Protecting The Aged Heart During Cardiac Surgery: Use of del Nido Cardioplegia Provides Superior Functional Recovery in Isolated Hearts

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No Disclosures
• Elderly hearts are not as well protected by some cardioplegia solutions

• The aged heart is similar to the immature heart
  – more susceptible to ischemia reperfusion injury
  – poorly equipped to handle intracellular calcium overload

• Our hypothesis:
  – A cardioplegia strategy developed for immature hearts may also provide superior myocardial protection for aged hearts
<table>
<thead>
<tr>
<th></th>
<th>del Nido</th>
<th>‘Standard’</th>
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</thead>
<tbody>
<tr>
<td>Base solution</td>
<td>Plasmalyte A</td>
<td>D5 0.225% NaCl</td>
</tr>
<tr>
<td>Dilution (blood:cardioplegia)</td>
<td>1:4</td>
<td>4:1</td>
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<tr>
<td>Final Composition</td>
<td></td>
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<tr>
<td>Hematocrit (%)</td>
<td>≈6</td>
<td>≈25</td>
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<tr>
<td>K⁺ (mmol/L)</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
<td>Ca²⁺ (mmol/L)</td>
<td>0.24</td>
<td>1.0</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>1</td>
<td>51</td>
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<tr>
<td>Lidocaine (mmol/L)</td>
<td>0.36</td>
<td>-</td>
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<tr>
<td>Strategy</td>
<td>Single dose</td>
<td>Induction + maintenance every ≈ 20 min</td>
</tr>
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O’Brien et al., Ann Thorac Surg 2009;87:1517-23
www.aats.org
Del Nido cardioplegia is associated with less activity during arrest and lower intracellular Ca$^{2+}$ in aged cardiomyocytes.

O’Blenes et al., J Thorac Cardiovasc Surg 2011;141:762-70
The objective of this study:

Determine if the benefits of del Nido cardioplegia seen in isolated cardiomyocytes from elderly animals translates into improved function in the whole heart.
- Elderly Rat Hearts (22-24 months)
- Isolated Working Heart Preparation
- Troponin release measured during reperfusion
- Flow measurements standardized to dry weights of ventricles

**Standard Cardioplegia**
- 15 ml/kg
- 5 ml/kg
- 5 ml/kg

**Del Nido cardioplegia**
- 15 ml/kg

**Baseline Working Heart** (5 min)

**Cardioplegic Arrest (60 min)**

**Reperfusion (20 min)**

**Post-Reperfusion Working Heart (60 min)**
Results

• 16 of 20 (80%) hearts met baseline inclusion criteria:
  – Heart rate > 200 bpm
  – Regular rhythm
  – Cardiac output > 25 mL/min
  – Coronary flow > 10 mL/min

• Hearts arrested with:
  – Standard cardioplegia (n=8) or
  – Del Nido cardioplegia (n=8)
Spontaneous Activity during Arrest

- ECG (mV)
- Ao Pressure (mmHg)

p = 0.01
Return of Rhythm at Reperfusion

![Bar graph showing time to first heartbeat for Standard and Del Nido methods.](image)

- **Standard**
- **Del Nido**

Time in Reperfusion (s)

<table>
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<tr>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>80</th>
<th>90</th>
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Time to First Heartbeat (s)

- **Standard**
- **Del Nido**

$p = 0.0007$
Coronary Vascular Resistance

CVR during reperfusion

ΔCVR

p=0.0497

p=0.0065
Troponin-I Release During Reperfusion

p=0.02
Left Ventricular Developed Pressure

**Standard**

**Del Nido**

Aortic Pressure (mmHg)

LV Developed Pressure (mmHg)

Cardioplegic arrest

Reperfusion

**=*p≤0.001**

Time in Working Heart (min)
Cardiac Output

Stroke Work

*=p≤0.001

**Cardiopulmonary arrest**

**Reperfusion**

**Cardiopulmonary arrest**

**Reperfusion**

*Del Nido*

*Standard*
Conclusion

- Del Nido cardioplegia prevents spontaneous activity during cardioplegic arrest, reduces myocardial injury, and results in superior myocardial function after reperfusion in aged hearts.
- Del Nido cardioplegia has the potential to provide superior myocardial protection for older patients undergoing cardiac surgery.
Future Directions

• Single vs. multi-dose
• Whole animal model
• Phase 1 clinical trial with elderly patients undergoing cardiac surgery
Acknowledgements

Rick Livingston – technical support
Karen Buth – statistical support