>
</tr>
<tr>
<td>RF 4</td>
<td>5,353</td>
<td>5,237</td>
<td>0.264</td>
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<tr>
<td>RF 5</td>
<td>5,916</td>
<td>4,125</td>
<td>0.264</td>
<td>4</td>
</tr>
<tr>
<td>RF 6</td>
<td>8,416</td>
<td>2,497</td>
<td>0.236</td>
<td>4</td>
</tr>
</tbody>
</table>

**D** Myocardial infarction

<table>
<thead>
<tr>
<th>Rutherford Category</th>
<th>Patients</th>
<th>Myocardial Infarctions</th>
<th>Cumulative Risk</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF 1-3</td>
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<td>2,620</td>
<td>0.275</td>
<td>4</td>
</tr>
<tr>
<td>RF 4</td>
<td>5,353</td>
<td>1,597</td>
<td>0.251</td>
<td>4</td>
</tr>
<tr>
<td>RF 5</td>
<td>5,916</td>
<td>1,410</td>
<td>0.251</td>
<td>4</td>
</tr>
<tr>
<td>RF 6</td>
<td>8,416</td>
<td>1,472</td>
<td>0.245</td>
<td>4</td>
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</table>

**E** Ischemic stroke

<table>
<thead>
<tr>
<th>Rutherford Category</th>
<th>Patients</th>
<th>Ischemic Strokes</th>
<th>Cumulative Risk</th>
<th>Years</th>
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<td>RF 1-3</td>
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<tr>
<td>RF 5</td>
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<td>0.251</td>
<td>4</td>
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<tr>
<td>RF 6</td>
<td>8,416</td>
<td>1,456</td>
<td>0.245</td>
<td>4</td>
</tr>
</tbody>
</table>

**Figure 2** Major adverse events during follow-up. Kaplan–Meier probabilities for death (**A**), amputation (**B**), a combined endpoint of death or amputation (**C**), myocardial infarction (**D**), and ischaemic stroke (**E**) are presented, with the number of patients at risk given below each chart. Between the distinct Rutherford categories highly significant differences were observed (% P, 0.001).

Footulcers in diabetic patients
Delivery of care in daily practice in Europe

Referral
6-55% late referral (i.e. >3 months) to a dedicated foot clinic

Pressure off-loading
0-68% casting in plantar fore- or midfoot ulcers

Vascular imaging
14-68% in patients with ABPI <0.5 or persistent ulcer (i.e. >1yr) or after major amputation; revascularization in 43%.
Critical Limb Ischemia
An interdisciplinary approach

Identification of CLI
- Suspicion of ischemia
- Hemodynamic evaluation
- Anatomical evaluation

Identification of comorbidities
- Contributors to tissue loss
  - Diabetes, neuropathy, infection, vasculitis, malnutrition...
- Cardiac disease CHF; CAD; HTN; HLP; CVD...
- Renal disease...,
### Peripheral arteriel disease

#### Grading of severity

<table>
<thead>
<tr>
<th>Fontaine Stage</th>
<th>Rutherford Category</th>
<th>Ankle Pressure</th>
<th>Ankle Brachial Index</th>
<th>Asympt. Claudication</th>
<th>Critical Limb Ischemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>III</td>
<td>140</td>
<td>0.9</td>
<td>1</td>
<td>0.0</td>
</tr>
<tr>
<td>Ila</td>
<td>IV</td>
<td>50</td>
<td>(70)</td>
<td>2</td>
<td>0.0</td>
</tr>
<tr>
<td>IIb</td>
<td></td>
<td>(70)</td>
<td>0</td>
<td>3</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Critical Limb Ischemia Definitions

### Fontaine Stage

<table>
<thead>
<tr>
<th>III</th>
<th>IV</th>
</tr>
</thead>
</table>

### Rutherford Category

<table>
<thead>
<tr>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ischemic Rest Pain</strong>&lt;br&gt;Ankle pressure&lt;br&gt;&lt;70mmHg&lt;br&gt;Toe pressure&lt;br&gt;&lt;50mmHg&lt;br&gt;TcPO&lt;sub&gt;2&lt;/sub&gt; &lt;40mmHg&lt;br&gt;Skin perfusion pressure&lt;br&gt;&lt;40mmHg</td>
<td><strong>Ischemic Ulceration</strong>&lt;br&gt;Ankle pressure&lt;br&gt;&lt;50mmHg&lt;br&gt;Toe pressure&lt;br&gt;&lt;30mmHg&lt;br&gt;TcPO&lt;sub&gt;2&lt;/sub&gt; &lt;20mmHg&lt;br&gt;Skin perfusion pressure&lt;br&gt;&lt;30mmHg</td>
<td><strong>Ischemic Gangrene</strong>&lt;br&gt;Ankle pressure&lt;br&gt;&lt;50mmHg&lt;br&gt;Toe pressure&lt;br&gt;&lt;30mmHg&lt;br&gt;TcPO&lt;sub&gt;2&lt;/sub&gt; &lt;20mmHg&lt;br&gt;Skin perfusion pressure&lt;br&gt;&lt;30mmHg</td>
</tr>
</tbody>
</table>

Critical Limb Ischemia Diagnostic approach

ABI
Toe Pressure
TcPO
SPP
DUS
CTA
MRA
iaDSA
Critical Limb Ischemia
Diagnostic approach

Very often, vascular imaging is more readily available than adequate hemodynamic assessment. However, with the exception of the "desert foot" CLI is not defined by angiograms!
"CLI", first defined in 1982, was intended to delineate a subgroup of patients with a threatened lower extremity primarily because of chronic ischemia.

Perfusion is only one determinant of outcome.

Risk stratification is based on three major factors that impact amputation risk and clinical management: Wound, Ischemia, and foot Infection (WIfI).
Critical Limb Ischemia Diagnostic approach

The Society for Vascular Surgery Lower Extremity Risk stratification based on Wound, Ischemia, and foot infection (WIfI)

Critical Limb Ischemia
Non-angiographic workup

Rutherford 5
Ischemic wound
Mild infection

Rutherford 5 (6?)
Ischemic toe

Rutherford 6
Ischemic limb

Ankle pressure
70mmHg

Ankle pressure >200mmHg
Toe pressure 0 (30) mmHg

Ankle pressure 30mmHg
Toe Pressure 0mmHg

WIfI 121

WIfI 320

WIfI 330
Critical Limb Ischemia
Risk stratification according to WIfI

Estimate risk of amputation at 1 year for each

<table>
<thead>
<tr>
<th></th>
<th>Ischemia – 0</th>
<th>Ischemia – 1</th>
<th>Ischemia – 2</th>
<th>Ischemia – 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>W-0</td>
<td>VL</td>
<td>VL</td>
<td>L</td>
<td>M</td>
</tr>
<tr>
<td>W-1</td>
<td>VL</td>
<td>VL</td>
<td>L</td>
<td>M</td>
</tr>
<tr>
<td>W-2</td>
<td>L</td>
<td>L</td>
<td>M</td>
<td>H</td>
</tr>
<tr>
<td>W-3</td>
<td>M</td>
<td>M</td>
<td>H</td>
<td>H</td>
</tr>
</tbody>
</table>

Estimate likelihood of benefit of / requirement for revascularization (assuming infection can be controlled first)

<table>
<thead>
<tr>
<th></th>
<th>Ischemia – 0</th>
<th>Ischemia – 1</th>
<th>Ischemia – 2</th>
<th>Ischemia – 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>W-0</td>
<td>VL</td>
<td>VL</td>
<td>VL</td>
<td>VL</td>
</tr>
<tr>
<td>W-1</td>
<td>VL</td>
<td>VL</td>
<td>L</td>
<td>M</td>
</tr>
<tr>
<td>W-2</td>
<td>VL</td>
<td>VL</td>
<td>M</td>
<td>H</td>
</tr>
<tr>
<td>W-3</td>
<td>VL</td>
<td>VL</td>
<td>M</td>
<td>M</td>
</tr>
</tbody>
</table>

fI, foot infection; I, Ischemia; W, Wound.
Critical Limb Ischemia
Non-angiographic workup

Rutherford 5
Ischemic wound
Mild infection

Rutherford 5 (6?)
Ischemic toe

Rutherford 6
Ischemic limb

Risk of Amp.: Moderate
Need of Revasc.: Moderate

Risk of Amp.: High
Need of Revasc.: High

Risk of Amp.: High
Need of Revasc.: High

Ankle pressure 70mmHg

WIfI 121 / Stage 3

Ankle pressure >200mmHg
Toe pressure 0 (30) mmHg

WIfI 320 / Stage 4

Ankle pressure 30mmHg
Toe Pressure 0mmHg

WIfI 330 / Stage 4

Wounds and foot ulcerations (WIfI): 121/Stage 3, 320/Stage 4, 330/Stage 4.
Critical Limb Ischemia
Validation of risk stratification according to WIfI

Distribution of WIfI clinical stages 1 to 4 among amputation and limb salvage cohorts

Incidence of major amputation and 1-yr amputation-free survival (AFS) among WIfI clinical stages 1 to 4

Angioplasty
Critical Limb Ischemia @ LINC 2016

17/45 PAD Cases

→ ABI (median)*: 0.41
   ABI (range): 0.34 - >1.3

→ Severity of Ischemia:
   Rutherford 4: n = 6
   Rutherford 5: n = 11

*only 9 values available
## Critical Limb Ischemia Management – General principles

<table>
<thead>
<tr>
<th>Fontaine Stage</th>
<th>I</th>
<th>IIa</th>
<th>IIb</th>
<th>≥1 Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rutherford Category</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Ankle pressure</td>
<td>140</td>
<td>≥x mmHg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankle Brachial Index</td>
<td>≥ 0.10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residual stenosis [%]</td>
<td>&lt;30%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Rutherford Category
- **0**: No symptoms or signs of chronic limb ischemia.
- **1**: Mild symptoms (claudication).
- **2**: Moderate symptoms (intermittent claudication).
- **3**: Severe symptoms (rest pain).
- **4**: Critical limb ischemia (ischemic rest pain, gangrene).
- **5**: Critical limb ischemia with amputation.
- **6**: Critical limb ischemia with death.

### Ankle Pressure
- Pressure levels are measured in mmHg.

### Ankle Brachial Index (ABI)
- ABI is a ratio of the ankle artery pressure to the brachial artery pressure. It is used to assess peripheral arterial disease.

### Residual Stenosis
- Stenosis is measured in percentage (%).
Chronic Limb Ischemia Management – General principles

I  IIa  IIb  III  IV

Lifestyle Modification
Best Medical Treatment
Exercise

Revascularisation
Prostanoids

Local Therapy, Control of Infection, Amputation
Critical Limb Ischemia
Management – General principles

Management of critical limb ischaemia

- Rest pains
- Ischaemic lesion, gangrene

Pain control (morphine)
Treatment of infection (antibiotics)

Feasible
- Endovascular revascularization
- Technical failure, endovascular revascularization unsuitable
- Surgical revascularization

Unfeasible
- Re-do procedure

Clinical and non-invasive assessment of haemodynamic result (Table 8)

Favourable
- Control CVD risk factors, debridement, shoe adaptation (removal of weight-bearing stress to lesion), surveillance
- Prostaglandins, consider spinal cord stimulation
- Amputation, rehabilitation

Unfavourable
- Control CVD risk factors, pain control (morphine), wound care

Revascularisation

Risk-Modification

Prostanoids

Painkillers (opiates)

Antibiotics

I IIA IIB
Diabetic Foot Infection (DFI) Antibiotic Therapy

**Guidelines 2011**

*Diab Metab Res Rev 2012, 28 (Suppl 1);234-5.*

- In clinical infection only
- 1° empirical S.aureus [MRSA?], Strep., Gram$_{\text{neg}}$ with severe infection
- Cultures of deep tissue specimens (after debridement) assist in optimizing antibiotic selection
- Available data do not favour any particular antibiotic treatment strategy
# Chronic Limb Ischemia Management – General principles

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>For limb salvage, revascularization is indicated whenever technically feasible.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>When technically feasible, endovascular therapy may be considered as the first-line option.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>If revascularization is impossible, prostanoids may be considered.</td>
<td>IIb</td>
<td>B</td>
</tr>
</tbody>
</table>

ESC Guidelines 2011  
doi:10.1093/eurheartj/ehr211
Chronic Limb Ischemia Management – General principles

Relative Indication
2nd Line Therapy

Revascularisation

Absolute Indication
1st Line Therapy

Prostanoids

Absolute Indication
(?) 2nd Line Therapy

* when revascularisation is not feasible

I  IIa  IIb  III  IV
Chronic Limb Ischemia
Modification of Risk – General principles

<table>
<thead>
<tr>
<th>Therapy</th>
<th>RRR</th>
<th>MACE/10a</th>
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<tbody>
<tr>
<td>∅</td>
<td></td>
<td>40%</td>
</tr>
<tr>
<td>Smoking</td>
<td>50%</td>
<td>20%</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>25%</td>
<td>15%</td>
</tr>
<tr>
<td>Statins</td>
<td>30%</td>
<td>10%</td>
</tr>
<tr>
<td>LDL-C 100 → 70</td>
<td>20%</td>
<td>8%</td>
</tr>
<tr>
<td>ACE-I / ARB</td>
<td>25%</td>
<td>6%</td>
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<tr>
<td>ß-Blocker</td>
<td>25%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Fonarow GC et al. Am J Cardiol 2000;85:10A-17A.
Critical Limb Ischemia

Conclusions

Early recognition matters!

Teamwork matters!

Keep the foot in the shoe!

- There is only one report of a successful leg-transplantation in the literature!

[The Miracle of Cosmas and Damian]