Mild Therapeutic Hypothermia for Deceased Kidney Donors

Just do it?

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Risk of Bias

- Concealed randomization
- Baseline comparability
  - Donors
  - Recipients - Longer CIT in normothermic group; adjusted analysis
- Blinding
  - Donor caregivers, only
  - Recipient outcome assessors
- Cointerventions
  - K and Mg repletion prior to Rx in hypothermia group
- Modified intention to treat analysis
- Completeness of follow up
- Stopped early - 370 donors, 572 recipients, 191 events
<table>
<thead>
<tr>
<th></th>
<th>HYPOTHERMIA</th>
<th>NORMOTHERMIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initially assigned</td>
<td>197</td>
<td>197</td>
</tr>
<tr>
<td>(dis-enrolled)</td>
<td>(17)</td>
<td>(7)</td>
</tr>
<tr>
<td>Assigned</td>
<td>180</td>
<td>190</td>
</tr>
<tr>
<td>Actual donors</td>
<td>150</td>
<td>152</td>
</tr>
<tr>
<td>Recipients</td>
<td>285</td>
<td>287</td>
</tr>
</tbody>
</table>

“Non-transplant or delayed graft function”
Risk of Bias

- Concealed randomization
- Baseline comparability
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  - Recipients - Longer CIT in normothermic group; adjusted analysis
- Blinding
  - Donor caregivers
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- Minimal cointerventions
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394 Donors were enrolled

197 Donors were initially assigned to hypothermia group
197 Donors were initially assigned to normothermia group

17 Disenrolled
13 Had medical condition that was identified later and precluded transplantation
3 Had hemodynamic instability
7 Had preexisting renal disease
1 Had coagulopathy
2 Had low electrolyte levels
2 Withdrew consent
2 Became donor of thoracic organs instead

7 Disenrolled
1 Had medical condition (preexisting renal disease) that was identified later and precluded transplantation
4 Withdrew consent
2 Became donor of thoracic organs instead

P < 0.05
Moderate Risk of Bias

- Concealed randomization
- Baseline comparability
  - Donors
  - Recipients - Longer CIT in normothermic group; adjusted analysis
- Blinding
  - Donor caregivers
  - Recipient outcome assessors
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Surrogate outcome

Large treatment effect
  - DGF 28.2% vs 39.2%; RR 0.72

Statistically significant
  - Unadjusted p = 0.008
  - Adjusted p = 0.02

Signal of benefit for both subgroups
  - Standard and expanded criteria donors
Clinical Context

- Common methods for temperature control
- Donor number needed to treat: 7
- Theoretical harm
  - Split liver donors
    - Hypothermia could result in mild coagulopathy dissection
- Relatively non-invasive, inexpensive
Summary: sources of uncertainty

1. Early/single studies can mislead
2. Mechanism of potential benefit not elucidated
3. Moderate risk of bias
   ▪ blinding
   ▪ loss to follow-up of all potential kidneys
   ▪ stopping early
4. Surrogate renal endpoints
5. No report of graft function for other organs
Reasonable - but not imperative - to use hypothermia

- Kidney-only donors
- Kidney-plus-other organ donors
Congratulations!