Angiosome interpretation – what to open, how many to open, when to stop

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I have the following potential conflicts of interest to report:

- Consulting: NIPRO, Canon
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s) Honoraria: Medtronic, Boston Scientific, Gore, NIPRO, Canon, Kaneka, Cook
- I do not have any potential conflict of interest
**Different Comorbidities in CLI but Almost Comparable Amputation-Free Survival**

Key baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>OLIVE EVT</th>
<th>PRVENT III BSX+Drug</th>
<th>CIRCULASE Drug</th>
<th>BASIL EVT/BSX</th>
<th>CRITISH EVT</th>
<th>BSX</th>
<th>SPINACH EVT</th>
<th>BSX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age&gt;80 yrs</td>
<td>26%</td>
<td>18%</td>
<td>18%</td>
<td>26%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>65%</td>
<td>65%</td>
<td>79%</td>
<td>66%</td>
<td>63%</td>
<td>68%</td>
<td>66%</td>
<td>72%</td>
</tr>
<tr>
<td>DM</td>
<td>71%</td>
<td>62%</td>
<td>51%</td>
<td>39%</td>
<td>48%</td>
<td>48%</td>
<td>74%</td>
<td>73%</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>52%</td>
<td></td>
<td></td>
<td></td>
<td>10%</td>
<td>5%</td>
<td>51%</td>
<td>51%</td>
</tr>
<tr>
<td>Tissue loss</td>
<td>88%</td>
<td>74%</td>
<td>69%</td>
<td>75%</td>
<td>78%</td>
<td>73%</td>
<td>88%</td>
<td>85%</td>
</tr>
<tr>
<td>Isolated BTK lesions</td>
<td>41%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-year AFS</td>
<td>74%</td>
<td>74.0% - 79.9%</td>
<td>75%</td>
<td>72%</td>
<td>76%</td>
<td>79%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Despite heterogeneity characteristics, 1-year AFS reveals around 75%. However, it is clinically difficult to simply compare to each study.
When and How to decide treatment strategy in BTK reconstruction?

My opinion

• Both angiosome and angiogaphosome concepts play an important role for achieving better clinical outcomes (wound healing [WH], limb salvage [LS] and freedom from major adverse limb events [MALEs]).
My understanding in BTK reconstruction
-There are 3 steps (chance) for decision making of target BTK lesion-

**STEP 1**
@Outpatient clinical
based on wound location and severity without angiogram

**STEP 2**
@Catheter laboratory
after angiogram but before wire crossing

**STEP 3**
@Catheter laboratory
after wire crossing or after angioplasty for 1st target lesion
Why Angiosome concept?

Despite an aggressive approach for revascularization, amputation rates of up to 20% can occur despite a patent bypass in patients with CLI presenting tissue loss.

This has led to the proposal of an angiosome-based revascularization strategy (where the specific artery perfusing the corresponding diseased territory is revascularized).

Severe stenosis AT to DP
Poor flow to the calcaneal region (from DPA-pedal arch).

Angioplasty for ATA-DPA

Poor flow to calcaneal region despite ATA-DPA revascularization (1-straight line)

Major amputation (BK amputation)

74 years, Male, tissue loss at heel (R6), DM, ESRD on HD
Angiosome is an anatomical concept, defined as the blood supply from a main secondary or distributing artery to a specific tissue area.

Worse limb prognosis for IR vs. DR only in patients with CLI complicated with wound infection and DM (N=718)

CLI complicated with both wound infection and DM, when IR has a poorer outcome.

The angiosome-oriented revascularization for CLI patients without concurrent wound infection and DM

There was no significant difference in terms of AFS and freedom from MALE for patients without concurrent wound infection and DM.

The angiosome-oriented revascularization for CLI patients without concurrent wound infection and DM

After propensity matching of characteristics, analysis showed better wound healing in the DR group than in IR group.

“What to open?”

Wound healing speed was significantly faster in less severe condition of CLI (non-DM and non wound infection), ➡ All CLI should be primarily considered for direct revascularization if lesions are technically feasible.

Meta-analysis of Angiosome concept

Forest plot for effectiveness in **wound healing**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Hazard Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Hazard Ratio IV, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varela 2010</td>
<td>-0.29</td>
<td>0.27</td>
<td>13.9%</td>
<td>0.75 [0.44 – 1.27]</td>
<td>2010</td>
</tr>
<tr>
<td>Azurna 2012 a</td>
<td>-0.2</td>
<td>0.2</td>
<td>25.3%</td>
<td>0.82 [0.55 – 1.21]</td>
<td>2012</td>
</tr>
<tr>
<td>Azurna 2012 b</td>
<td>-0.59</td>
<td>0.22</td>
<td>25.9%</td>
<td>0.55 [0.36 – 0.85]</td>
<td>2012</td>
</tr>
<tr>
<td>Kabra 2013</td>
<td>-0.6</td>
<td>0.29</td>
<td>12.0%</td>
<td>0.65 [0.31 – 0.97]</td>
<td>2013</td>
</tr>
<tr>
<td>Söderström 2013</td>
<td>-0.58</td>
<td>0.19</td>
<td>26.0%</td>
<td>0.56 [0.39 – 0.81]</td>
<td>2013</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td><strong>0.64 [0.52 – 0.78]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Forest plot for effectiveness in **limb salvage**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Hazard Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Hazard Ratio IV, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varela 2010</td>
<td>-0.28</td>
<td>0.6</td>
<td>12.7%</td>
<td>0.78 [0.28 – 2.01]</td>
<td>2010</td>
</tr>
<tr>
<td>Alexandrescu 2011</td>
<td>-0.65</td>
<td>0.4</td>
<td>16.1%</td>
<td>0.62 [0.24 – 1.14]</td>
<td>2011</td>
</tr>
<tr>
<td>Blanes Ori 2011</td>
<td>-0.59</td>
<td>0.98</td>
<td>6.6%</td>
<td>0.55 [0.18 – 1.14]</td>
<td>2011</td>
</tr>
<tr>
<td>Ferrufino-Merida 2012</td>
<td>-4.16</td>
<td>0.92</td>
<td>6.2%</td>
<td>0.70 [0.30 – 1.43]</td>
<td>2012</td>
</tr>
<tr>
<td>Iida 2012</td>
<td>-0.38</td>
<td>0.25</td>
<td>19.0%</td>
<td>0.70 [0.43 – 1.14]</td>
<td>2012</td>
</tr>
<tr>
<td>Kabra 2013</td>
<td>-0.89</td>
<td>0.67</td>
<td>9.4%</td>
<td>0.50 [0.13 – 1.89]</td>
<td>2013</td>
</tr>
<tr>
<td>Lejay 2013</td>
<td>-1.17</td>
<td>0.42</td>
<td>14.6%</td>
<td>0.31 [0.14 – 0.71]</td>
<td>2013</td>
</tr>
<tr>
<td>Söderström 2013</td>
<td>-0.48</td>
<td>0.36</td>
<td>16.2%</td>
<td>0.62 [0.31 – 1.25]</td>
<td>2013</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td><strong>0.44 [0.26 – 0.75]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Angiosome Targeted PTA is More Important in patients with diabetes

In diabetic patients, indirect endovascular revascularization leads to the poorest wound healing and leg salvage rates.

→ Endovascular procedures should be targeted according to the angiosome concept.

## Impact of angiosome differs from studies

<table>
<thead>
<tr>
<th>Publication</th>
<th>Country</th>
<th>Limbs (Pts)</th>
<th>Outcomes</th>
<th>DM</th>
<th>ESRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexandrescu, 2008</td>
<td>Retro</td>
<td>124 (98)</td>
<td>Wound Healing</td>
<td>124 (100%)</td>
<td>27 (22%)</td>
</tr>
<tr>
<td>Iida, 2010</td>
<td>Retro</td>
<td>203 (177)</td>
<td>Limb Salvage</td>
<td>120 (68%)</td>
<td>96 (54%)</td>
</tr>
<tr>
<td>Alexandrescu, 2011</td>
<td>Retro</td>
<td>232 (208)</td>
<td>WH, LS, Mortality</td>
<td>232 (100%)</td>
<td>42 (18%)</td>
</tr>
<tr>
<td>Blanes Orti, 2011</td>
<td>Retro</td>
<td>34 (32)</td>
<td>Wound Healing</td>
<td>27 (73%)</td>
<td>13 (35%)</td>
</tr>
<tr>
<td>Iida, 2012</td>
<td>Retro</td>
<td>369 (329)</td>
<td>LS, Mortality</td>
<td>172 (73%)</td>
<td>149 (63%)</td>
</tr>
<tr>
<td>Soderstrom, 2013</td>
<td>Retro</td>
<td>250 (226)</td>
<td>Wound Healing</td>
<td>250 (100%)</td>
<td>39 (16%)</td>
</tr>
<tr>
<td>Fossaceca, 2013</td>
<td>Retro</td>
<td>201 (201)</td>
<td>WH, LS</td>
<td>201 (100%)</td>
<td>15 (7.4%)</td>
</tr>
<tr>
<td>Acin, 2014</td>
<td>Retro</td>
<td>101 (92)</td>
<td>WH, LS, Mortality</td>
<td>101 (100%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**More effective, Less effective**

Angiosome-guided angioplasty is more or less effective strongly depending on the patient characteristics and endpoints (wound healing vs. limb salvage).

2017 ESC Guidelines on the Diagnosis and Treatment of PAD, in collaboration with the ESVS

1) The decision of revascularization **should** also consider the angiosome concept, targeting the ischaemic tissues.

2) The angiosome model **should not** be used as an absolute strategy for interventions on patients with CLTI.

3) Further, well-structured prospective studies are needed to assess the value of the angiosome concept.
Main criticism for angiosome concept

✓ Angiosomes has multiple definitions that makes comparisons between studies.

✓ Angiosomes were designed as dynamic concept to be applied to non-vascular patients.

✓ The foot vascular anatomy is seriously affected in CLI. The regional vascular foot perfusion cannot be statically schematized.

✓ Diffuse distal vascular lesions prevent the DR of the injured angiosome in more than a half of the revascularization procedures and patent foot medium-sized collateral vessels (arterial-arterial connections) could be the only way to achieve ulcer local blood perfusion.
2019 Global Vascular Guidelines on the management of chronic limb-threatening ischemia

Debatable points

1. Unambiguous assignment of foot wounds to an individual angiosome is possible in only a minority of cases.
2. Tibial and peroneal bypasses perform equally well for limb salvage, and DP bypass can be effective for some hindfoot lesions.
3. Systematic reviews have yielded conflicting results, and data are inextricably confounded by the quality of the confounding effect of limb staging.

GVG finally summarized that it may be reasonable in selected patients with advanced limb threat (eg, WIfI stages 3 and 4) undergoing endovascular therapy if it can be safely accomplished without risking loss of a bypass target or compromising runoff to the foot.
Endovascular treatment of more than one artery was associated with better wound healing rates. The length of the procedure, the use of contrast, and the amount of radiation exposure were significantly larger in procedures that treated more than one artery.

Why angiosome is clinically important?
- Know limitations of BTK angioplasty -

Repeat EVT @ 1 year 40%
Restenosis @ 3 months 70%
Early Recoil @ 15 min. 97%


Multiple vessel approach could provide continuing healing of the wound; even if restenosis occurs in one vessel, the perfusion from the other vessel could compensate. Therefore, a possible delay in restenosis time achieved by having more inflow vessels to the foot could result in a better wound healing course.
All clinicians should specifically think how amount of blood supply would be continuously needed for each wound.

Endpoints of technically acceptable compromise should be individually imagined based on wound and anatomical severity.
First step: Angiosome based angioplasty
First step: Angiosome based angioplasty

Angioplasty 2mm for BTA, 3mm for BTK

BTK-post

BTA-post
Direct angioplasty but delayed wound healing

Day 1 - EVT for AT-DPA
Day 23 - Antibiotics
Day 25 - Minor amputation
Day 45 - NPWT
Second step: More selective angioplasty based on angiographosome

Day 50
Partially insufficient granulation
Second step: More selective angioplasty based on angiographosome.
After Angiosome and Angiographosome based angioplasty

Day 1
Day 23
Day 25
Day 45
Day 48

EVT
Antibiotics
Minor amputation
NPWT
Skin transplantation
The goal of CLI treatment

- Limb salvage
- Wound healing
- Restoring wound-related artery and acquiring wound brush by appropriate angioplasty
- Accurate diagnosis for wound and anatomy
- CLI master!

My conclusion

Both angiosome and angiographosome concepts play an important role for achieving better clinical outcomes (wound healing, limb salvage and free from major adverse limb events).