What is the SOLUTION to Vein Graft Failure?

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Vein Graft Failure: An Unsolved Problem

- 20-40% at one year
- Data suggests similar for LEB and CABG
- Early graft injury, especially endothelial damage, plays an important role
- Arterialization response, inflammation
- Optimal harvest and storage solution would preserve structure and function, metabolic state
- Limited pharmacotherapy; unmet need

Disclosures

- NONE
Mechanisms of Early Vein Graft Injury

- Harvest trauma - stretch, torsion, distension
- Warm ischemia and reperfusion
- Alterations in osmolarity, pH
- Oxidative stress
- Lack of nutrients
- Toxins (e.g. surgical skin markers)
- Arterialization

Molecular engineering of vein grafts

- **Rationale**: minimize injury/redirect the healing response at the time of implantation
- **Types of interventions**
  - Metabolic/biochemical (cytoprotective)
  - Anti-inflammatory
  - Anti-thrombotic
  - Anti-proliferative
- **Local delivery approaches**
  - Enhanced vein preservation solutions
  - Gene/ODN transfection methods
  - Adventitial treatments

K08 HL04189 (1999-2004): "Genetic Engineering of a Failure-Resistant Vein Graft"
Vein Graft Failure (≥ 75% stenosis)

Failure of the anti-proliferative E2F Decoy strategy in lower extremity and coronary vein bypass grafting was unambiguous and disappointing

<table>
<thead>
<tr>
<th></th>
<th>Edifoligide</th>
<th>Placebo</th>
<th>P value</th>
<th>Edifoligide</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per Patient</td>
<td>436/965</td>
<td>442/955</td>
<td>0.660</td>
<td>601/2295</td>
<td>597/2242</td>
<td>0.829</td>
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</tbody>
</table>

*Adjusted for intra-pt graft correlation

The factors influencing early patency of coronary artery bypass vein grafts

- Early (30-day) graft patency (P<.01)
  - 93% buffered crystalloid (Plasma-Lyte with heparin and papaverine)
  - 80% heparinized blood

- SEM and TEM findings
  - Endothelial slough and ruffling
  - Microthrombi, platelet and leukocyte aggregates

Catinella FP et al J Thor Cardiovasc Surg 1982;83:686-700
Vein Graft Storage Solutions

- Heparinized blood
  - No buffering capacity: Acidic (pH<6.0)
  - Lacks cytoprotectants or nutrients
- Heparinized saline
  - Plasma-Lyte-A
  - Add vasodilator e.g. papaverine

<table>
<thead>
<tr>
<th>Solution</th>
<th>Sodium (mmol/L)</th>
<th>Potassium (mmol/L)</th>
<th>Magnesium (mmol/L)</th>
<th>Calcium (mmol/L)</th>
<th>Chloride (mmol/L)</th>
<th>Other Components</th>
<th>pH (measured)</th>
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<tbody>
<tr>
<td>Plasma-Lyte A (Baxter)</td>
<td>140</td>
<td>3.0</td>
<td>1.4</td>
<td>1.2</td>
<td>101</td>
<td>None</td>
<td>7.4 (6.3-6.8)</td>
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<tr>
<td>0.9% normal saline (Baxter)</td>
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<td>14.0</td>
<td>1.4</td>
<td>1.2</td>
<td>101</td>
<td>None</td>
<td>7.4 (6.5-7.0)</td>
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<tr>
<td>University of Wisconsin solution</td>
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<td>4.0</td>
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<td>1.2</td>
<td>132</td>
<td>Lactoboric acid, 190</td>
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<tr>
<td>Gehner solution</td>
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<td>1.4</td>
<td>1.2</td>
<td>132</td>
<td>Glutathione, 3</td>
<td>7.3</td>
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<tr>
<td>Autologous whole blood</td>
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<td>1.2</td>
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<td>Glutathione, 20</td>
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<tr>
<td>GALA solution</td>
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<td>1.4</td>
<td>1.2</td>
<td>132</td>
<td>Glutathione, 1, L-arginine, 0.5</td>
<td>7.4</td>
</tr>
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</table>
Vein preparation for LEB

- Minimize harvest trauma and ischemia time
- GENTLE manipulation during exposure
- Don’t divide until arterial sites fully exposed and prepared for anastomoses; excess length (2-4 cm) allows for unexpected issues
- Role for endoscopic harvest—may be injurious
- Gentle distension with harvest solution
  - Buffered isotonic solution/neutral pH (Plasma-Lyte)
  - Papaverine (60 mg/500 ml), Heparin (2000 u/500 ml)
- Role for other additives (Ca-channel blockers, antioxidants, L-arginine) is unclear