Relation Between Time to Arousal and Neurologic Outcomes in Cardiac Arrest Patients Treated with Therapeutic Hypothermia

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Speaker Disclosures

• Presenter: Anne V Grossestreuer, MSc

• Disclosures: None
Penn Alliance for Therapeutic Hypothermia (PATH) registry

- National US registry for data sharing and collaboration on therapeutic hypothermia after cardiac arrest
- Tracks data points related to cardiac arrest and post-cardiac arrest care
- Benchmarks between institutions across the country
- Uses this data to implement the best practice of therapeutic hypothermia (TH) nationally
Objectives

• To determine the length of time it takes cardiac arrest patients to regain arousal after cardiac arrest and TH

• Examine factors that affect time to arousal
Background

• **Neuroprognostication before Targeted Temperature Management**: American Academy of Neurology neuroprognostication guidelines for comatose SCA patients
  - detailed neurologic exam at 72 hours after arrest
    • myoclonic status epilepticus
    • serum neuron-specific enolase (NSE)
    • somatosensory evoked potential (SSEP)
    • pupillary light response
    • corneal reflexes
    • **motor responses**

Background

• Literature support both ways?
Studies Looking at Time to Arousal

• Chandra-Strobos “A Paradigm Redefined: Time Course of Neurological Recovery Following Hypothermia Therapy Post Non-Traumatic Out-of-Hospital Cardiac Arrest”
  – Patient population: 47 patients with out of hospital arrests; 15 treated with TH (57% with VF as initial rhythm)
  – Findings: Meaningful awakening can occur 7+ days post arrest in patients treated with TH

• Mayo Neurology paper
  – Patient population: 227 patients with out of hospital arrests; 128 treated with TH (88% with VF as initial rhythm)
  – Findings: Hypothermia does not delay time to arousal past 72 hours post-arrest
Methods

• **Inclusion Criteria:**
  • Patients had a cardiac arrest (any initial rhythm) with ROSC and received therapeutic hypothermia between 2005-2011
  • 3 Hospitals Cohort:
    • Hospital of the University of Pennsylvania
    • Penn Presbyterian Medical Center
    • Pennsylvania Hospital

• **Exclusion Criteria:**
  • Traumatic arrests
  • < 18 years of age

• **Definition of Regaining Arousal:**
  • Purposeful movement
  • Measured by a patient’s first recorded Glasgow Motor Score of 6 or a chart notation of purposefully following commands

• **Definition of Neuro Outcome:**
  • return to neurologic baseline (pre-arrest) or GCS 14-15
Hypothermia Protocol

• Temperature management was provided using a surface cooling device; most patients also received chilled saline and/or ice bags

• Target temperature, 33°C (with an acceptable range of 32-34°C), was maintained for 24 hours

• Rewarming, at 0.33°C/hour, was done actively using a surface cooling device
• N = 192
• Mean age = 57±16 years
• 108/192 (56%) were male
• Initial rhythm was VF/VT in 73/190 (38%)
• Survival to hospital discharge was achieved in 82/192 (43%)
• 59/82 (72%) had a good neurological outcome
• Hypothermia was maintained for 24.0±7.0 hours
• Rewarming took place over a mean of 17.4±12.4 hours
# Results

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
<th>Mean Time (days)</th>
<th>Range (days)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who Regained Arousal</td>
<td>81 (42)</td>
<td>3.8±2.6</td>
<td>0.5 - 14.5</td>
<td></td>
</tr>
<tr>
<td>Survival to Discharge</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>70 (86)</td>
<td>3.6 ± 2.4</td>
<td>0.5 - 14.5</td>
<td>0.26</td>
</tr>
<tr>
<td>No</td>
<td>11 (14)</td>
<td>4.5±3.4</td>
<td>1.3 - 13.7</td>
<td></td>
</tr>
<tr>
<td>Discharged Neurologically Intact</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>59 (84)</td>
<td>3.2±1.6</td>
<td>0.5 - 7.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>No</td>
<td>11 (16)</td>
<td>6.2±4.5</td>
<td>2.5 - 14.5</td>
<td></td>
</tr>
</tbody>
</table>
Results

Time to Arousal by Neurologic Outcome at Discharge

Days to Arousal

- Neurologically Intact
- Not Neurologically Intact

- Survived to Discharge
- Did Not Survive to Discharge
Alternate Chart

Number of Patients

Days Post-Arrest

- Discharged Neurologically Intact
- Discharged Not Neurologically Intact
- Did Not Survive to Discharge
Results

• No Association with Time to Arousal
  – Age, Gender (female: 3.6 ± 2.4 days; male: 3.9 ± 2.7 days), Race

• DNR
  – 94 patients were made DNR by family during their hospital course
  – 39/94 (41%) patients had care withdrawn during the 72 hours post-arrest
  – Of the patients who regained arousal but expired before discharge, 9/11 (82%) were made DNR (comfort care only) by family
### Important Findings

<table>
<thead>
<tr>
<th></th>
<th>Mean Time to Wake Up (days)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurologically Intact</strong></td>
<td>3.2 ± 1.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Not Neurologically Intact</td>
<td>6.2 ± 4.5</td>
<td></td>
</tr>
<tr>
<td>No Renal Insufficiency</td>
<td>3.4 ± 2.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Renal Insufficiency</td>
<td>5.2 ± 3.9</td>
<td></td>
</tr>
<tr>
<td>Paralytic Used</td>
<td>3.5 ± 2.1</td>
<td>0.07</td>
</tr>
<tr>
<td>No Paralytic Used</td>
<td>5.4 ± 6.0</td>
<td></td>
</tr>
<tr>
<td>VF/VT Arrest</td>
<td>3.1 ± 1.6</td>
<td>0.02</td>
</tr>
<tr>
<td>PEA/Asystole Arrest</td>
<td>4.4 ± 3.3</td>
<td></td>
</tr>
<tr>
<td>Out of Hospital</td>
<td>3.5 ± 2.2</td>
<td>0.17</td>
</tr>
<tr>
<td>In Hospital</td>
<td>4.4 ± 3.5</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions

• Time to arousal after resuscitation and TH use is highly variable, and often longer than 3 days
• Earlier arousal is associated with better neurologic status on hospital discharge
• Time to arousal is prolonged in patients with renal insufficiency
• Further research is required to determine optimal timing of neuroprognostication in the post-arrest setting
Acknowledgments
Out of Hospital Shockable Arrests

- 62/192 (32%) of patients who received TH arrested outside of the hospital and had a shockable initial rhythm
- 38/62 (61%) survived to discharge
- Mean time to wake up was 3.0 ± 1.5 days (range: 0.5 – 7.4 days)
- Of those who regained arousal
  - 33/35 (94%) survived to discharge
  - 31/35 (89%) had a good neurologic outcome at discharge
  - 12/35 (34%) regained arousal later than 72 hours post-arrest and were discharged with a good neurologic outcome
Causes of in-hospital death after arousal

- re-arrest (27%)
- hemodynamic instability (27%)
- sepsis (9%)