Efficacy of an angiosome-directed versus indirect revascularisations for wound healing in patients with diabetes and critical limb ischaemia: a literature review
Disclosure of Interest

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- I do not have any potential conflict of interest

I declare no funding was accepted in the course of undertaking this literature review
## Critical Limb Ischaemia (CLI)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Fontaine Classification (Fontaine et al., 1954)</th>
<th>Clinical description</th>
<th>Category</th>
<th>Rutherford Classification (Rutherford et al., 1997)</th>
<th>Clinical description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Asymptomatic</td>
<td>0</td>
<td>Asymptomatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Intermittent claudication</td>
<td>1</td>
<td>Mild claudication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- IIa</td>
<td>Mild claudication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- IIb</td>
<td>Moderate to severe claudication</td>
<td>2</td>
<td>Moderate claudication</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>Severe claudication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Ischaemic rest pain</td>
<td>4</td>
<td>Ischaemic rest pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Ulceration or gangrene</td>
<td>5</td>
<td>Minor tissue loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(non-healing ulcer, focal gangrene with diffuse pedal ischaemia)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td>Major tissue loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(extending above transmetatarsal level, foot no longer salvageable)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Figure: Nunan et al., 2014*
The Trans-Atlantic Inter-Society Consensus (TASC-II) (Norgren et al., 2007) defines CLI as:

- the presence of ischaemic rest pain or tissue lesions, such as non-healing wounds, necrosis or gangrene,
- which typically presents at the extremities of the affected limb for more than two weeks.

• This is usually associated with haemodynamic quantification of:
  - ankle pressures <50–70 mm/Hg,
  - toe pressures <50 mm/Hg, or
  - TcPO₂ levels of <30 mm/Hg.
Current Practice

‘Best Vessel’ Strategy

- **Target vessel:** Guided by the least diseased artery as identified on angiography
- **Pros:** Best quality conduit
- **Cons:** Indirect perfusion, may require a good collateral supply to reperfuse site of ulceration

Persistence of ischaemic ulcerations **despite technically successful revascularisations** achieving the restoration of pedal pulses and vessel patency

(Carsten et al., 1998; Seeger et al., 1999; Attinger et al., 2006; Söderström et al., 2009; Simons et al., 2010; Forsythe et al., 2014).
The Angiosome Concept

Target vessel: Guided by site of ulceration

Figure: Cook Medical, 2014
Comparing the efficacy of:

Indirect / ‘Best Vessel’ strategy

- **Target vessel**: Guided by the least diseased artery as identified on angiography
- **Pros**: Best quality conduit
- **Cons**: Indirect perfusion, may require good collateral supply to reperfuse site of ulceration

Angiosome-directed strategy

- **Target vessel**: Guided by site of ulceration
- **Pros**: Direct perfusion from source artery, not dependent on collaterals
- **Cons**: May be required to recanalise a more calcified and occluded vessel, over one which might be more pliable and patent
Comparing the efficacy of:

**Indirect / ‘Best Vessel’ strategy**
- **Target vessel:** Guided by the least diseased artery as identified on angiography
- **Pros:** Best quality conduit
- **Cons:** Indirect perfusion, may require good collateral supply to reperfuse site of ulceration

**Angiosome-directed strategy**
- **Target vessel:** Guided by site of ulceration
- **Pros:** Direct perfusion from source artery, **not dependent on collaterals**
- **Cons:** May be required to recanalise a more **calcified** and **occluded** vessel, over one which might be more pliable and patent
Peripheral Arterial Disease (PAD)

### Comparison of PAD characteristics

(Boulton & Armstrong, 2006; Graziani et al., 2007; Setacci & Ricco, 2011; Forsythe et al., 2015)

<table>
<thead>
<tr>
<th></th>
<th>With diabetes</th>
<th>Without diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age of onset</strong></td>
<td>Younger</td>
<td>Older</td>
</tr>
<tr>
<td><strong>Disease progression</strong></td>
<td>Aggressive</td>
<td>Gradual</td>
</tr>
<tr>
<td><strong>Anatomical localisation</strong></td>
<td>• Mainly distal</td>
<td>• Mainly proximal</td>
</tr>
<tr>
<td></td>
<td>• Distinctly infrapopliteal</td>
<td>• Lesions tend to affect</td>
</tr>
<tr>
<td></td>
<td>affliction, involving all</td>
<td>femoral and aortic-iliac</td>
</tr>
<tr>
<td></td>
<td>three tibial arteries</td>
<td>arteries more frequently</td>
</tr>
<tr>
<td></td>
<td>• Relative sparing of</td>
<td>than the distal arteries</td>
</tr>
<tr>
<td></td>
<td>inframalleolar arteries &amp;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>supragenicular arteries</td>
<td></td>
</tr>
<tr>
<td><strong>Type of atherosclerotic lesion</strong></td>
<td>• Stenosis &lt; Occlusions</td>
<td>• Stenosis &gt; Occlusions</td>
</tr>
<tr>
<td></td>
<td>• Diffuse, occurring over</td>
<td>• Focal, occurring over</td>
</tr>
<tr>
<td></td>
<td>long segments</td>
<td>short segments</td>
</tr>
<tr>
<td><strong>Calcification</strong></td>
<td>Commonly present</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Collateral network</strong></td>
<td>Poor</td>
<td>Unaffected</td>
</tr>
</tbody>
</table>

Figure: lower limb arterial tree

(Memorize, 2016)
## Methods

<table>
<thead>
<tr>
<th>8 databases</th>
<th>AMED, CINAHL, MEDLINE, ProQuest Health &amp; Medicine Complete, ProQuest Nursing &amp; Allied Health Source, The Cochrane Library, TRIP database, ScienceDirect</th>
</tr>
</thead>
</table>
| Search terms | S1 - “critical limb isch?emia” OR “isch?emi*”  
S2 - “peripheral arter* disease” OR “peripheral vascular disease”  
S3 - “diabetic foot” OR “diabet*”  
S4 - “bypass” OR “angioplasty” OR “endovascular” OR “revasculari?ation” OR “reconstruct*”  
S5 - “angiosom*” OR “direct revasculari?ation” OR “indirect revasculari?ation”  
S6 - S1 OR S2 OR S3  
S7 - S4 AND S5 AND S6 |
| Critical appraisal tool | Newcastle-Ottawa Scale |
## Methodological Rigour of Studies

<table>
<thead>
<tr>
<th></th>
<th>Fossaceca et al., 2013</th>
<th>Söderström et al., 2013</th>
<th>Acín et al., 2014</th>
<th>Lejay et al., 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strengths</strong></td>
<td>✓ TASC-II diagnostic criterion satisfied* ✓ Complete follow-up of all subjects ✓ Diagnostic criteria of diabetes indicated ✓ Subjects’ duration of diabetes provided</td>
<td>✓ TASC-II diagnostic criterion satisfied* ✓ Complete follow-up of all subjects ✓ Diagnostic criteria of diabetes indicated ✓ Utilised wound classification system ✓ Presence of infection accounted for ✓ Consecutive sample</td>
<td>✓ TASC-II diagnostic criterion satisfied* ✓ Comparable inter-group baseline characteristics ✓ Diagnostic criteria of diabetes indicated ✓ Presence of infection accounted for ✓ Consecutive sample</td>
<td>✓ TASC-II diagnostic criterion satisfied* ✓ Complete follow-up of all subjects ✓ Comparable inter-group baseline characteristics of subjects ✓ Utilised wound classification system ✓ Presence of infection accounted for ✓ Consecutive sample</td>
</tr>
<tr>
<td><strong>Limitations</strong></td>
<td>• Non-consecutive sample • Wound classification system not utilised • Presence of infection not documented • Omission of subjects’ baseline characteristics</td>
<td></td>
<td>• No data on subjects’ duration of diabetes • Wound classification system not utilised • Drop-outs unaccounted • Patients with ESRD excluded</td>
<td>• No data on subjects’ duration of diabetes • Wound classification system not utilised • Drop-outs unaccounted • Patients with ESRD excluded</td>
</tr>
<tr>
<td><strong>NOS Scores</strong></td>
<td>6/9</td>
<td>8/9</td>
<td>5/9</td>
<td>7/9</td>
</tr>
</tbody>
</table>

- **Abbreviations:** End-Stage Renal Disease (ESRD); Newcastle-Ottawa Scale (NOS); Trans-Atlantic Inter-Society Consensus (TASC-II)
- **Additional details:** TASC-II (Norgren et al., 2007)’s diagnostic criterion is for the clinical diagnosis of critical limb ischaemia to be confirmed with objective quantifications of haemodynamic compromise.
Findings

• Focusing on methodologically stronger studies (Söderström et al., 2013; Lejay et al., 2014), giving a representative sample of 280 subjects.

• Angiosome-directed revascularisations found to be superior to indirect revascularisations (p-values: <0.001 and 0.04).

• Results in a nearly twofold increased probability for subjects to achieve wound healing in 12 months (hazard ratios: 1.97; 95% confidence intervals, 1.34-2.90).
Clinical Relevance & Implications

**Focal point:** to reduce avoidable lower-limb amputations, especially those relating to diabetes and peripheral arterial disease (PAD)

*(All-Party Parliamentary Group (APPG) on Vascular Disease, 2015)*

**PAD** is the **chief** contributing factor to non-healing diabetic foot ulcerations

*(International Diabetes Federation & International Working Group on the Diabetic Foot, 2015)*

**Over 80%** of diabetes-related amputations are preceded by a non-healing foot ulcer

*(National Institute for Health and Care Excellence, 2015)*
Within the limits of technical feasibility, it appears that re-calibrating the revascularisation strategy to incorporate the angiosome concept may be more efficacious than an indirect approach in optimising wound healing outcomes for patients with diabetes and critical limb ischaemia.
Recommendations for future research

• Evidence for angiosome-directed revascularisations in a purely diabetic population is limited, but do appear promising and would merit from further investigation

  - To rigorously assess and substantiate the short- and long-term safety and viability of pursuing an angiosome-directed over an indirect strategy
  
  - Comply with the European Wound Management Association’s recommendations (Gottrup et al., 2010; Price et al., 2014) to ensure consistency in outcome measurements and reporting

  - To stratify patients according to disease type, to aid in the development of targeted management strategies


References


References


