Stem cell therapy is promising.

Preliminary evidence of:
- Feasibility
- Safety
- Efficacy

42 trials
Beneficial role:
- ↓ amputations
- ↑ quality of life

<table>
<thead>
<tr>
<th>Risk</th>
<th>Risk ratio</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Amputation</td>
<td>0.91</td>
<td>0.57</td>
</tr>
<tr>
<td>Amputation-free survival</td>
<td>1.03</td>
<td>0.77</td>
</tr>
<tr>
<td>Ulcer healing</td>
<td>1.48</td>
<td>0.06</td>
</tr>
<tr>
<td>ABI difference</td>
<td>0.31</td>
<td>&lt;0.0001</td>
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<tr>
<td>TlPO2</td>
<td>11.88</td>
<td>&lt;0.0001</td>
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<tr>
<td>Pain score</td>
<td>-0.72</td>
<td>0.03</td>
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</table>
What are the barriers to performing stem cell therapy for patients with lower extremity vascular disease?

Stem cells are not drugs!
- Animal models may not provide guidance
  - Little pre-clinical knowledge available
  - Rapidly growing field
  - Stem cells are very complex
    - Harder to investigate

Problems with randomized trials - I
- Assessing risks and benefits unique to each trial
  - Cell type
  - Requires invasive procedure to deliver
  - Sham / control procedure
  - Informed consent more difficult
- Outcome measures not uniform
  - Amputation-free survival
  - Ulcer healing
  - Walking distance

Problems with randomized trials - II
- High level of commercial interest
  - Need for “return on investment”
- High level of public interest
  - Stem cell clinics becoming very popular
  - Do they put patients at risk?
    - Potential for non-evidence-based treatments being used

Which patient population to focus on?
- Claudication vs. CLI
  - Claudication is more benign
    - Treatment must be low risk, especially in the long term
  - CLI patients are more severe
    - Can we treat them in time?
    - Does the treatment work quickly enough?
- Thromboangiitis Obliterans (Buerger’s disease)

How can we practically treat patients?
- Best cells to use?
  - How do we identify and obtain them?
  - Will they work in diseased patients?
- How do we make enough of them?
  - Role of stimulation (G-CSF)
  - Single-step, bedside, closed isolation system
    - Without specialized subservices
    - Without legal issues
- Where and how do we deliver them?
Will these treatments be safe for long term treatment?

- Recurrent symptoms
  - Pain, ulcers
- Off target angiogenesis
  - Development of AV shunting
- Retinopathy
- Malignancy
  - Teratomas

Lessons from cardiac surgery

- Move to a vascular specific stem cell

Lessons from cardiac surgery

- Improve cell delivery technology
  - Optimize cell numbers
  - Optimize delivery site
  - Optimize delivery system

Lessons from cardiac surgery

- We need to continue our research in this area

Stem cell therapy is still promising.*

*Details not shown